

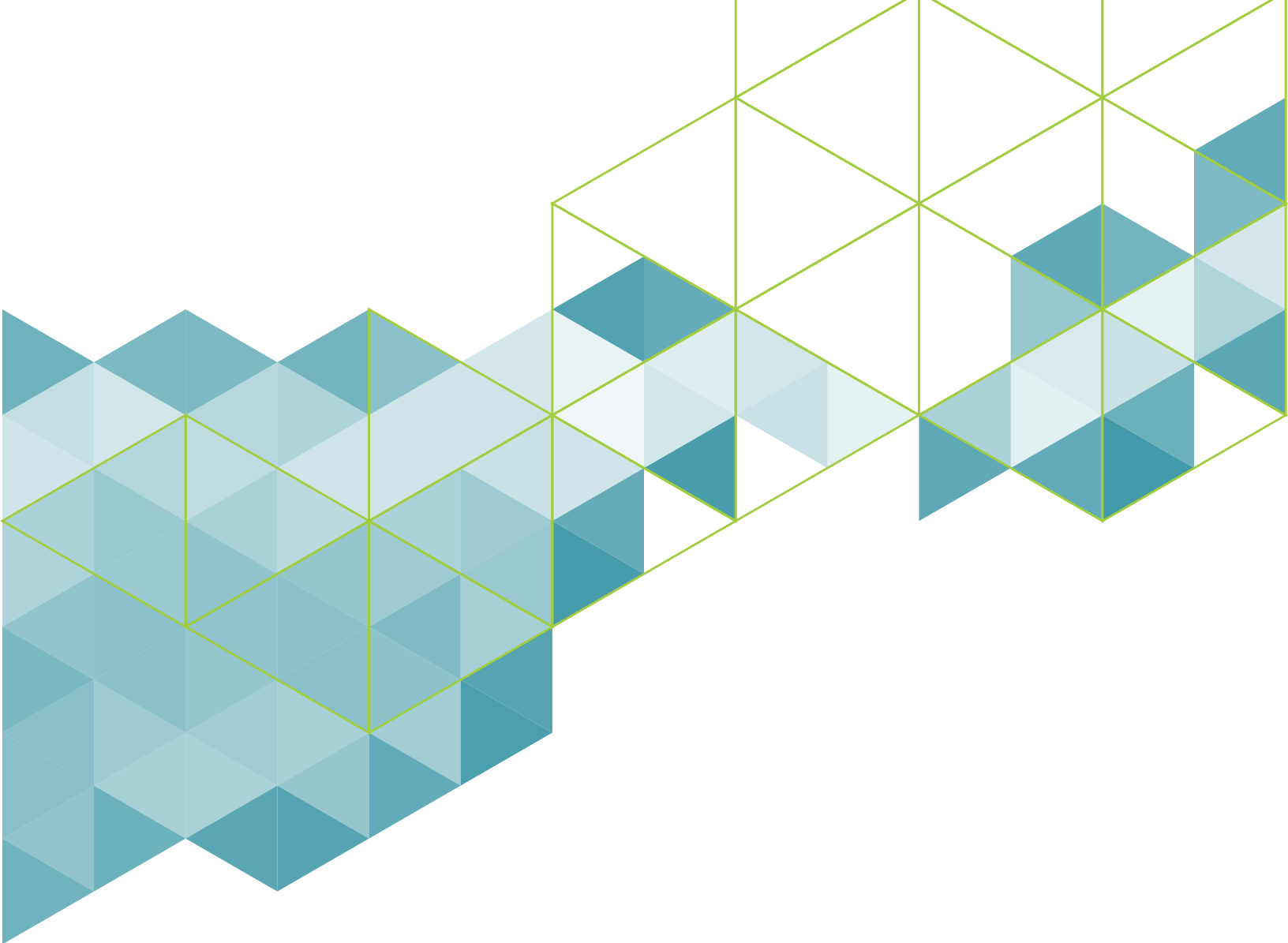


Research Appreciation Day

VIRTUAL CONFERENCE

MARCH 27 - 31, 2023

ABSTRACT BOOK



Gibson D. Lewis Library

presents

The University of North Texas Health Science Center's

Research Appreciation Day 2023 Abstract Book

COMPETITION POSTERS

Novel Kinase Inhibitor Screen on Estrogen Receptor (ER)-positive Breast Cancer and ER Mutants

PRESENTER

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COLLEGE/SCHOOL

School of Biomedical Sciences

ABSTRACT TOPIC

Cancer

ABSTRACT

Purpose: Breast cancer is the second leading cause of death in women in the United States. Triple-negative breast cancer is named for its lack of estrogen (ER), progesterone (PR) receptors, and HER2. The lack of receptors makes these tumors increasingly more challenging to treat, resulting in worse clinical outcomes than other receptor-positive subtypes. Some ER-positive tumors mutate to express an ER-negative phenotype, effectively reducing sensitivity to common anti-estrogenic drugs and making them more triple-negative and metastatic. Most estrogen-receptor mutations (both naturally occurring and genetically engineered) in ER-positive breast cancers occur at the ligand-binding site, rendering them ineffective. This change in estrogen receptor effectiveness can alter signaling cascades and affect downstream events in the cell, thereby promoting uncontrolled cell growth and insensitivity to drugs. Kinases are responsible for signal propagation in cells. Therefore, alterations to estrogen receptor signaling could significantly affect kinase expression and activity. Little is known about the 538 kinases encoded in the human kinome; consequently, they must be studied more thoroughly. Suppose a kinase inhibitor drug effectively inhibits the growth of cells with mutated estrogen receptors. In that case, there may be an effective treatment option against triple-negative breast cancer and these naturally occurring mutations.

Methods: Wild-type ER-positive breast cancer cells (MCF-7) were treated with 1 μ M KCGS Drug Library kinase inhibiting compounds from Dr. David Drewry at the SGC at UNC Chapel Hill. After 72 hours, cells were stained with crystal violet and imaged for cellular viability and morphologic changes. In addition, ER-mutated ER-positive breast cancer cells (MCF-7 Y537S and MCF-7 S167A) were treated with the same compounds at 100nM for 72 hours and stained with crystal violet.

Results: The data from the screening indicate that eight kinase inhibitors affected the morphology and viability of Y537S and S167A mutants to a greater extent than the wild-type MCF-7 cells at a log-dose lower concentration. One kinase inhibitor affected the S167A mutant to a greater extent than the Y537S mutant at the same attention (100nM).

Conclusions: Mutations to the estrogen receptor of typically ER-positive breast cancers may give insight into the development of interventions for triple-negative breast cancers. In the future, additional ER mutants will be screened against the same kinase inhibitors. In addition, kinase inhibitors may also give insight into the kinases essential to cancer viability and metastasis.

Single Agent Opioid vs Combination Agent Opioids in Postoperative Pain Control

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Other

ABSTRACT

Introduction: Treating post-surgery pain in pediatric populations often involves combination opiates, commonly hydrocodone and oxycodone. Unfortunately, this approach can lead to confusion for parents and concerns for overdose, as half of pediatric opioid prescriptions are considered high-risk. An opioid stewardship committee was established to oversee prescribing guidelines at Cook Children's Medical Center (CCMC). This large-scale retrospective study examined whether educational interventions increased the likelihood of single-agent opioid prescriptions for post-surgery pain. This practice allows providers to more freely utilize NSAIDs and acetaminophen for postoperative pain.

Methods: This was a retrospective single-center quality improvement (QI) project of all patients, who were prescribed opioids after surgery at CCMC in Fort Worth, TX between 3/1/2018 and 2/28/2022. Logistic regression was used to determine whether likelihood of single-agent (vs. combination) opioid prescriptions differed by intervention and department.

Results: There were 5227 (38.30%) pre-intervention procedures and 8419 (61.70%) post-intervention procedures. Post-intervention procedures (vs. pre-intervention) were statistically significantly more likely to result in single-agent, rather than combination, opioid prescriptions (88.10% vs. 8.84%, OR=79.62, $p<0.0001$), and likelihood of single-agent opioid prescriptions significantly differed by department ($p<0.0001$). The proportion of single-agent opioids prescribed increased post-intervention in all 7 departments examined, and the proportion increased by 70% in the 3 departments with the most procedures: orthopedics, urology, and otolaryngology.

Conclusion: Ongoing educational efforts by the Opioid Stewardship Committee have resulted in a sustained change in prescribing practices in multiple surgical departments from the use of combination to single-agent opioids.

Outcomes of Patients Treated with Neoadjuvant Chemotherapy for Breast Cancer at John Peter Smith Hospital

PRESENTER

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COLLEGE/SCHOOL

Dual Degree

ABSTRACT TOPIC

Cancer

ABSTRACT

Purpose: Neoadjuvant chemotherapy (NAC) is administered before surgery and expected to benefit certain breast cancer (BC) patients. This study inspected outcomes of triple negative BC (TNBC), hormone receptor (HR) positive (+) HER2 negative (-), and HER2+ BC patients treated with NAC at John Peter Smith Hospital (JPS) in Tarrant County, TX. Our primary aim is to analyze pathologic complete response (pCR) rates in patients and any differences among groups. These results can give oncologists (surgical, medical, and radiation) a better idea on how to navigate patients through this journey of complex decision making for overall better outcomes.

Methods: This study is an IRB exempted retrospective review of JPS Oncology and Infusion Center's registry data. Eligible patients were diagnosed with TNBC, HR+ HER2-, or HER2+ BC from 1/1/2016 to 12/31/2019 and underwent NAC. Age, race, NAC regimen, tumor grade, recurrence, and patient survival were collected from EPIC EMR. National Comprehensive Cancer Network (NCCN) guidelines were used to standardize clinical prognostic and pathologic anatomic stages. Decrease in stage by at least one level was considered as improvement.

Results: Total of 104 patients (TNBC: 32; HR+ HER2-: 29; HER2+: 43) were analyzed. Median age was 53 years. 103 were women. 89 (85.6%) patients received full doses of prescribed NAC regimen. 22 (21.2%) had recurrence of cancer and 14 (14.5%) had died. Using the full cox proportional hazard model, TNBC patients had a 3.214 times higher hazard of death/recurrence when compared to other subsets (95% CI: 1.261, 8.193; $p=0.0145$). We noted improvement in stage in 65 (62.5%) patients: TNBC 78%, HR+ HER2- 38%, HER2+ 93%. 34 (32.7%) patients achieved pCR: TNBC 22%, HR+ HER2- 10%, HER2+ 56%. pCR in Black TNBC patients was only 16%. Patients that achieved pCR had a 71.6% reduced hazard of death/recurrence when compared to patients who had residual disease (HR: 0.284; 95% CI: 0.095, 0.849; $p=0.0243$). For HR+ HER2- patients, only 11 (38%) showed improvement in stage, 12 (41%) showed no change, and 6 (21%) were upstaged. In this subset, 6 (21%) showed improvement in LN while 11 (37.9%) upstaged in LN.

Conclusions: A clear unmet need is poor survival of Black TNBC patients. Safety net hospitals, like JPS, disproportionately treat Black patients. We show that attaining pCR correlates with improved survival, but less than a quarter of TNBC patients attained pCR. New NAC regimens with Pembrolizumab has become standard of care for TNBC patients since 2021 due to higher pCR rates. Still, there is a need for better NAC regimens to improve pCR in TNBC overall and clinical trials on new regimens should include Black patients. Also, more than a third of HR+ HER2- patients upstaged in LN after NAC. This suggests a need for better pre-NAC radiology staging methods and better NAC regimen testing for this subset.

Novel use of Light Adjustable Lenses to improve visual acuity in patients with corneal abnormalities: a case report.

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Eye / Vision

ABSTRACT

Background: Keratoconus is characterized by thinning and protrusion of the cornea that produces an irregular astigmatism and decreased visual acuity. Individuals with these corneal abnormalities commonly experience undesirable visual acuity outcomes due to lack of effective traditional treatment options. We postulate Light Adjustable Lens (LAL) may be a safe and effective treatment where neither multifocality nor Laser-Assisted In Situ Keratomileusis (LASIK) are a viable method to achieve decreased spectacle dependence following surgery. This report presents a single patient diagnosed with forme fruste keratoconus undergoing LAL intraocular lens (IOL) replacement surgery. The patient was selected based on their history of corneal abnormalities and ability to benefit from IOL replacement. Potential benefit from IOL replacement was determined based on the patient's ocular complaints and visual test results in clinic. Lens selection parameters were made based on keratotomy and biometry data obtain from the Lenstar LS900. Visual acuities after LAL implantation and postoperative light treatments were recorded and compared with preoperative visual acuities. The patient received LAL, made of foldable silicone, implanted through phacoemulsification and standard IOL implantation techniques in both eyes (OU), and after completion of 1-month postsurgical healing received postoperative light treatments for lens adjustment.

Case Presentation: A 69-year-old man presented in clinic with complaints of decreased central vision. His brightness acuity test (BAT) was 20/40 OU and slit lamp examination (SLE) and oxidative stability index (OSI) revealed nuclear sclerotic (NS) cataracts of 2+ grade OU. Scheimpflug imaging (Figure 1.1) showed corneal abnormalities consistent with FFK OU. Imaging measured a topographic irregularly irregular astigmatism of 0.50 D at 115 degrees with a total corneal power (TCP) of 0.44 D at 127 degrees in the right eye (OD) and 0.33 D at 80 degrees with a TCP of 0.32 D at 88 degrees in the left eye (OS). Keratotomy measurements can be found in Table 1. The patient's primary goal was to achieve reduced spectacle dependency. Preoperative serial refraction established refractive stability OU. RxSight LAL of +20.5 D and +20.0 D were selected for the OD and OS respectively. 1-month UDVA was 20/20 in the OS and UNVA was Jager 5 (20/50) OD. Following 2 postoperative UV light treatments spaced 4 days apart and 1 lock-in UV light treatment after 3 days, the patient maintained UDVA of 20/20 in the OS and achieved UNVA of Jager 1 (20/25) OD.

Conclusions: This case shows the potential of LAL to be a reliable and reproducible treatment method that can result in positive visual acuity outcomes in patients with corneal abnormalities. It also demonstrates that in patients with FFK and mild keratoconus, LAL has potential to utilize spherical aberration to successfully achieve extend depth of the focus (EDOF) vision.

Leading Predictors of Economic Burden Among Postmenopausal Women with Heart Failure: An Application of Machine Learning with XGBoost and SHapley Additive exPlanations

PRESENTER

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COLLEGE/SCHOOL

School of Biomedical Sciences

ABSTRACT TOPIC

Other

ABSTRACT

Objective: Heart Failure is associated with high direct healthcare costs, including out-of-pocket spending by the patients. However, there are knowledge gaps in HF research among postmenopausal women. Therefore, this study uses machine learning methods to identify leading predictors and their associations with economic burden among postmenopausal women (age > 50 years) with heart failure.

Methods: This cross-sectional study used data from postmenopausal women with heart failure from the 2020 Medical Expenditure Panel Survey (MEPS: weighted N= 600,742). The economic burden was measured with total healthcare expenditures by the payors (third-party expenditures) and out-of-pocket expenditures by the patients and their families. We employed eXtreme Gradient Boosting (XGBoost) regression to determine key predictors. Global and local interpretations of associations were performed using SHapley Additive exPlanations (SHAP). Our predictive model used 21 features such as age, health status including comorbidities (anxiety, arthritis, asthma, cancer, COPD, depression, diabetes, high cholesterol, hypertension, and thyroid disease), perceived physical and mental health status, and polypharmacy. Social determinants of health (SDoH) consisted of marital status, health insurance coverage, prescription drug coverage, education, poverty status, and region. The model building included 70% training and 30% testing split of the data, 10-fold cross-validations, and up to six rounds of optimization using Python 3.9.12. Model performance metrics included absolute mean squared errors, root mean squared error and coefficient of determination; these were evaluated using the test dataset.

Results: The model offered excellent accuracy as evidenced by its low mean absolute errors (0.442,0.310), root mean square errors (0.452,0.342), and high coefficients of determination (0.935,0.987) for third-party and out-of-pocket expenditures, respectively. The top 10 leading predictors of third-party expenditures included polypharmacy, age, resident of the Midwest region, asthma, perceived physical and mental health, anxiety, hypertension, white race, and low income. The SHAP plots from the third-party expenditures revealed complex relationships of age, physical, and mental health with the target variable. Polypharmacy, low income, anxiety, and asthma were associated with higher third-party expenditures. Non-Hispanic white Women and those with hypertension had lower third-party expenditures. The top 10 leading predictors of out-of-pocket expenditures included age, Latinx ethnicity, asthma, cancer, being poor, having middle income and high income, prescription drug coverage, private insurance, and polypharmacy. Out-of-pocket expenditure plots only highlighted age as the key complex factor. Being poor, having middle income, and reporting Latinx ethnicity were associated with lower out-of-pocket expenditures. High income, prescription drug coverage, private insurance, polypharmacy, and the presence of asthma and cancer were associated with higher out-of-pocket expenditures.

Conclusion: The leading predictors differed by payor source. SDoH were associated with economic burden, suggesting that addressing SDoH may reduce healthcare costs. Cost-containment policies, programs, and interventions at the payor and patient levels need to include effective comorbidity management strategies. The

limitations of this study include cross-sectional study design, self-reported data that may be subject to recall bias, and severity of comorbidities that may affect the economic burden. However, the study also has several strengths, such as nationally representative data, the inclusion of SDoH, validated information on expenditures, and robust interpretable machine learning methods.

EXTERNAL FUNDING SOURCE

NIH-Artificial Intelligence/Machine Learning Consortium to Advance Health Equity and Researcher Diversity

Assessing the Impact of Senate Bill 8 on Texas Medical Students' Future Specialty Choice and Intended Location of Practice

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Purpose: On June 24, 2022, the Supreme Court overturned their 1973 ruling on Roe v. Wade, spurring Texas to enact "trigger law" 170A, extending the ban on abortion beginning at fertilization. The goal of our research is to evaluate whether Texas medical students' choices of women's health related specialties such as OB-Gyn and Family Medicine (FM) and/or intended location of practice have been impacted in response to these legal changes. Although many professional organizations released statements in response to these law changes, the impact this legislature has on medical students has not been summarized. It is important to understand how medical students are influenced by legal changes in healthcare, as the future distribution and availability of physicians is dependent on their choices.

Methods: An anonymous, Qualtrics survey consisting of six multiple choice and one free response question was dispersed via email list-serves to all current students at the Texas College of Osteopathic Medicine in Fort Worth, Texas. Only responses from students who indicated they have ever been interested in Ob-Gyn and/or FM specialties were included in the final data set. Data was collected for four weeks and then analyzed.

Results: We received 200 total responses, with 163 qualifying for our final data set. Of the total respondents (n=163), 89.57% answered they intended to practice medicine in Texas prior to the overturning of Roe v. Wade, and 84.05% answered they are currently interested in practicing medicine in Texas. Regarding the decision to pursue Ob-Gyn and/or FM specialties in response to the law change, our survey shows 28.83% of students were deterred, 26.99% were encouraged, and 44.17% were not impacted. Out of those indicating their specialty choice was impacted, 51.65% (n=91) were deterred. Regarding their decision to practice in Texas, our survey shows 45% were deterred by the law changes, 18.75% were encouraged, and 36.25% were not impacted. Out of those indicating their location of choice was impacted, 70.59% (n=102) were deterred from practicing in Texas. The alternative desired locations were Colorado (10), California (17), New York (7), New Jersey (2), Illinois (2), Washington (2) or abroad.

Conclusions: Our data shows the majority of students' decisions to pursue Ob-Gyn and/or FM and to practice in Texas were impacted by the overrule of Roe v. Wade, with higher percentages of students being deterred than encouraged for both decisions. Overall, there was a decrease in students who currently want to practice in Texas compared to before the legislative changes. Per answers to our free-response question, one motivation for practicing outside of Texas is wanting to practice somewhere with less limitations on women's health care and abortion. Alternatively, some students indicated they were encouraged to remain in Texas, as an advocate for reproductive rights. Although there are many variables that influence where one practices medicine, such as family, military commitment, etc., our survey shows that the recent changes in Texas legislation play a strong role in this decision for some students.

Gaps in the Knowledge of Sexually Transmitted Infections in Young Adults: A Review of the Literature

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

General Public Health

ABSTRACT

Purpose: Almost half of the 26 million sexually transmitted infections (STI) occur in young adults, although they are only 25% of the sexually active population in the US. Common STIs include chlamydia, gonorrhea, syphilis, genital herpes, Hepatitis B (HBV), Human Immunodeficiency Virus (HIV), and Human Papillomavirus (HPV). STIs are often associated with adverse health outcomes if left untreated, such as pelvic inflammatory disease, infertility, and ectopic pregnancies in women. The high rates of STIs in young adults, ages 18-25, may be due in part to a lack of knowledge about screening recommendations, symptoms, and available services for care. Because knowledge is a key factor associated with the prevention of STIs, the purpose of this study is to explore the current literature related to STI knowledge among young adults and identify the gaps in knowledge.

Methods: A literature review process was conducted using the following electronic databases: PubMed, Scopus, Medline, ScienceDirect, WILEY, EbscoHost. In addition to database search, the reference lists of the relevant articles were screened for titles and abstracts containing the keywords. The keywords used included: STI, STD, sexually transmitted infection, sexually transmitted diseases, knowledge, awareness, health literacy, health attitudes, information literacy, primary prevention, and secondary prevention. This retrospective search was limited to: (i) articles written in English, (ii) studies conducted in the United States, (iii) articles addressing genital herpes, HBV, HIV, HPV, chlamydia, or gonorrhea in the title or abstract, and (iv) included young adults 18-25 years old as participants. We excluded syphilis in the STI category, and the final search resulted in 41 articles that included qualitative and quantitative studies and systematic reviews.

Results: Gaps in the knowledge of STIs in young adults was subset into five categories: prevalence, transmission, symptoms, treatment and prevention, and testing services. Young adults lack awareness about the high STI rate in their age group, transmission factors such as skin-skin contact, or oral/genital sex, and that STIs can be asymptomatic. Many young adults have misconceptions about HPV vaccines, pre-exposure prophylaxis for HIV prevention, and condom use. Two of the most important factors to the success of STI prevention in programming are the promotion of self-efficacy and the reduction of stigma around STIs. Self-efficacy is defined as the "belief in one's own ability to execute a particular behavior related to a specific domain of functioning." A high level of self-efficacy in college students is one of the best predictors of STI and HIV testing and condom use. Additionally, higher levels of STI knowledge have been correlated with less stigma surrounding the diseases.

Conclusion: Understanding what the specific gaps are in young adults' STI knowledge can guide college and community programs in narrowing their focus to provide complete education concerning STIs. Specifically, more programs should implement effective theory-based approaches, including those that focus on improving self-efficacy of STI prevention and treatment and decreasing the stigma around these diseases. Addressing these specific points among young adult populations may have a role in reducing the rates of STIs and preventing the adverse health outcomes.

Analysis of survivin expression in black and white breast cancer patient tissue

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Cancer

ABSTRACT

Purpose: Survivin is a protein that belongs to the inhibitor of apoptosis family. It inhibits the activation of caspases and is also involved in the regulation of the cell cycle. Survivin is normally expressed during development with no expression detected in most adult differentiated tissues. However, high expression of this protein is found in many cancers which correlates with poor prognosis. Breast cancer disproportionately affects black women who have significantly higher mortality rates compared to white women with breast cancer. We hypothesize that higher expression of Survivin in Black cancer patients correlates with their higher mortality rates. In this project, we compared the level of expression of survivin in breast tumor tissue from Black and White cancer patients. This was done using immunohistochemical (IHC) staining technique of tumor tissue sections and analysis of The Cancer Genome Atlas database. Detecting differential expression of Survivin between the two racial groups and within different subtypes of breast cancer could lead to the development of Survivin as a diagnostic and/or prognostic marker as well as a possible therapeutic target.

Methods: Our first approach was to analyze the TCGA database to confirm our hypothesis that there is differential expression of survivin between the two racial groups and within different subtypes of breast cancer. This involved RNA-seq data analysis using various tools available online. Secondly, breast tumor tissue, representing different subtypes of breast cancer, from Black and White patients, was analyzed by immunohistochemistry (IHC) using survivin specific antibodies. The protocol for nuclear and cytoplasmic Survivin detection was standardized. The IHC data, in the form of percent staining (nuclear and cytoplasmic), was then analyzed by semi-quantitative methods using H-score and Allred scores.

Results and Conclusions: Results from the analysis of TCGA database and our IHC data indicate significantly higher expression of survivin in tumors from Black patients compared to White. Differential expression was also observed between different subgroups of breast cancer, with high expression in the most aggressive triple negative (TNBC) form of breast cancer. Coincidentally, the occurrence of TNBC is higher in Black women compared to White women. We also observed higher nuclear expression in Black patients compared to White patients, which has been associated with poor outcomes. Based on the vast literature suggesting that survivin plays a key role in cancer progression, we believe that survivin could be a useful diagnostic and/or prognostic marker or a therapeutic target to combat the racial disparity in breast cancer.

IRB NUMBER

2018-093

Changes in cerebral inflammation and blood pressure in postpartum preeclamptic rats

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Introduction: Postpartum (PP) preeclamptic (PE) women have an increased risk of developing hypertension (HTN) and cerebrovascular diseases later in life. Studies show that women who experience preeclampsia go on to develop HTN 7-8 years earlier than women with normal pregnancies, increasing their risk for developing cerebrovascular diseases such as stroke. While the timing and mechanisms contributing to a rise in blood pressure (BP) and cerebrovascular dysfunction in postpartum preeclamptic women are unknown, they are hypothesized to be influenced by inflammation. Previous studies in our lab indicate postpartum PE rats at 10 weeks have HTN and increased inflammation (PMID: 34727994). Our current study will examine BP and inflammation in postpartum PE rats at an earlier time point, 6 weeks (PP6), to determine the relationship between cerebral inflammation and the pathophysiology of HTN. We hypothesize that postpartum PE rats will have an increase in BP and cerebral inflammation 6 weeks after delivery.

Methods: Pregnant Sprague Dawley rats were divided into 2 groups: normal pregnant (NP) rats, and preeclamptic (RUPP) rats. Placental ischemia was surgically induced in the preeclamptic group via the reduced uterine perfusion pressure (RUPP) model. All rats gave birth naturally and were weaned for 3 weeks. At PP6, BP was measured via carotid catheterization, and brain tissue was collected to measure pro-inflammatory (TNF- α and IL-17) and anti-inflammatory (IL-4 and IL-10) factors via colorimetric assays and ELISAs.

Results: Blood pressure was elevated in RUPP PP vs NP PP (128 ± 6 vs 106 ± 4 mmHg, $p < 0.05$). Cerebral TNF- α drastically increased by ~ 2.4 fold in RUPP PP vs NP PP (2576 ± 445.6 vs 1058 ± 212.5 pg/mL, ns). Cerebral IL-17 (331.2 ± 41.1 vs 297.6 ± 48.6 pg/mL, ns) and IL-4 (178.4 ± 23.4 vs 154.8 ± 14 pg/mL, ns) also increased in RUPP PP vs NP PP. Cerebral IL-10 (103.9 ± 21.4 vs 147.6 ± 11.3 pg/mL, ns) was decreased in RUPP PP vs NP PP rats.

Conclusion: PP6 preeclamptic rats have HTN and increased cerebral inflammation. It is yet to be determined whether cerebral inflammatory markers are the cause or consequence of HTN in PP6 PE rats. Future studies will explore the sequence of HTN and cerebral inflammation in postpartum PE rats and determine how brain inflammation contributes to HTN and cerebral damage. We will also target specific areas of the brain that modulate autonomic function and BP. This study is clinically relevant because it will inform providers on the pathophysiology of HTN and/or cerebral damage in women after a PE pregnancy. Our findings suggest that the use of inflammatory therapeutic targets improves HTN and cerebrovascular dysfunction in postpartum PE women.

EXTERNAL FUNDING SOURCE

This research was supported by start-up funds and the American Heart Association Early Career Development Award [AHA 18CDA34110264 (Cunningham)]. Also the National Heart Lung and Blood Institute (NHLBI) of the National Institutes of Health Award [5R25HL007786-29 (Jones)]

IACUC NUMBER
IACUC-2021-0037

Examining Familiarity with Location and People in Association with Protective Behavioral Strategy Use Among Adolescents and Young Adults at the Daily-Level

PRESENTER

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COLLEGE/SCHOOL

School of Public Health

ABSTRACT TOPIC

Other

ABSTRACT

Purpose: Despite protective behavioral strategies (PBS) often being a central component to alcohol prevention programs, many adolescents and young adults who drink alcohol use few to no PBS. Therefore, it is important to determine factors associated with PBS use. Situational factors such as social and physical environments have shown to influence drinking behavior. In addition, many PBS are often related to peers and location and thus may influence PBS use or nonuse. The study aimed to investigate the associations between situational familiarity (i.e., familiarity with locations and people) and PBS use at the daily level among adolescents and young adults.

Method: Participants were recruited in Texas for a longitudinal ecological momentary assessment (EMA) study that involved a 3-week EMA burst design (8 surveys per week; up to 2x/day) with bursts occurring quarterly over 12-months. Participants who reported drinking days and answered PBS items were included in the current analyses.

Data: The analytical sample consisted of 3,921 drinking days from 579 participants (55.44% females; 45.12% White, Non-Hispanic; ages 15 to 25 (mean = 21.04)). Data were analyzed with mixed effects zero-inflated Poisson models for each PBS outcome (i.e., serious harm reduction, limiting/stopping, manner of drinking).

Results: Within-person results indicated when participants had elevated (i.e., higher than their own average) familiarity with location (e.g., How familiar are you with the locations you were at yesterday?), they were less likely to use harm reduction PBS (RR = 0.94, $p < 0.001$) and limiting/stopping PBS (RR = 0.96, $p = 0.001$). Results showed that on drinking days with elevated familiarity with people (e.g., How familiar are you with the people you were with yesterday?), individuals were more likely to use limiting/stopping PBS (RR = 1.04, $p = 0.01$). There were no significant daily-level associations between familiarity with people or location and manner of drinking PBS.

Conclusion: Results suggest that adolescent and young adult PBS use, particularly serious harm reduction and limiting/stopping PBS, can vary based on familiarity with people and location on a daily level. Alcohol prevention approaches, such as just-in-time intervention strategies, should consider how to increase PBS use even when drinking in more familiar situations or with less familiar people.

IRB NUMBER

2018-077

Osteogenesis Imperfecta: Implications of Using Micro-CT for Visualizing Developmental Variation in the Middle and Inner Ear of OIM Mice

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Structural Anatomy

ABSTRACT

Osteogenesis imperfecta (OI), also known as brittle bone disease, is a genetic bone disorder caused by mutations in the genes COL1A1 and COL1A2, which are responsible for encoding type I collagen. Much is known regarding the effects of the disease on cranial and postcranial elements. However, little is known regarding the pathogenesis and physical manifestations of OI in the ear despite the high rates of hearing loss in patients with OI (~60% of the population is affected). Because ossification or demineralization of structures in the ear may affect the efficacy of certain treatments like cochlear implants, this information deficit limits the treatment options available for OI patients. Thus, the purpose of our research is to visualize and document anatomic variation in the ears of mice bred to have the Type III OI genetic variant in order to better understand the cause of OI-related hearing loss. 3D models of the middle and inner ears were created from micro-CT scans that also employed two new contrast-enhanced methods to visualize the cochlea and middle ear (malleus, incus, and stapes). All CT scanning were done on the UNTHSC campus using the new Small Animal Imaging Facility (SAIF) as part of a previous study. The scan resolution was approximately 20 μ m. The studied WT and OIM mouse samples include three time points intended to capture a developmental sequence: 0-day-old (WT=20, OIM=29), 7-day-old (WT=23, OIM=23), and 14-day-old mice (WT=22, OIM=18). The visualization software Avizo was then used to digitally segment the bone of the inner ear and middle ear. Gross anatomic differences are currently being documented for each region.

Previous work has shown higher levels of ossification and marked bony encroachment of the otic capsule onto the cochlea in the adult OIM mouse model, potentially damaging the soft tissue of the membranous labyrinth. This research uses micro-CT imaging designed to capture a developmental sequence, giving us the potential to elucidate how and when the bony intrusions are impacting surrounding structures. Insight into this anatomical damage may help further clarify OI-related pathology, including the distinction between hearing loss associated with the middle ear (conductive hearing loss) vs. hearing loss associated with the inner ear (sensorineural hearing loss). Furthermore, a preliminary analysis of the developmental sequence should provide insight into when these anatomical changes are first occurring. Upon completion, this research will demonstrate the efficacy of using these new imaging approaches for studying minute structures of the ear and may markedly advance our understanding of the pathogenesis of OI-related hearing loss.

Creation of an Affordable and Realistic Ultrasound Pericardiocentesis Model

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Cardiovascular

ABSTRACT

Purpose: The pericardium is a protective fluid filled sac that surrounds the heart. In cardiac tamponade, the pericardium fills with excess fluid (blood, pus, etc.) resulting in decreased cardiac output. Ultrasound guided pericardiocentesis is a dangerous, but potentially lifesaving procedure that can be performed to relieve cardiac tamponade. Teaching institutions often obtain lifelike trainers that cost upwards of \$20,000. More cost-effective models using balloons or Styrofoam eggs have been created but lack realism and durability. Our objective was to develop an affordable model utilizing a 3D printed heart for ultrasound-guided pericardiocentesis.

Methods: Models of the heart and pericardium were created using Mimics 3D software (Materialise) and printed on a Stratasys J750 printer utilizing Digital Anatomy materials. An alternative model was created utilizing a cup and saline IV bag. Gel wax was then melted at 220 degrees Fahrenheit and the two models were submerged to simulate the acoustic properties of surrounding thoracic tissues.

Results: The 3D model and alternative model were successfully created and ultrasound-guided pericardiocentesis was attempted. The echogenicity of the 3D printed pericardium was sufficient for visualization; however, the material was too thick to penetrate. In the alternative model, the saline IV bag was amenable to needle puncture, but was anechoic preventing sufficient visualization and did not sufficiently reseal after needle removal.

Conclusion: While gel wax has appropriate ultrasound properties, a material that can reseal after needle insertion is needed to make plastic bags and cups viable alternatives. Additional trials need to be done to identify a material for the 3D printed pericardium that is compatible with both ultrasound and repeat procedure attempts. Overall, 3D printing offers the most promising results and with future attempts, after fine-tuning the thickness of the pericardial sac, we anticipate a successful model will be produced.

The One Where Hepatic Encephalopathy Presented in the Setting of Normal Ammonia Levels

PRESENTER

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ABSTRACT TOPIC

General Medicine

ABSTRACT

Background: Ammonia has long been used as an independent predictor of hospitalization with liver-related complications and mortality as well as directly linked to hepatic encephalopathy. Ammonia is able to cross the blood-brain barrier and employ toxic neuroinflammation and alterations in neurotransmission.

Case Presentation: A 67 year-old-male with a history of cirrhosis status post TIPS, varices with multiple upper and lower GI bleeding episodes presented to the Emergency Department with abdominal pain, fever, and altered mental status. Vital signs were notable for fever and tachycardia. The initial consideration for the patient's altered mental status involved infectious vs metabolic concern. He was started on empiric antibiotic treatment while awaiting blood cultures. Upon examination, the patient was disoriented with abnormal coordination, inattentive and impaired cognition. Initial labs shown were notable for a WBC of 6.31, Hemoglobin (Hgb) of 10.4, Hematocrit (Hct) of 30.2, MCV of 98.1, and Platelets (plt) of 56. His ammonia levels were 30, in the high normal range.** Given immunocompromised state, a lumbar puncture was obtained, revealing 97 protein and 4 WBC (insignificant). CT and Ultrasound of the abdomen revealed occlusion of TIPS shunt, along with MRI revealing hepatocellular carcinoma. GI was consulted and based on clinical suspicion of hepatic encephalopathy S/P TIPS occlusion, he was started on Rifaxmin 550 mg BID and Lactulose 20 g q2 hours. After 9 bowel movements, the patient had a surprising improvement in his mentation, considering his normal ammonia levels. On exam, he had returned to baseline mentation, AO x3. Following changes in mentation, labs revealed IgG AB reactive to Treponema Pallidum, and the patient was started on Penicillin. It is important to note that the improvement in the patient's mentation was prior to the initiation of the penicillin.

Conclusion: Hyperammonemia in cirrhosis involves interactions amongst many different organs as it may arise due to declining liver synthetic function, portosystemic shunting, or renal dysfunction. Ammonia, a neurotoxic metabolite, is believed to play a central role in the abnormal brain function that is seen in hepatic encephalopathy. It is important to note that inflammation has been shown to play a role in the encephalopathic symptoms of liver disease, as the liver is inflamed and the gut leaks bacteria, cytokines produced from these processes can reach the brain, inducing further inflammation of the CNS. This case demonstrates the importance of not ruling out Hepatic Encephalopathy as the cause of abnormal brain function in the setting of normal ammonia levels, as there are many other inflammatory processes that are taking place as a result of hepatic dysfunction. Treatment options involve the use of Rifaximin, an antibiotic that targets ammonia-producing bacteria in the gut, and lactulose which aids in creating an acidic intestinal environment converting ammonia to ammonium for excretion. Our patient provides a unique example where all of the mechanisms and solutions imply rising levels of ammonia leading to hepatic encephalopathy, in the rare setting of a normal-ranging blood ammonia level.

Area deprivation index and cognitive function: A cross-sectional study of the HABS-HD cohort

PRESENTER

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ABSTRACT TOPIC

Aging / Alzheimer

ABSTRACT

Purpose: Dementia is an ever-growing group of disorders worldwide. It is proposed that neighborhood socioeconomic status (NSES) is linked with overall health, and this study will evaluate whether NSES is cross-sectionally associated with cognition in non-Hispanic White, African American, and Mexican American participants of the Health and Aging Brain: Health Disparities Study (HABS-HD).

Methods: The HABS-HD is a longitudinal study conducted by the Institute for Translational Research at the University of North Texas Health Science Center. Participants (n=1634) were age 50 years or older, and underwent a clinical interview, neuropsychological exam battery, functional examination, head MRI, amyloid PET scan, and blood draw for clinical and biomarker analysis. NSES was measured using the national area deprivation index (ADI) percentile ranking, which considered the variables of education, employment, income, occupation, and housing. Cognition was assessed by the Mini-Mental State Examination, Trails B Exam, FAS Test, Spanish English Verbal Learning Test, and Digit-Symbol Substitution Test. The cognitive performance in those living in the 20% most disadvantaged neighborhoods was compared to those in the 80% least disadvantaged neighborhoods using multiple linear regression models with age, sex, education, and ethnicity as control variables.

Results: Those in the most deprived neighborhood group were statistically significantly ($p < 0.05$) younger, less educated, more likely to be female, and more likely to be Mexican American. The means of MMSE and Trails B test were lower in those living in the more deprived neighborhood group ($p < 0.05$). When looking at the linear model of ADI and cognition, after adjusting for covariates, only Trails B scores were related to the higher deprived neighborhood group ($t = -0.62$, $p < 0.0001$).

Conclusion: Our study revealed that some measures of cognitive impairment were higher in people living in the top 20% disadvantaged neighborhoods. In future studies, specific markers of deprivation should be analyzed along with cognitive impairment to more specifically advocate for beneficial change. Further, due to sex and ethnicity being significant cofounders, analysis should be run by ethnicity to investigate this distinction.

EXTERNAL FUNDING SOURCE

National Institute for Aging

IRB NUMBER

2016-128

An Analysis of Student Satisfaction with Active Learning Techniques in an Online Graduate Anatomy Course: Consideration of Demographics and Previous Course Enrollment

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ABSTRACT TOPIC

Education

ABSTRACT

Purpose: Online learning has become an essential part of mainstream higher education, allowing greater access for students. With the increase in online course enrollment, specifically that of anatomy, understanding online teaching best practices is critical. Active learning has previously shown many benefits in face-to-face anatomy courses, including increases in student satisfaction. Currently, no research has measured the satisfaction of several active learning techniques implemented in an asynchronous, online graduate anatomy course.

Methods: This study compared the student satisfaction achieved by four active learning techniques with consideration of demographics and previous course enrollment. Survey questions consisted of multiple-choice and Likert-style that asked students to indicate their level of satisfaction with the active learning techniques. One hundred seventy (170) students completed the online anatomy course and surveys.

Results: Students were more satisfied with question constructing and jigsaw than with concept mapping and team-learning module. Additionally, historically excluded student groups (underrepresented racial minorities) were more satisfied with active learning than White students. Age, gender, previous anatomy experience and/or online course experience did not influence the satisfaction of the active learning techniques. However, students with higher GPAs and those who had no graduate degree were more satisfied with the active learning techniques than students who had lower GPAs and those with a graduate degree.

Conclusion: These findings provide evidence that students enrolled in an online graduate anatomy course were satisfied with the active learning techniques, dependent on the specific technique, demographics, and previous course enrollment. Results provide anatomy educators with a better understanding of which techniques work best in an online anatomy course. Currently, there is a lack of research comparing active learning techniques in an online learning environment. These findings provide online anatomy educators with evidence that active learning techniques improve satisfaction, with consideration of student demographics and previous course enrollment.

EXTERNAL FUNDING SOURCE

American Association for Anatomists

IRB NUMBER

1792843

Effect of Monocarboxylate Transporter 2 Loss on Retinal Ganglion Cell Survival and Function

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ABSTRACT TOPIC

Eye / Vision

ABSTRACT

Purpose: There is currently no cure for the vision loss in glaucoma that is characterized by retinal ganglion cell (RGC) loss and irreversible optic neuropathy. Monocarboxylate transporter 2 (MCT2s) that transport pyruvate, lactate, and ketone bodies, are exclusively found in neurons such as the RGCs. We have previously shown that MCT2 is lost during glaucoma, in advance of RGC loss, and MCT2 overexpression protects RGC number and function. This study was undertaken to test whether MCT2s are necessary for RGC survival and function.

Methods: To test this hypothesis, we used tamoxifen injection into Thy1-ERT2-cre: MCT2^{fl/fl} mice to conditionally knock out MCT2 from Thy1-positive RGCs. Control mice carried the MCT2 floxed allele but were Thy1-ERT2-cre-negative. Control and experimental mice were subjected to ocular hypertension using the magnetic microbead model; separate naïve controls from each genotype were also evaluated. Intraocular pressure (IOP) was measured using the TonoLab rebound tonometer. Pattern electroretinogram (PERG) was used to analyze RGC function. We used unbiased stereology (Stereo Investigator, Micro Brightfield) to count the number of retinal ganglion cells in wholemount retina, and ATP levels in retina were also measured.

Results: IOP was higher in the ocular hypertension (OHT) groups. MCT2 knockout alone did not impact IOP, nor did it alter baseline PERG amplitude or latency. After OHT, PERG amplitude was significantly lower in the MCT2-knockout mice ($p=0.0013$). MCT2 knockout alone did not change RGC density. After OHT, RGC density decreased, though in this preliminary analysis, RGC density among the groups was not significantly different. ATP production in the OHT+ Tamoxifen group was significantly higher (1.81 ± 0.89 ug/ul) than in the naïve control group (0.68 ± 0.42 ug/ul).

Conclusions: MCT2 knockout from RGCs did not change IOP or PERG, suggesting that MCT2 is not necessary for RGC survival. Ocular hypertension decreased PERG amplitude and RGC density, though the magnitude of the decrease may not have been increased by MCT2 knockout. These preliminary data suggest that RGCs are capable of meeting their immediate metabolic needs through means beyond MCT2.

EXTERNAL FUNDING SOURCE

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IACUC NUMBER

IACUC-2022-002

Assessment of Patient Engagement in Pediatric Mental Health Calls in Mothers of Young Children Since COVID-19 with Improvement Solutions

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ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Purpose: COVID-19 restrictions led to a rise in telehealth visits. To combat the issue of limited in-person visits, Pediatric Mental Health Calls (PMHC) were created to bridge the gap and provide continued mental health support to UNTHSC Pediatric patients and their caregivers during the pandemic and beyond. Patient engagement was analyzed to gain a better understanding of the impact of PMHC during COVID-19 in 2020 and 2021-22 and to provide improvement for future calls.

Methods: PMHC was completed by HSC student volunteers. Quantitative analysis of patient involvement was made in mothers whose children were infants in 2020 and toddlers in 2021-2022. Patients no longer with UNTHSC clinic or phone numbers no longer in service were omitted from the count. Participation of these mothers (n=292) was assessed using the percentage of the total number of responses in open or close-ended questions (<5, ≥5, or no response at all) and the number of word sentences in open-ended questions (<5 in any category, ≥5 in 1 category, ≥5 in 3 categories). Analysis used chi-square test of independence. Statistical significance was set at $p < 0.05$. Additionally, Edinburg Postnatal Depression Scale (EPDS) phone screenings and referrals in mothers of infants were compared with early COVID-19 in 2020 to follow-ups in 2021-2022. In 2020, 199 out of 543 infant mothers who agreed to complete the EPDS screenings over the phone were compared to 229 out of 473 mothers of infants in 2021-2022. A comparison was also evaluated for 2020 (n=165) and 2021-2022 (n=190) postnatal mothers with an EPDS score of ≥10 indicating an increased risk for depression, thereby given referrals based on volunteer judgment.

Results: There was a positive response in patient engagement in early 2020 compared to 2021-2022. Chi square test showed a statistically significant decline in both the number of responses in open or closed-ended questions (<5, ≥5, with an increase in no response at all category) and in the number of word sentences in open-ended questions (<5 in any category, ≥5 in 1 category, ≥5 in 3 categories) in 2021-2022. In 2020, from the 199 infant mothers willing to complete the EPDS screening over the phone, 127 answered yes and 72 answered no. In 2021-2022, from the 229 infant mothers, 147 answered yes and 82 answered no. There was a drop in percentage in the number of referrals made for mothers of infants with an EPDS score of ≥10 in 2021-2022 when compared to 2020.

Discussion: Modifications of the PMHC are recommended to increase patient participation beyond the pandemic. Volunteers are encouraged to connect with patients using motivation and interpersonal interaction. Demographic data must be considered to assess patterns of patient engagement. Mothers should be educated on the data and the importance of completing EPDS screenings. Specific questions relevant to current concerns in the country affecting maternal and pediatric health should be focused upon. Alternatives should be suggested to patients who are less likely to respond.

Hyperkalemia in Adolescent Idiopathic Scoliosis Patients with Tranexamic Acid Administration

PRESENTER

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ABSTRACT TOPIC

Other

ABSTRACT

Introduction: Tranexamic acid (TXA) is used intraoperatively to reduce blood loss in various fields such as obstetrics, spine, and major joint replacement surgeries. Between May and June 2022, we identified more than three cases of intraoperative hyperkalemia that we believed to be influenced by TXA administration in our adolescent idiopathic scoliosis posterior spinal fusion (AISPSF) patient population.

Methods: A systematic review of our intraoperative hyperkalemia patients was conducted and narrowed to three patients with minimal pharmacodynamic, metabolic, or pathological influences. Each patient's timeline of intraoperative hyperkalemia was charted along with medical interventions to reduce patient's potassium levels.

Results: Patients 1-3 received a bolus of 5000 mg TXA an hour prior to the initial incision. Their maintenance doses were set to 10 mg/kg/hr, with infusion rates ranging from 4.95 mL/kg – 8.93 mL/kg. TXA administration was halted when potassium levels exceeded 5.5 mmol/L, and anesthetic intervention ensued to ensure patients rapidly reduced intraoperative potassium and avoided any unnecessary untoward effects of hyperkalemia. Of note, most interventions involved the administration of 10% CaCl, four puffs of (45 mcg/act) Levalbuterol, and an increase in ventilation in addition to cessation of TXA administration. Cessation of TXA administration alone was able to reduce hyperkalemia as well.

Conclusion: Upon initial review, we could not identify preoperative factors or intraoperative changes that could have led to hyperkalemia. To prevent potential complications associated with acute intraoperative hyperkalemia, we are currently working on a retrospective review of institutional TXA administration for AISPSF cases and matching patients that did and did not suffer from episodes of intraoperative hyperkalemia by age, gender, diagnosis, levels of surgery, length of procedure, and preoperative potassium to better identify the influence TXA administration plays on AISPSF intraoperative hyperkalemia.

Pediatric Rhabdomyolysis and Plasmapheresis - A Review of Two Cases

PRESENTER

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ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Background: Rhabdomyolysis is the breakdown of skeletal muscles causing leakage of cellular components like creatine kinase (CK) into the bloodstream. Clear guidelines for managing pediatric rhabdomyolysis currently do not exist. Traditional treatment involves prompt administration of intravenous (IV) fluids to counteract dehydration and prevent acute kidney injury (AKI). However, there have been limited case studies involving plasma exchange to treat severe cases of rhabdomyolysis in pediatrics.

Case Information:

Case 1: A 14-year-old female presented with muscle pain, headache, decreased urine output, and tea-colored urine. Her history included lifting weights and dehydration. Her presenting CK was 281,483 U/L and creatinine was 2.88 mg/dL. She was diagnosed with rhabdomyolysis, AKI, and transaminitis. CK levels rose to 410,000 U/L. On the second day, plasmapheresis was performed, and CK levels decreased after two more treatments. However, creatinine levels continued to increase. Renal biopsy showed acute tubular injury secondary to rhabdomyolysis. Hemodialysis was performed. Upon discharge, creatinine was 2.43 mg/dL, and she no longer required dialysis.

Case 2: An 11-year-old female presented with a respiratory illness for two days. Her CK was 41,671 U/L. She was diagnosed with AKI and rhabdomyolysis induced by COVID-19. Standardized treatments were initiated with no improvement. CK levels reached over 410,000 U/L. Plasmapheresis was then initiated for three days, which lowered the CK levels significantly. Upon completion of plasmapheresis, her CK level dropped down to 40,000 U/L. Her CK levels normalized and her AKI became stable.

Conclusions: Given the risks associated with high CK levels resistant to traditional IV hydration, it is crucial that the levels are brought down quickly to prevent long-term complications such as AKI. Therefore, plasmapheresis may be considered in severe, life-threatening rhabdomyolysis in pediatrics.

Development of a mouse model to study the long-term effects of chemotherapy on brain function

PRESENTER

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ABSTRACT TOPIC

Neuroscience

ABSTRACT

Purpose: While remaining an effective life-saving intervention for cancer patients, chemotherapy has been associated with many neurotoxic side effects, including chemotherapy-related cognitive impairments (CRCI). Chemotherapy exposure leads to a decline in learning, memory, processing speed, attention, and executive functions, which may persist for more than 20 years post-treatment, impairing the quality of daily lives of survivors. Childhood cancer survivors are particularly vulnerable to chemotherapy and have been impacted in their educational achievements, employment, social relationships, and even life expectancy. Most common childhood cancers are often treated with the folate-inhibitor methotrexate (MTX). Our study aimed at establishing a tumor-free mouse model of MTX-induced brain impairments. We hypothesized that early exposure to MTX would induce impairment in cognition, as well as motor and affective functions.

Methods: Male and female C57BL6/J postnatal day 15 pups received intraperitoneal injections of saline or MTX (2 mg/kg) once a day for 3 days. Pups were weaned on PND21, and subsets were behaviorally characterized at 1 or 7 months after MTX exposure (n=6-8 for 1.5 months old, and n=11-13 for 8 months old) for motor, affective and cognitive functions using a comprehensive behavioral test battery.

Results: At 1.5 months, coordination and motor learning was significantly impaired in males and improved in females. All other measures did not reveal any other significant effects, however trends of impaired motor and cognitive functions could be discerned. At 8 months, there were no effects of MTX on motor, affective and some cognitive functions. However, MTX exposure led to an impairment on spatial learning and memory and increased swimming speed.

Conclusions: Studies at 1.5 months will need to be repeated to increase power and ascertain conclusions on brain functions. Early exposure to MTX treatment led to long-term impairments in both male and female mice and could be used as a model to test interventions to limit CRCI.

EXTERNAL FUNDING SOURCE

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IACUC NUMBER

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Clinical significance of Annexin A2 overexpression in kidney renal clear cell carcinoma

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ABSTRACT TOPIC

Molecular Genetics

ABSTRACT

Purpose: Invasion and metastasis led to poor prognosis and death of kidney renal clear cell carcinoma (KIRC) patients. In this study, we focus on the characterization of Annexin A2 (AnxA2), which plays an essential role in cell growth, angiogenesis, migration, invasion, and metastasis. Although the role of Annexin A2 (AnxA2) has been studied in many cancers, its function in KIRC is still unexplored. Therefore, in this study, we investigated the AnxA2 expression in tumor tissues of KIRC patients to determine its association with disease characteristics.

Methods: We utilized data from The Cancer Genome Atlas (TCGA) to observe AnxA2 gene expression in KIRC and its association with survival. Additionally, immunohistochemical (IHC) analysis was performed to examine the AnxA2 expression in tumor tissues of KIRC patients.

Results: In our analysis of TCGA data, AnxA2 mRNA expression was found significantly higher in KIRC tumor tissues compared to the adjacent noncancerous tissues. In addition, AnxA2 expression was significantly associated with higher tumor stage and grade. The high expression of AnxA2 in KIRC patients was significantly correlated to decreased survival [hazard ratio (HR), 1.75; 95% confidence interval (CI), 1.29 - 2.36; $p = 0.00023$] as compared to low expression. In addition, our IHC staining suggests that AnxA2 was overexpressed in tumor tissues of KIRC patients compared with adjacent noncancerous tissues.

Conclusion: AnxA2 is overexpressed in KIRC tumor tissues, and has a direct relationship to the advanced clinicopathological variables and adverse prognosis associated to patients with KIRC.

Presentations of Cutaneous Disease in Various Skin Pigmentations: Atopic Dermatitis

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ABSTRACT TOPIC

General Medicine

ABSTRACT

Background: Atopic dermatitis (AD), commonly known as eczema, is a chronic inflammatory skin disorder classically affecting flexural areas of the body. It presents in any age group, but commonly develops during infancy and early childhood and morphologic subtypes exist due to varying skin tones. Children with darker skin were approximately six times more likely to develop atopic dermatitis in comparison to children with lighter skin. African American and Asian patients more frequently have atopic dermatitis compared to Caucasian patients. Presentations of atopic dermatitis vary due to duration, age and color of skin. Acute lesions are clinically characterized as ill-defined pruritic, erythematous plaques (raised, >1cm) while chronic lesions are dry, hyperpigmented plaques (raised, >1cm) with lichenification and prurigo nodules. Differential diagnosis includes scabies, seborrheic dermatitis, ichthyoses, and psoriasis. This review article will showcase clinical images with varying presentations of atopic dermatitis in ranging age groups and skin color according to the Fitzpatrick scale.

Case Information: The Fitzpatrick scale provides a classification system for an individual's skin type based on the ability to burn and/or tan when exposed to ultraviolet light. It is used to approximate the degree of skin pigmentation. This review article focuses on 5 distinct cases of varying ages and skin types to present 5 atypical presentations of atopic dermatitis. Case 1 presents a 40-year-old, Fitzpatrick I, with chronic atopic dermatitis. Case 2 presents a 6-month-old, Fitzpatrick III, with acute atopic dermatitis. Case 3 presents a 11-year-old, Fitzpatrick IV, with subacute atopic dermatitis. Case 4 presents a 21-year-old, Fitzpatrick IV, with chronic atopic dermatitis. Case 5 presents a 3-year-old, Fitzpatrick V, with chronic atopic dermatitis.

Discussion: In the United States, atopic dermatitis affects approximately 11.3 – 12.7% and 6.9 – 7.6% of children and adults, respectively. Presentations of atopic dermatitis can vary due to duration, age and color of skin. Post inflammatory dyspigmentation is observed more in African American patients due to decreased healthcare access and different clinical manifestations, notably with erythema. Atopic dermatitis can have a significant quality of life impairment and disease burden in diagnosed individuals, especially those with darker skin pigmentation. The disease can progress to a systemic disorder, "atopic march" causing allergic conditions including asthma, allergic rhinitis and food allergies. Pruritus, a hallmark symptom of atopic dermatitis, may lead to increased sleep disturbances, fatigue, and mental health symptoms which ultimately affects growth, school performance, attention, and accident rates in children. Atopic dermatitis has been linked to attention-deficit hyperactivity disorder in children and increased rates of depression and anxiety in teenagers and adults. The purpose of this review article is to outline atypical presentations of atopic dermatitis to allow practitioners to gain a better understanding to aid in diagnosing patients with different skin tones.

Effects of the thromboxane receptor antagonist S18886 in the porcine coronary circulation

PRESENTER

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ABSTRACT TOPIC

Cardiovascular

ABSTRACT

Thromboxane A₂ (TxA₂) is a potent coronary vasoconstrictor that has been implicated in promoting decreases in myocardial perfusion in a variety of (patho)-physiologic conditions. S18886 is a promising orally-active TxA₂ receptor antagonist currently approved for investigational clinical use. However, the coronary vascular effects of S18886 are unknown and its specificity and affinity for the thromboxane receptor in the coronary circulation remain unclear. We tested the hypothesis that administration of S18886 dose-dependently attenuates coronary vasoconstriction to the TxA₂ mimetic U46619 without influencing coronary responses to prostaglandin F_{2α}, acetylcholine, or smooth muscle depolarization (K⁺).

Experiments to test this hypothesis were performed in male (n = 5) and female (n = 6) domestic swine. Hearts were excised and the left circumflex coronary artery isolated, cleaned of periadventitial fat, and cut into 3 mm rings. Isometric tension of coronary artery rings was measured in response to log order increments of U46619 (1 nM to 1 μM) with and without S18886 (0.1-100 nM). Similar isometric studies were conducted with prostaglandin F_{2α} (10 nM-10 μM), acetylcholine (0.1-10 μM), and KCl (5-90 mM).

U46619 induced concentration dependent increases in tension development of isolated coronary artery rings (average EC₅₀ of 42 ± 19 nM). Incubation of coronary arteries with S18886 (1 nM) significantly attenuated coronary vasoconstriction to U46619 resulting in a rightward shift of the EC₅₀ to 187 ± 38 nM (P < 0.02). Vehicle had no effect on U46619-induced contractions. Higher concentrations of S18886 dose-dependently reduced U46619-induced contractions. S18886 (1 nM) antagonized coronary vasoconstriction of prostaglandin F_{2α} (10 μM) by 68% ± 5 (P < 0.0001) but had no effect on either acetylcholine or KCl-induced contraction.

Data from this investigation indicate that S18886 is an effective antagonist of U46619-induced vasoconstriction in the porcine coronary circulation. While S18886 does not influence coronary smooth muscle response to either acetylcholine or activation of L-type Ca²⁺ channels, attenuation of prostaglandin F_{2α} suggests antagonists specificity may extend beyond TxA₂ receptor signaling.

EXTERNAL FUNDING SOURCE

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The length-tension characteristics of small coronary arteries vary with transmural origin

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School of Biomedical Sciences

ABSTRACT TOPIC

Cardiovascular

ABSTRACT

There are transmural differences in the structure of arteries across the left ventricular wall. For example, for arteries of the same size, wall thickness is greater in arteries of the epicardium than those from the endocardium. This observation suggests that there could be differences in their passive and active length-tension relationships, as different amounts of connective tissue or smooth muscle would be expected to alter these characteristics. We tested this hypothesis by studying similarly sized porcine coronary arteries from opposite transmural locations. Endocardial arteries had a diameter of $389 \pm 33 \mu\text{m}$ ($n = 8$), while epicardial arteries measured $388 \pm 50 \mu\text{m}$ ($n = 6$). A wire myograph was used to study the mechanical properties of these arteries under isometric conditions in Krebs-Henseleit buffer at 37 °C. Arteries were cut into rings with an axial length of 2 mm. Rings were repetitively stimulated to contract at increasing lengths with the addition of high extracellular K^+ (80 mM). Coronary arteries developed active tension to a plateau level over approximately 3-5 min and K^+ -induced contractions readily washed out. Arteries from the epicardium were stiffer, as the passive-length tension curve of these vessels was elevated over arteries from the endocardium. Passive tensions at optimal length were 3.2 ± 0.4 vs. 5.6 ± 1.5 mN/mm ($p < 0.05$). The active tension developed in response to K^+ depolarization was greater in epicardial arteries. Active tensions at optimal length were 3.4 ± 1.1 vs. 2.4 ± 0.3 mN/mm ($p < 0.05$). Our results represent the first comparison of transmural differences in coronary arteries under isometric tension. Our findings support the hypothesis that differences exist in the passive and active length-tension relationships of epicardial and endocardial arteries that correlate with wall thickness.

EXTERNAL FUNDING SOURCE

R01HL158723

Prediction of Ligand Selectivity and Efficacy Using Artificial Intelligence Algorithms

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COLLEGE/SCHOOL

Dual Degree

ABSTRACT TOPIC

Neuroscience

ABSTRACT

Purpose: Identifying target-specific ligands is extremely challenging in drug discovery, especially in cases where receptors display high structural similarity. Such is the case for metabotropic glutamate receptor subtype 2 (mGlu2) and metabotropic glutamate receptor subtype 3 (mGlu3), which are prime targets for various neurological treatments. However, signal transduction through these two receptors often yields opposing physiological function and differentially affects pathologies. The purpose of this study is to develop artificial intelligence (AI) methods to predict ligand selectivity and efficacy on similar targets.

Methods: Understanding the need to differentiate ligands based on their binding to mGlu2 and mGlu3, we employed a machine learning approach. Using patent-derived datasets, data was pre-processed into an eight-dimension vector space. Afterwards, the data was flattened, and a Multiple Input and Output (MIO) Model was designed to receive the incoming vectors. A classification arm was designated as an output, differentiating input structures as mGlu2 or mGlu3 ligands. In addition, this novel MIO Model with Functional application program interface (API) architecture also has the capacity to estimate efficacy of an input ligand by outputting Half-maximal inhibitory concentration (IC50) value.

Results: The model yielded greater than 96% accuracy in the classification task to predict the binding selectivity of the ligands, while simultaneously delivering satisfactory performance when predicting efficacy. With regards to the regression arm, the model attained about 81% accuracy in correctly identifying high-affinity mGlu2 compounds, and 62% accuracy in correctly identifying high-affinity mGlu3 compounds. We then used docking studies, and the trained model to screen an available ZINC database, selecting the top 39 compounds out of 9270 ligands.

Conclusions: This approach can pave the way for computer aided searches which screen for high efficacy ligands belonging to a certain class of interest. More specifically, this model can be used in combination with other established structure-based methodology like molecular docking, allowing for screening of even more drug candidates for further study and validation. With access to other high-quality datasets, this model has the potential to apply to other ligand classes of interest, posing great potential for drug repurposing studies.

EXTERNAL FUNDING SOURCE

This work is partially supported by a grant (#RP210046) from the Cancer Prevention and Research Institute of Texas.

The Effect of Trusted News Sources on the Confidence in the Safety of COVID-19 Vaccination

PRESENTER

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COLLEGE/SCHOOL

School of Public Health

ABSTRACT TOPIC

General Public Health

ABSTRACT

Purpose: COVID-19 vaccination prevents severe disease manifestations; yet uptake has been suboptimal. Confidence in the safety and efficacy of the vaccine influences COVID-19 vaccination decisions. Exposure to information from a trusted news source can impact perceptions and may contribute to vaccine decisions. This study assessed the association between trusted news sources and confidence in the safety of COVID-19 vaccination among Texas adults.

Methods: Participants were recruited through an online panel using quota sampling based on the racial and ethnic distribution of Texas in July 2022 (n=1089). The primary predictor variable was self-reported trusted news sources for COVID-19 related news (16 options), in which respondents were asked to endorse any news source they trusted, with options ranging from print media to cable news to local news. The outcome was confidence in the safety of the COVID-19 vaccine (not at all confident to very confident). Multinomial regression analyses were conducted to model confidence in COVID-19 vaccination and trusted news sources while controlling for education, age, gender, and self-reported race.

Results: Through an initial descriptive analysis, Fox News, local cable TV programs, and news broadcasting from one's home abroad were associated with lower confidence levels. After grouping those three sources as "top news sources" and assessing their effect on confidence through a multinomial model, it was found that individuals who trusted those top sources were significantly less likely to endorse "somewhat confident" (OR=0.59, 95%CI 0.4-0.89) or "very confident" (OR=0.41, 95%CI 0.27- 0.62) compared to being "not at all confident" in the safety of the COVID-19 vaccine.

Conclusions: Study findings show that some trusted news sources contributed to participants having less confidence or no confidence in the safety of the COVID-19 vaccine. Public health initiatives should consider how to address vaccine confidence among the public given the diversity of information sources people rely on.

IRB NUMBER

1858668-1

The Incidence of Distal Extremity Necrosis Associated with Vasopressor use in Critically Ill Patients

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ABSTRACT TOPIC

Cardiovascular

ABSTRACT

Purpose: Medication adverse events are associated with significant morbidity and mortality, increased hospital length of stay, and create a high burden of cost for both the patient and the healthcare system. Vasopressors are a class of medication with a known association with digital necrosis due to excessive peripheral vasoconstriction, in order to prioritize blood flow to the vital organs. We aim to identify the incidence of distal extremity necrosis in critically ill patients receiving vasopressors for cardiovascular support.

Methods: A retrospective analysis was performed of all patients treated with vasopressors including epinephrine, norepinephrine, phenylephrine, and vasopressin during the study period: January 1, 2012, through December 31, 2020, at a single institution. Patients treated with vasopressors with a concomitant documented diagnosis of distal extremity (upper and/or lower) ischemia, gangrene, or necrosis were identified. This subset of patients underwent further chart review to confirm the onset of digital necrosis was within 4 months of vasopressor use. The incidence of distal extremity necrosis in critically ill patients receiving vasopressors for cardiovascular support was then calculated.

Results: A total of 1,980,300 patients were screened, of which 46,792 had documented vasopressor use and were included in the at-risk population. Of all patients that had received vasopressors within our study period, 1,151 also had a documented diagnosis of distal extremity necrosis. Overall, a total of 56 (0.12%) patients had documented distal extremity necrosis within 4 months after sustained vasopressor use. 31 patients (36.1%) were given 3 or 4 vasopressors concurrently, 28 (50%) had isolated toe and/or foot necrosis, 15 (26.8%) had necrosis of both the distal upper and lower extremities, and 13 (23.2%) developed necrosis isolated to the hand and/or fingers. The average age of those who developed digital necrosis was 59 years. While there was more distal extremity necrosis when multiple pressors were used concurrently, the association was not significant ($p=0.77$)

Conclusion: The use of vasopressors for cardiac support in critically ill patients is often unavoidable. This treatment comes with the risk of inducing distal extremity ischemia and necrosis. The incidence of distal extremity necrosis is extremely low, but the risk increases when multiple vasopressors are used concurrently.

IRB NUMBER

1697545-1

Use of VMAT2 Inhibitors for Tardive Dyskinesia in Geriatrics - A Case Study

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ABSTRACT TOPIC

Aging / Alzheimer

ABSTRACT

Background: Tardive dyskinesia is a persistent, often irreversible movement disorder that may develop after chronic, cumulative exposure to antipsychotics. Geriatric populations are at increased risk of developing tardive dyskinesia as they age, leading to increased risk of injuries secondary to impaired gait and balance. VMAT2 inhibitors such as valbenazine, deutetrabenazine, and tetrabenazine are the first-line treatment and control of tardive dyskinesia.

Case Information: After developing tardive dyskinesia on aripiprazole, our patient was started on valbenazine before developing Parkinsonian symptoms and was subsequently switched to deutetrabenazine for management of the tardive dyskinesia. It has taken years of trial and error to adequately manage her tardive dyskinesia without significant untoward effects.

Conclusion: As use of VMAT2 inhibitors in managing antipsychotic induced tardive dyskinesia increases, special consideration regarding their efficacy and safety must be taken when starting in older patients. The case presented here highlights the increased risk of development of movement disorders in older adults on even short courses of antipsychotics, as well as the variability in response to VMAT2 inhibitors in resultant treatment. This case also represents the need for caution and concern when prescribing antipsychotics in patients >55, as older adults may have increased susceptibility to the development of tardive dyskinesia even with shorter term second generation antipsychotic use.

Correlative Findings of Maternal and Placental Health with Congenital Heart Disease and Post-Operative Acute Kidney Injury

PRESENTER

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Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Purpose: Acute kidney injury (AKI) is a common complication in pediatric patients with congenital heart disease (CHD) who undergo cardiopulmonary bypass (CPB). Besides established risk factors such as time on CPB, factors affecting fetal development may contribute to the prevalence of AKI within this population. Adverse intrauterine microenvironments associated with certain maternal conditions have been shown to impact nephrogenesis. These factors also increase the risk of preterm delivery, shortening the timeframe for nephrogenesis. Thus, infants that develop in these microenvironments may be predisposed to develop AKI when subjected to secondary insults such as CPB. This study aims to examine the incidence of AKI in this patient population and determine whether maternal or fetal variables predict the development of AKI.

Methods: Retrospective review of electronic medical records of pediatric patients at Cook Children's Medical Center (CCMC) between 3/1/2022 and 4/14/2022. Inclusion criteria were as follows: patients aged 0-12 months who underwent surgical repair or palliation of CHD with care in the cardiac intensive care unit (CICU). Data collected included maternal variables such as pre-eclampsia, gestational diabetes, obesity, and smoking status; individual variables such as gestational age and other congenital factors; and surgical variables such as CPB time and average PAO₂ during CPB. AKI was determined using creatinine levels from established Kidney Disease: Improving Global Outcomes (KDIGO) criteria.

Results: Twenty patients met inclusion criteria. No statistical significance was noted between maternal and surgical variables. Twenty percent of patients developed at least Stage 1 AKI.

Conclusions: Identification of maternal risk factors for AKI in the pediatric population may allow further insight into the mechanisms of the development of AKI. Our results were impacted by the low power of our study. Inclusion of more patients into our study will positively impact our power.

IRB NUMBER

2022-058

Evaluating the properties of extracellular vesicles that are affected by diabetic keratopathy.

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School of Biomedical Sciences

ABSTRACT TOPIC

Eye / Vision

ABSTRACT

Purpose: Extracellular Vesicles (EVs) are small-sphere like structures that are released from cells. They play a role in cell-cell communication by passing genetic information from one cell to another. EVs are thought to be critical in future diagnostic targets for various diseases and conditions. Diabetic Keratopathy (DK) can often lead to different manifestations such as scarring and corneal erosions. One of the receptors that plays a role in DK is Peroxisome Proliferator-Activated Receptor alpha (PPAR α), but its functions in the cornea is unknown, including its impact on the EVs formation. Our goal was to investigate the influence of PPAR α in the production of EVs and its role in cell-cell interaction.

Methods: Healthy Corneal Fibroblasts (HCFs), Type 1 Diabetes Mellitus (T1DM), and Type 2 Diabetes Mellitus (T2DM) corneal stromal cells were cultured on polycarbonate membranes for 4 weeks at a density of 1×10^6 cell/well in culture medium + 0.5mM stable Vitamin C. The culture media were processed and analyzed with the EV-TETRA-C chips paired with the ExoView R100.

Results: The results showed that total particle counts were upregulated in HCF compared to T1DM and T2DM, but were downregulated in T1DM when compared with T2DM, during weeks 2 and 4. The total particle count for HCFs were downregulated during week 4 when compared to weeks 1 and 3. When comparing week 1 to weeks 2, 3, and 4, week 1 revealed the most significance for changes of CD63+, CD63+/CD81+, CD81+/CD9+, and CD63+/CD81+/CD9+ in HCFs and T1DMs. CD9+ showed significance during weeks 2, 3, and 4 in HCFs and T1DMs. During week 1, T2DMs had significant downregulation of CD63+, whereas CD9+, CD63+/CD9+, and CD63+/CD81+/CD9+ showed significant upregulation. During week 4, T2DMs showed significant downregulation in CD63+/CD81+ and significant upregulation of CD81+/CD9+. T1DMs were the only cell type to show significance in CD81+, which was during week 4 when compared to week 2. CD63+, CD81+, and CD9+ showed significance during week 1 and 2 in HCF, T1DM, and T2DM. The co/triple colocalizations showed significance in weeks 1, 2, and 4 in HCF, T1DM, and T2DM.

Conclusion: EV formation (based on CD63+), immune system regulation (CD81+ and CD9+), and EV particle counts showed distinct phenotypes between HCF, T1DM, and T2DM. These distinctions could potentially serve as a diagnostic tool in the future and ultimately help individuals suffering from DK.

EXTERNAL FUNDING SOURCE

NIH/NEI EY028949

Craving for Change: Culturally Tailored E-Health Intervention to Support SMART Goal Setting of Lifestyle Modifications Among Underserved Racial/Ethnic Families to Combat Obesity

PRESENTER

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Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Health Disparities

ABSTRACT

Purpose: Examine the impact of the mixed-method intervention program Family Central E-Health, utilizing interactive, culturally tailored, e-health text messaging to promote healthy lifestyle behaviors in six domains (diet, physical activity, sleep, social connection, tobacco cessation, and stress management), and combat chronic disease such as obesity among a diverse racial/ethnic and low socioeconomic sample of caregivers of overweight/obese children.

Methods: A sample of 14 adult caregivers of overweight/obese children receiving care from the University of North Texas Health Science Center Pediatric Mobile Clinic participated in the e-health intervention group (n = 8) or a control group of usual care (n = 6). The transtheoretical behavior change framework was applied to health briefs shared through a bi-directional text messaging software to customize SMART (Specific, Measurable, Attainable, Relevant, and Time) goal setting, monitor attitude (motivation and confidence), and assess behavioral change on the six domains of lifestyle modifications. The study aims were accomplished through weekly surveys throughout the study (6-month duration), at study close, 3 months post-intervention, and 6 months post-intervention.

Results: Longitudinal analysis and differences in overall means of motivation and confidence between the two groups were minimal and not statistically significant. Descriptive thematic analysis of the participants' attitudes and experiences revealed lifestyle modification domains of physical activity, social connection, and stress management with the most utilization in SMART goal setting and initiating health-promoting behaviors.

Conclusion: The Family Central E-Health intervention may be an effective and culturally sensitive model for managing and preventing obesity, and alike chronic diseases among diverse racial/ethnic and/or low socioeconomic caregivers and their families. Reduction of harmful health behaviors and initiation of health-promoting behaviors through SMART goal setting within the six lifestyle domains can help address existing health disparities. Health education and lifestyle modification interventions are important and future directions include investigating participant empowerment, resiliency, and wellbeing, especially within underserved and diverse communities.

IRB NUMBER

IRB 2019-036

Inadequate Administration of Post-Intubation Sedation and Analgesia in the Pediatric Emergency Department (PED)

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ABSTRACT TOPIC

Patient Safety

ABSTRACT

Purpose: Previous adult studies demonstrate patients in emergency departments (ED) often do not receive subsequent sedative or analgesic medications within the intubation medication's duration of action (DOA). These patients can experience pain or remember events while still being under the effects of the paralytic medication. Inadequate sedation following intubation increases rates of adverse events. The purpose of this project was to evaluate if pediatric patients intubated in the Cook Children's Medical Center ED (CCMC ED) are administered timely post-intubation sedation and analgesia.

Methods: Chart review was performed for patients intubated in the CCMC ED between June and December 2021. Exclusion criteria included intubation at another facility and charts with incomplete data. Data were collected for medications administered, time of medication administration, and intubation time.

Results: There were 106 patients intubated in the CCMC ED meeting inclusion criteria. Following intubation, 17 (16%) patients were provided with a sedative or analgesic within the DOA of the sedative or analgesic used for induction, while the remaining 89 (84%) were inadequately medicated. Thirty-one patients (29%) did receive a sedative or analgesic following intubation but not within the DOA of the initial agent. The remaining 58 (55%) patients were inadequately medicated due to a lack of medication administration before intubation, following intubation, or both.

Conclusions: The majority of intubations in the CCMC ED were not adequately medicated with sedatives and/or analgesics after intubation. Thus, these patients were at risk of suboptimal levels of sedation while paralyzed following intubation. Given the adverse effects of inadequate sedation seen in previous studies, timely administration of further sedation and analgesia after intubation may lead to decreased adverse events. Quality improvement interventions are being implemented in the CCMC ED to improve post-intubation sedation and analgesia administration.

Use of Electronic Vapor Products and its association with Feelings of Depression

PRESENTER

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School of Public Health

ABSTRACT TOPIC

General Public Health

ABSTRACT

Background: Electronic vapor products (EVPs) are the second most common form of youth substance use. EVPs were principally a means of harm reduction or cessation for smokers of cigarettes made of combustible tobacco, but this new tendency is emerging in teenagers and youths as a coping mechanism for feelings of sadness, hopelessness, stress, anxiety, or depression. There is a need for continued assessment of EVP use among adolescents. The aim of the study was to understand the epidemiology of current use of EVPs among adolescents in the U.S. and identify the association between depression and current EVPs use.

Methods: Data from the Youth Risk Behavior Surveillance System – 2019 was used. Students from grades 9 through 12 were sampled ($n = 13,677$) to obtain information on trends and sociodemographic disparities related to the use of EVPs. Variables included "During the past 12 months, did you ever feel so sad or hopeless almost every day for two weeks or more in a row that you stopped doing some usual activities" and operationalized as yes/no and, "During the past 30 days, on how many days did you use an electronic vapor product?" (Response: 0 days, 1 or 2 days, 3 to 5 days, 6 to 9 days, 10 to 19 days, 20 to 29 days, and All 30 days) and operationalized as "no" EVP use for 0 days and "yes" for other options. Demographic variables included grade, sexual orientation (sexual identity and sex of sexual contact), and race/ethnicity. The associations were analyzed using t-tests and chi-square tests, with a 0.05 level of significance.

Result: Among high school students, 32.7% (95% CI: 30.7–34.8%) reported use of EVPs. Non-Hispanic-Whites were more likely to use EVPs as compared to NH-Black, Hispanic/Latinos and Asian (p -value < 0.001). 9th graders were less likely than other grades (10th, 11th, and 12th) to be using EVPs currently (p -value = 0.001). Bisexuals (34.5%) and gay, lesbian, or bisexual (34.1%) students used EVPs at a higher rate than heterosexual students (32.1%), but there was no statistically significant difference between them. Among high school students who reported feeling sad or hopeless, 43.5% (95% CI: 40.8–46.2) were currently using EVPs, compared to 73.5% (95% CI: 71.6 - 75.4) who did not feel sad or hopeless and were not using EVPs currently.

Conclusion: A difference was observed in the use of EVPs based on race/ethnicity and grade level, while no significant differences were observed for EVP use and sexual identity. Moreover, feeling sad or hopeless was associated with the current use of EVPs. Additional research is needed to disentangle the relationship between EVP use and mental health among adolescents, especially as mental health is a growing concern among youth in the United States.

IRB NUMBER

2020-092

Proteomic Profiles of Tau Positivity among an Ethnically Diverse Cohort: An HABS-HD Study

PRESENTER

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Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Aging / Alzheimer

ABSTRACT

Purpose: PET tau has been well documented to precede Alzheimer's Disease (AD) and mild cognitive impairment (MCI). In the pursuit of increasing the accessibility of AD diagnosis, studies have shown that blood biomarkers including ptau181 trend with PET tau in Non-Hispanic Whites (NHW). Current literature shows limited studies on Mexican Americans (MA) who have a higher risk of AD at earlier ages. MA populations have shown to have significantly higher burden of blood biomarkers/metabolic markers that are associated with MCI including ptau181, insulin, and glucagon, but lower in plasma amyloid. Our aim is to look at the utility of AT(N) (amyloid, tau, neurodegeneration) biomarkers in the detection of PET Tau positivity status among MA and NHWs

Methods: Data were analyzed from n=401 participants (Total sample [n=21 Tau positive, n=380 Tau negative]; Black [n=11 Tau positive, n=216 Tau negative]; Hispanic [n=5 Tau positive, n=50 Tau negative]; Non-Hispanic whites [n=5 Tau positive, n=114 Tau negative]) from a community-based study of brain aging the Health and Aging Brain Study- Health Disparities (HABS-HD). HABS-HD participants underwent a clinical interview, neuropsychological testing, blood draw, functional medical exam and neuroimaging as a part of the study's protocol. Plasma blood biomarkers used in this study consisted of Amyloid Beta 40, 42, Total Tau, Ptau181 and NFL derived using Single Molecule Array Technology (SIMOA) on an HDX platform. PET Tau positivity status was determined based on a clinical read. Support Vector Machine (SVM) models were used with plasma ATN biomarkers as predictors of PET Tau positivity status (Positive; Negative). SVM models were run with 10 times, five-fold repeated cross-validation and included models with and without demographics.

Results: In the total sample, ATN biomarkers produced an area under the curve (AUC) of 98% with a sensitivity [SN] of 100% and Specificity [SP] of 73% for distinguishing PET Tau Positive cases from PET Tau Negative. The same ATN biomarkers produced for Black participants an AUC of 98% (SN=100%, SP=80%), for Hispanic participants an AUC of 100% (SN=100%, SP=100%), and for Non-Hispanic White participants an AUC of 98% (SN=100%, SP=70%). The addition of demographic variables of age, gender, and education produced a slight increase in the AUC for both black and non-Hispanic white participants by 1%. The top biomarkers were shown to vary by race and ethnic group.

Conclusions: The results further support the AT(N) biomarkers as a viable method in predicting AD/PET tau positivity, as well as confirming that ptau181 has heavy influence in MA. The varying results of top biomarkers between groups confirm that ethnic background plays a strong role in biomarker profiles contributing to AD. An interesting finding was that demographic factors were ranked higher in black participants in distinguishing PET Tau positivity as compared to NHW and MA. Future work should expand on ptau181 value in relation to MCI state/AD progression in MA.

EXTERNAL FUNDING SOURCE

National Institute of Aging of the National Institutes of Health under Award Numbers: R01AG054073 and R01AG058533, P41EB015922 and U19AG078109

IRB NUMBER
2016-128

Addressing Age-Appropriate Cancer Care for Adolescents and Young Adults

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ABSTRACT TOPIC

Cancer

ABSTRACT

Purpose: Adolescents and young adults (AYAs), normally defined as patients between 15 and 39 years of age, are often lost in the healthcare system that concentrates primarily on pediatric and adult cancers¹. AYA cancer presentation can differ and treatments are less established compared to pediatric and adult cancers². Many AYA patients are treated in pediatric facilities, which can lead to age-appropriate needs not being met. The goal of this project is to examine the AYA patient experience and assess if AYAs receive age-appropriate care at Cook Children's Hospital in Fort Worth, Texas.

Methods: Patient reported outcomes surveys were administered to AYA patients diagnosed between 1/1/2016 and 1/1/2020 with at least one of the following cancers: acute lymphoblastic leukemia, acute myeloblastic leukemia, Hodgkin lymphoma, non-Hodgkin lymphoma, testicular germ cell tumor, ovarian germ cell tumor, or sarcoma. Eighty-five patients were eligible to participate in the study. The survey and chart review included information pertaining to demographics, socioeconomic factors, treatment, and diagnosis-related questions.

Results: Seventeen patients have completed the survey. Patients rated age-appropriateness and quality of care on a five-point Likert scale. On average, patients rated the following aspects of their care as highly satisfactory for age-appropriateness: communication with medical staff ($M = 4.80$, $SD = 0.40$), staff recognition of life events ($M = 4.71$, $SD = 0.46$), provider attitude ($M = 4.86$, $SD = 0.37$), and support provided to their families ($M = 4.82$, $SD = 0.40$). Although still highly rated, the physical environment ($M = 4.38$, $SD = 0.91$) and recreational activities ($M = 4.35$, $SD = 0.87$) were reported to be slightly lower than the other categories for age-appropriateness.

Conclusions: AYA patients face unique challenges related to their cancer presentation and psychosocial needs. Interactions between patients, their physicians, and their environment all contribute to the patients' treatment experience and providing comprehensive, age-appropriate care is important. Overall, patients reported receiving age-appropriate care at Cook Children's Hospital but reported slightly less satisfaction with the facilities and age-related activities. Based on these findings, continuing to establish age-appropriate resources and physical spaces for AYA patients can greatly enhance their quality of care and treatment experience. Beginning in 2016, Cook Children's AYA clinic had already initiated changes to establish more supportive resources for AYAs, including creating and renovating a designated AYA lounge and implementing more programmatic psychosocial care through psychological interventions and AYA-specific support groups.

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IRB NUMBER

2019-017

Redox Profiling of NAD Kinase in Acute Kidney Injury

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ABSTRACT TOPIC

Pharmaceutical Sciences

ABSTRACT

Background: Acute kidney injury (AKI) is a common clinical disorder in hospitalized patients and is characterized by a rapid decline in kidney function reflected by a rapid decrease in glomerular filtration rate and a decrease in urine output or anuria. Besides supportive therapy for AKI, there are no effective treatments. Therefore, further understanding of the underlying pathology of this disorder is needed.

Purpose: Oxidative stress has been postulated to be one of the major mechanisms underlying AKI; and NAD kinase (NADK), the sole enzyme making NADP from NAD, is a key player in oxidative stress and redox imbalance. Nevertheless, the role of NADK in AKI remains unknown. In this study, we propose to investigate the redox profile of cytosolic NADK in mice models.

Methods: AKI-induced mice model by a single intraperitoneal injection of folic acid (250 mg/kg). Three days after the folic acid injection, mice will be euthanized followed by the collection of blood and the kidneys. Kidney function will be measured by quantitation of blood urea nitrogen, serum uric acid, and creatinine. For NADK profiling, we will analyze NADK protein expression, enzymatic activities, and NADK protein oxidative modifications. NADK protein oxidation will be quantitated by Western blot detection of protein carbonyls labeled with biotin-linked reactive aldehyde probes.

Results: The NADK protein oxidation is expected to increase upon AKI induction concurrent with a decreased enzymatic activity of NADK. Additionally, we expect to observe changes in NADK protein expression in AKI.

Conclusion: the results of our study will provide insights into the role of NADK in AKI and may also indicate that NADK could be a potential target for future prevention and therapy for acute kidney injury.

EXTERNAL FUNDING SOURCE

PDRT

Development of Reconstituted High-Density Lipoprotein Nanoparticles Utilizing Fluorescence Resonance Energy Transfer for Ocular Applications

PRESENTER

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ABSTRACT TOPIC

Eye / Vision

ABSTRACT

Purpose: Macular degeneration and glaucoma are considered age-related degenerative eye diseases. Both conditions can lead to vision change and loss. While glaucoma and macular degeneration have similarities, they affect different eye regions and require targeted drug-delivery systems. Significant limitations of current ocular therapies are poor bioavailability and delivery barriers in the eye. Developing an efficient ocular delivery system is thus critical to improving the efficacy of therapeutic agents. Specifically, reconstituted high-density lipoprotein (rHDL) mimics the structure and function of endogenous human plasma HDL and thus presents a non-toxic therapeutic strategy for delivering various drugs and imaging agents to ocular tissue. Moreover, rHDL nanoparticles (rHDL NPs) are ideal for transporting lipophilic therapeutic agents and imaging dyes since they are small in size, non-immunogenic, can circulate in the body fluids for an extended time, and have specific receptor-protein interactions to release their lipophilic payloads. Our study aims to employ a reconstituted rHDL drug delivery vehicle that mimics the structure and function of endogenous human plasma HDL and offers a novel strategy for the delivery of drugs and imaging agents to the eye.

Methods: A stable rHDL-payload complex (rHDL NPs) was prepared by combining lipophilic fluorescent dyes using phosphatidylcholine and apolipoprotein A-I (Apo A-I) via a novel preparation method. Dual fluorescent rHDL NPs have been used as Förster resonance energy transfer (FRET) probes and were assessed by dynamic light scattering (DLS), spectrophotometry, and fluorescence spectroscopy.

Results: Dual fluorescence rHDL NPs were generated with 64.4% and 79.2% encapsulation efficiency for the donor and acceptor fluorophores, respectively. rHDL NPs were found to have a polydispersity index (PDI) of 0.302 ± 0.023 , an average size of 10.96 ± 1.47 nm, and a zeta potential of -7.65 ± 0.63 mV. The fluorescent signals were characterized by anisotropy measurements while the FRET signal was detected by the change in fluorescence lifetime between the donor and acceptor fluorophores.

Conclusions: A stable rHDL NP formulation that includes a FRET pair was successfully prepared through an optimized protocol. The rHDL NPs can be utilized for biodistribution studies and dynamic kinetic characterization in vivo to assess the efficacy of drug-loaded rHDL NPs for the treatment of ocular degenerative diseases such as glaucoma and macular degeneration.

Hemodynamic Responses to Oscillatory Thigh Cuff Inflations

PRESENTER

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COLLEGE/SCHOOL

School of Biomedical Sciences

ABSTRACT TOPIC

Integrative Physiology

ABSTRACT

Background: In the clinical setting, individuals have varying tolerance to hypovolemia induced by blood loss. Experimental generation of 0.1 Hz oscillations (~10-s cycle) in arterial pressure and cerebral blood flow via oscillatory lower body negative pressure (OLBNP) increases tolerance to this simulated hemorrhage, and protects cerebral tissue oxygenation. However, use of OLBNP as a method of inducing hemodynamic oscillations in the clinical setting is limited as: 1) it is a large and cumbersome technique, and; 2) it induces central hypovolemia, which would only worsen the magnitude of hemorrhage. In this study we evaluated a more clinically applicable method of inducing 0.1 Hz oscillations in arterial pressure and cerebral blood flow, using intermittent inflation of bilateral thigh cuffs. We *hypothesized* that the amplitude of arterial pressure and cerebral blood flow oscillations at 0.1 Hz would increase in response to repeated thigh cuff inflations at 0.1 Hz when compared with a baseline control condition.

Methods: Ten healthy human subjects were tested (6 male, 4 female; 26.8 ± 4.1 y). Middle cerebral artery velocity (MCAv) was measured via transcranial doppler ultrasound, arterial pressure was measured via finger photoplethysmography, and end tidal CO₂ (etCO₂) was measured via capnography. Following a 10-min baseline period, intermittent thigh cuff inflations at 0.1 Hz and 230 mmHg (5-s inflation, 5-s deflation) were performed for 10-min ("oscillations"). 0.1 Hz oscillatory amplitude of mean arterial pressure and mean MCAv were quantified using Fast Fourier transformation during the last 5-min of baseline and the oscillatory period, and compared via two-tailed paired t-tests.

Results: The amplitude of 0.1 Hz oscillations increased during the oscillatory period vs. baseline for mean arterial pressure (baseline: 1.7 ± 1.0 mmHg² vs. oscillations: 9.0 ± 6.2 mmHg²; $P = 0.004$) and mean MCAv (baseline: 1.1 ± 0.6 (cm/s)² vs. oscillations: 3.4 ± 3.1 (cm/s)²; $P = 0.04$). Absolute mean arterial pressure was similar between baseline and the oscillatory period (baseline: 97.2 ± 8.1 mmHg vs. oscillations: 99.1 ± 15.0 mmHg; $P = 0.54$), but absolute mean MCAv was lower during the oscillatory period (baseline: 61.7 ± 14.6 cm/s vs. oscillations: 53.2 ± 13.1 cm/s; $P = 0.02$). This reduction in mean MCAv was most likely due to hypocapnia (indexed by etCO₂) induced by pacing the breathing of all subjects at ≥ 10 breaths/min (baseline: 33.2 ± 4.8 mmHg vs. oscillations 27.2 ± 4.5 mmHg; $P = 0.005$).

Conclusions: Intermittent thigh cuff inflations at 0.1 Hz induced 0.1 Hz oscillations in both arterial pressure and cerebral blood flow when compared to baseline. These findings indicate that intermittent thigh cuff inflations could be developed as a method to induce pulsatile perfusion as a potential new therapy for individuals experiencing major blood loss.

EXTERNAL FUNDING SOURCE

American Heart Association #19TPA34910073; UNTHSC 2021 Physiology and Anatomy Seed Grant

IRB NUMBER

2021-067

Therapeutic Effects of Bone Marrow Aspiration Injection for Refractory Osteoarthritis of the Knee: A Case Series

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Rehabilitative Sciences

ABSTRACT

Case Diagnoses: This case series includes 3 cases of patients with refractory osteoarthritis of the knee who have received bone marrow aspirate concentrate injections in office.

Case Description: The case series examines the patient's perception of pain, symptoms, activities of daily living, sports/recreation, and quality of life following bone marrow aspirate concentrate injections used to treat osteoarthritis of the knee. Osteoarthritis is a challenge to treat and can be an indication for knee replacement when pain persists after treatments with available therapies. Bone marrow aspirate concentrate injection is a type of therapy that uses regenerative cells found in the patient's own bone marrow. Bone marrow is extracted from the pelvis of the patient, then placed into a centrifuge to separate regenerative cells from the other blood products. The bone marrow is then injected into the knee.

The Knee Injury and Osteoarthritis Outcome Score (KOOS) was used to evaluate each patient's perception of pain, symptoms, activities of daily living, sports/recreation, and quality of life. The survey was administered retrospectively, and patients were asked to complete the survey based on their perceptions before and after receiving the injection. The score is calculated on a scale of 0 to 100, with 0 representing extreme problems and 100 representing no problems.

Results/Discussion: The KOOS scores for each patient were calculated before the injection and after the injection. On average, the results of the case series showed 53% decrease in pain, 70% decrease in symptoms, 36% improvement in activities of daily living, 150% improvement in sports/recreation, and 132% improvement in qualities of life. All 3 cases reported an increased score in each of the 5 measured outcomes. While this is a small case series with only 3 cases, it shows promising results. These patients have also shown clinical improvement following the injection, which correlates well with the improvements in KOOS score. The findings are relevant, as bone marrow aspirate concentrate injections could be an option for patients who desire to avoid knee replacement with refractory osteoarthritis of the knee.

Conclusions: Based on the results of the case series, bone marrow aspirate concentrate injections may be an appropriate recommendation for patients with refractory osteoarthritis of the knee. More research is indicated in this regard. We are planning to investigate these results further with a cross-sectional descriptive design survey.

Hyperemesis Cannabinoid Syndrome Chart Review

PRESENTER

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Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Community Medicine

ABSTRACT

Purpose: The purpose of this research study is to determine if the combination of Compazine and Benadryl is a superior method of treatment for patients who present with nausea and vomiting symptoms due to a diagnosis of Hyperemesis Cannabinoid Syndrome. Based on patient charts from a regional hospital emergency department in Oklahoma, an analysis was performed to determine if this combination of medications is more effective in quickly reducing the nausea, vomiting, and other symptoms associated with cannabis use.

Methods: An agreement was created between a regional hospital in Duncan Oklahoma and The University of North Texas Health Science Center which allowed students at the Texas College of Osteopathic Medicine to review and analyze a total of 75 patients' charts from the regional hospital. IRB approval was obtained for this project. The chart review process consisted of evaluating the patient's age, chief complaint, abnormal lab values, history of present illness (HPI), and medications administered in the emergency department. The important variables that assisted in this study were drug screening values, and the medications administered. The main outcome for which statistical efficacy of drug treatment was measured by duration of stay in the emergency department and whether or not an additional dose of medication was given.

Results: This chart review showed that the 12 patients that used the Benadryl and Compazine combination had a decreased time spent in the emergency department by an average of 56 minutes when compared to 38 patients who received alternative medications. The average time spent in the emergency department for those who received Benadryl and Compazine was 127 minutes vs the average time spent for those using an alternative medication was 183 minutes. The typical dose was 50 mg of Benadryl and 10 mg of Compazine. While using an ANOVA statistical analysis these doses showed a significantly statistical relationship by decreasing provider-to-discharge time with a p value of 0.012. It was also found while using a logistic regression analysis that those patients who received this combination as their initial dose were less likely to receive a second dose. This relationship also was statistically significant with a p value of 0.005. It was also noted in the logistic analysis that females were more likely to receive a second dose when compared to men. This relationship also showed a relationship with significance and a p value of 0.037.

Conclusions: The findings from this study recommend and encourage providers who are in a setting where Hyperemesis Cannabinoid Syndrome is prevalent to consider the medication combination of 50 mg of Benadryl and 10 mg of Compazine when providing treatment. There may be multiple ways to alleviate the discomfort and symptoms that patients may present with, however the combination stated above appears most effective to reduce provider-to-discharge time 56 minutes and eliminate second doses of medication based off of the data reviewed from the charts provided.

Analyzing the Effectiveness of Wellness Resources Provided for Medical School Students

PRESENTER

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ABSTRACT TOPIC

General Public Health

ABSTRACT

Background: There exists well-documented evidence demonstrating that physicians and medical school students practicing preventative lifestyles are more likely to promote prevention to their patients, which is especially important given the escalation of chronic conditions in the United States. The arduous nature of medical school challenges the student's ability to initiate or sustain healthy lifestyle habits even with the various resources available. Several interventions have been created to address medical student wellness; however, there remains a discrepancy in the literature regarding the effectiveness of these resources long-term. Student burnout, which is defined as emotional exhaustion, is still a prevalent issue in the medical profession. Medical schools must emphasize the importance of program evaluations to address the issues that contribute to poor medical student wellbeing.

Goal: To create a simple and inexpensive survey that can track the effectiveness of wellness resources that medical students use over the long-term.

Methods: A survey that could be implemented at a single point in time or a yearly fashion was developed. The survey was created to collect information on wellbeing markers, resources used, and basic demographic information. The wellness questionnaires used were the WHO-5 Wellbeing Index, Modified Maslach Burnout Inventory (M-MBI), International Physical Activity Questionnaire Short Form (IPAQ-SF), Single Item Sleepy Quality Scale (SQS), and the nutritional questionnaire section from the American Association of Family Medicine's (AAFP) Lifestyle Assessment Form. The effectiveness of the wellness resources will be assessed in three ways. First, a question will be asked regarding the user's opinion about the value of the resource to their wellness. Second, the students with poor wellbeing will be identified, and the prevalence of usage of that resource will be documented. Third, the wellbeing markers will be compared to students who use the resource versus students who do not use the resource. Propensity score matching will be used to reduce the confounding variables associated with demographic information and academic factors (average grades, amount of time spent studying in a day, etc.). The data will be collected through Qualtrics and analyzed using IBM SPSS Version 29.0.

The first round of the survey will be distributed to first- and second-year medical students between the dates of February 1st -15th. Subjects will be recruited through verbal announcements at the end of mandatory lectures.

Discussion and Future Implications: Due to the numerous wellness programs at medical schools, it can be difficult to assess their efficacy because of the time and resources needed. The survey design is built to help medical schools track the performance of their wellness resources in a quick and affordable manner. The data from this survey can help guide decisions about how medical schools can improve the quality of their wellness resources. It is important for medical schools to continue to evaluate their wellness initiatives over the long-term so that they can adapt to the evolving needs of their students.

IRB NUMBER

1996167-1

A Rare Case of Synchronous Familial Adenomatous Polyposis and Endometrial Carcinoma

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ABSTRACT TOPIC

Cancer

ABSTRACT

Familial adenomatous polyposis (FAP) is a rare autosomal dominant disease characterized by numerous polyps in the colon. It is caused by a germline mutation of the adenomatous polyposis coli (APC) gene. Patients have a guaranteed risk of having colorectal cancer and can also develop multiple extra-intestinal manifestations, including cutaneous lesions, brain tumors, desmoid tumors, osteomas, and thyroid cancer. Thus, extensive screenings for both colorectal cancer and the manifestations mentioned above are recommended on a frequent basis. Ovarian and endometrial malignancies are not known to be associated with FAP. Here, we present a case of synchronous FAP and endometrial carcinoma.

A 51-year-old female with family history of autosomal-dominant-patterned colon cancer, subtotal colectomy at 17 due to multiple polyps, ileostomy with a J-pouch at 35, and recent upper endoscopy suspicious for ampullary adenoma, presented with one-month history of fatigue and night sweats. Review of system was positive for heartburn and easy bruising. The patient did not have formal genetic testing. She has close follow-ups with yearly surveillance upper GI endoscopy (EGD), flexible sigmoidoscopy, and thyroid ultrasound. At 44, she underwent dilation and curettage due to menorrhagia; samples revealed endometrial cancer, which led her to undergo a bilateral salpingo-oophorectomy.

Reports of endometrial and ovarian cancers in FAP are rare. In another case, a 57-year-old female with FAP was found to have bilateral ovarian microcystic stromal tumors (MCSTs), papillary thyroid carcinoma, and endometrial carcinoma. Histopathology from the MCSTs and thyroid was positive for beta-catenin, an important marker in FAP. MCST is a rare subtype of ovarian cancer that has been found concurrent with FAP on several occasions. Although our patient did not have genetic testing, the large number of polyps and autosomal dominant pattern of inheritance are consistent with FAP, rather than Lynch or MUTYH-associated polyposis (MAP) syndromes, which could present similarly. It would be important to look at histopathology in our patient to determine whether there is overlapping genetic expression with FAP. Nevertheless, our case represents another rare instance of co-occurrence of endometrial cancer and FAP. More research needs to be done to explore the potential association between endometrial/ovarian malignancies and FAP. Holistic care is an integral part of osteopathic medicine, thus it is important for osteopathic physicians to provide well-rounded care for every patient. This case gives evidence that there might be benefits in future screening of endometrial/ovarian cancer in patients with FAP that could potentially increase life expectancy in these patients.

Factor VII Deficiency: A Diagnostic Dilemma

PRESENTER

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ABSTRACT TOPIC

General Medicine

ABSTRACT

Background/Introduction: Factor VII deficiency is a rare bleeding disorder, estimated to affect 1 in 300,000 to 500,000 individuals in the general population. The disease is associated with autosomal recessive inheritance or could be acquired. Clinical manifestations range from asymptomatic to severe, life-threatening bleeds. There is poor correlation between the level of factor VII and the severity of symptoms, thus making diagnosis and management a challenge. Here we present a case of incidental finding of elevated international normalized ratio (INR) and found to have factor VII deficiency.

Description of Case: Patient is a 74 year-old male with a history of CREST, pulmonary fibrosis, Raynaud's Disease, COPD, referred by his cardiologist for recurrent, unresolved pericardial effusion. Compared to his previous echocardiogram, the pericardial effusion is now circumferential and enlarged, leading to an immediate need for pericardiocentesis. Due to the urgency of the patient's condition and lack of bleeding history, we proceeded with the procedure without obtaining INR. CT scan taken during the course of hospitalization revealed a cavitory lesion of the lung, which prompted planning of a CT biopsy with Interventional Radiology. At this time, INR was 1.8 (Ref 0.8-1.1) with normal PTT and there was no reported anticoagulants use. Due to increased INR, ultrasound of the liver was done and showed no features of fibrosis. Vitamin K was preemptively administered without improvement of INR. Mixing study resulted in correction for PT and the ensuing factor assay revealed a deficiency of factor VII. FFP was administered prior to other procedures.

Discussion/Conclusion: Factor VII deficiency is an extremely heterogeneous disorder with regard to clinical presentation, sites, and severity of bleeding. Symptoms exist on a continuum of severity, ranging from epistaxis, gum bleeds, easy bruisability, and menorrhagia to hemarthrosis, gastrointestinal and intracranial bleeds (3). Despite being a prime protein in the coagulation system, patients mostly present with mucocutaneous bleeding, which sometimes can be confused with platelet-related bleeding and hence require thorough evaluation (2). Most patients with Factor VII deficiency are diagnosed incidentally with abnormal PT, which can then be confirmed by one-stage PT-based assay for factor VII level. However, PT and factor VII levels do not correlate with the severity of bleeding symptoms and future risk of bleeding (3). In addition, previous studies have shown a marked phenotype-genotype disparity among patients (4). This could be attributed to various genetic polymorphisms of the gene or environmental factors, such as pregnancy, increasing age, obesity, underlying disorders, and vitamin K deficiency. The lack of correlation also poses a challenge for management strategies. Treatment cannot depend on the level of Factor VII alone, but also on severity of disease, risk of certain medications or procedures, and patient's age and comorbidities. Several modalities have been used as treatment, such as recombinant activated factor VII (rFVIIa), plasma-derived factor VII, fresh frozen plasma, and IV prothrombin complex concentrates (5).

Neuroprotection of Rodent Retinal Ganglion Cells using Hybrid Molecule SA-10

PRESENTER

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School of Biomedical Sciences

ABSTRACT TOPIC

Eye / Vision

ABSTRACT

Purpose: Oxidative stress is the imbalance between the activity of antioxidants and free radical production, which has been shown to be associated with glaucomatous retinal ganglion cell (RGC) degeneration. In this study, we aimed to promote RGC survival by treatment with SA-10, a second-generation hybrid molecule with nitric oxide donating and sulfone reactive oxygen species (ROS) scavenging moieties *in vitro* and *ex vivo* following oxidative stress-induced injury.

Methods: Endothelin-3, a vasoactive peptide, was used to induce oxidative stress *in vitro* in rat primary RGCs (n=3 biological replicates) and *ex vivo* in C57BL/6J mice retinal explants (n=8-9 explants/group). Primary RGCs were isolated from Sprague Dawley rat pups (post-natal days 4-7) and cultured for seven days with neurotrophic factors to allow for neurite outgrowth. The RGCs and retinal explants were pretreated with vehicle (DPBS) or SA-10 [10 μ M] for 30 minutes, following which ET-3 treatment [100 nM or 400 nM] was carried out for 1 hour. CellROX™ Green was then used to stain for ROS produced by the cells, and the integrated density was analyzed. Analysis of Variance (ANOVA) or nonparametric Kruskal-Wallis was performed for all experiments.

Results: In primary RGCs, ET-3-mediated ROS production decreased by 25.9% (p<0.01) following SA-10 treatment compared to the vehicle. In mice, retinal explants, 400 nM ET-3 induced a 24.4% increase in ROS production compared to the vehicle [0 nM ET-3]. With the SA-10 treatment, the ROS production was decreased by 14.74% (p<0.001) in the ET-3 and SA-10 treated group compared to the ET-3-only treated group.

Conclusion: SA-10 effectively protects rodent RGCs *in vitro* and *ex vivo* from ET-3-mediated oxidative stress.

EXTERNAL FUNDING SOURCE

NEI Grant EY029823

The one where all paths point to ITP

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

General Medicine

ABSTRACT

Background: Immune Thrombocytopenic Purpura (ITP) is an autoimmune condition where antibodies against platelets can eventually lead to sequestration by the spleen and liver inducing a thrombocytopenia. Although primary idiopathic ITP is most common, secondary ITP associated with a trigger such as malignancy, infection, and drugs have also been reported.

Case Description: We report a case of a 66 year old male status post two years of chemoradiation for invasive squamous cell carcinoma of oropharynx. This is a unique case where our patient presented to the ED with vomiting, generalized weakness, and a low grade fever. Initial physical exam was negative for mucosal bleeding and petechial rash. Initial labs indicated severe thrombocytopenia with platelets as low as 36,000/UL, AKI with creatinine of 3.73, and elevated LFTs. There was concern for TTP vs. ST-HUS vs Tick borne illness given the extent of thrombocytopenia and subsequent upper extremity petechiae appearing a few days into the patient's admission. However ADAMTS13 and coagulation function were normal, our patient was shiga-toxin negative, and Rickettsia serology negative. The patient was found to have coagulase negative staphylococcus bacteremia which was successfully treated with 7 days of doxycycline. Bone marrow biopsy was notable for schistocytes suspicious for a low grade hemolytic process with no evidence of hematopoietic neoplasia or myelodysplasia. Platelets did not initially improve with blood transfusions remaining 30,000-50,000. In concordance with the transfusions oral prednisone was given, however thrombocytopenia was refractory to this therapy as well. Lastly plasma exchanges were continued and Rituximab once weekly for three weeks was started; after the first dose our patients' platelets began to improve. Platelet count rose above goal of 150,000 and the patient was discharged with plan for once weekly Rituximab infusions for four weeks outpatient and oral Prednisone 40 mg daily.

Discussion: ITP is usually found in females and is mostly asymptomatic. When symptoms appear they are characterized by things such as petechiae, purpura, gingival bleeding. The diagnosis is one of exclusion where patients present with thrombocytopenia and no other abnormalities. Treatment options for first line refractory ITP involve identifying and treating the underlying cause as well as interventions with thrombopoietin receptor agonists, Rituximab, and even splenectomy. These solutions can prove to be expensive and each provides their own risks. Cases such as this emphasize the importance of broadening differential diagnosis when presentation is not typical and initial treatments seem to be refractory.

RETROSPECTIVE ANALYSIS OF A HYPERGLYCEMIA SCREENING PROTOCOL IN PEDIATRIC PATIENTS WITH ALL AND LLY

PRESENTER

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ABSTRACT TOPIC

Cancer

ABSTRACT

Background: Approximately 4-35% of pediatric patients undergoing treatment for acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LLy) develop drug-induced hyperglycemia. Hyperglycemia is associated with poor outcomes including increased infections, weight loss, diabetic ketoacidosis, and greater mortality. However, no guidelines for identifying drug-induced hyperglycemia currently exist and the time course of hyperglycemia development remains relatively uncharacterized past induction therapy.

Objective: The present study aims to evaluate a hyperglycemia screening protocol (HSP) that was implemented to identify hyperglycemia more promptly and to further describe the time course of hyperglycemia during ALL and LLy therapy.

Design/Methods: A retrospective medical records review of 154 patients diagnosed with ALL or LLy at Cook Children's Medical Center between March 2018 and April 2022 was performed. The HSP included more frequent blood glucose monitoring, criteria for removal of dextrose from IV fluids, consultation with other providers (case management, patient educator, registered dietitian), and robust care coordination between the hematology-oncology and endocrinology teams. Predictors of hyperglycemia were examined with univariate Cox regression.

Results: The HSP was ordered for 88 (57%) of the patients. Fifty-four (35%) patients developed hyperglycemia: 28 (52%) during induction therapy and 26 (48%) patients after induction therapy. Enrollment in the HSP increased the likelihood of a hyperglycemia diagnosis compared to those not enrolled (41% vs. 27%, HR=1.76, $p<0.050$). Age ≥ 10 years was an independent predictor of hyperglycemia development (HR=3.72, $p<0.0001$). Patients who did not gain weight during the induction period were more likely to also have hyperglycemia (weight loss: HR=5.42, $p=0.001$; weight steady: HR=3.48, $p=0.012$). The development of pancreatitis was also associated with drug-induced hyperglycemia (HR=2.45, $p=0.007$). Blood glucose values were significantly more likely to be ≥ 200 mg/dL during days 5-8 of induction therapy compared to days 1-4 (29% vs. 10%, OR=4.18, $p<0.001$). Compared to blood glucose measurements taken in the morning (10%), values were more likely to be ≥ 200 mg/dL when acquired overnight (20%, OR=4.42, $p<0.001$), in the afternoon (16%, OR=2.34, $p=0.011$), and in the evening (38%, OR=10.57, $p<0.001$).

Conclusion: Implementation of the HSP helped detect hyperglycemia more frequently in enrolled patients compared to controls and readily identified individuals at the greatest risk of developing hyperglycemia. These findings highlight a population of patients that develop hyperglycemia past induction therapy and give guidance on the timing of continued blood glucose monitoring in at-risk patients.

IRB NUMBER

2022-009

The Neuroprotective Effects of Hybrid SA-10 Nanoparticles in a Glaucoma Mouse Model of Retinal Ischemia/Reperfusion Injury

PRESENTER

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ABSTRACT TOPIC

Eye / Vision

ABSTRACT

Purpose: The progression of glaucoma is largely dependent on the gross functionality of retinal ganglion cells (RGCs), which transmit visual signals to the brain. Current treatments for glaucoma focus on lowering intraocular pressure (IOP), yet other risk factors such as oxidative stress and poor blood perfusion also contribute to RGC damage. Furthermore, no treatments exist which revitalize dysfunctional RGCs. One promising neuroprotective agent is SA-10, a hybrid compound with reactive oxygen species (ROS) scavenging sulfone moiety and perfusion-enhancing nitric oxide (NO) donor moiety. This study aims to investigate the *in vivo* neuroprotective effects of the nanoparticle (NP) formulation of SA-10 (SA-10-NPs) on RGCs in an acute rodent model of ischemia/reperfusion (I/R).

Methods: C57BL/6J mice were separated into 3 groups (n= 5-8 per group): Sham control, 1% Blank NPs-treated, and 1% SA-10-NPs. Aside from sham, all groups received 4 μ L of different blinded topical pre-treatments: poly(lactic-co-glycolic-acid) (PLGA) nanoparticles suspended PBS for the Blank-NPs group, and 1% SA-10 loaded in PLGA for the SA-10-NPs group. Besides the sham, all groups had their anterior chambers cannulated with normal saline to achieve an elevated IOP of 120 mmHg for 60 minutes. After I/R all groups received 4 μ L of their respective treatments 3 times a week over 14 days. Pattern electroretinogram (PERG) and pattern visual evoked potential (PVEP) tests were independently performed both prior to I/R insult (baseline) and after completing the treatment regimen. Mouse eyes were then enucleated. Their retinas were stained with an RNA binding protein with multiple splicing (RBPMS) RGC-specific marker for quantification of cell survival. Parametric Analysis of Variance (ANOVA) and its non-parametric equivalent, the Kruskal-Wallis test, were performed for statistical analysis.

Results: I/R injury (Blank-NPs-treated) produced a 52.1% decline ($p<0.01$) in PERG and a 17.9% decreasing trend in PVEP amplitudes as compared to sham. SA-10-NPs prevented this decline by a trend of 33.5% and 14%, respectively. I/R injury (Blank NPs-treated) caused a 33% decrease ($p<0.01$) in RGC survival in the inner retina in comparison with sham control, which was alleviated with the SA-10-NPs treatment by 33.4% ($p<0.001$).

Conclusions: SA-10-NPs enhanced RGC survival and function following ischemia-induced damage in the mice I/R model and have the potential to be used as a neuroprotective therapy for glaucoma.

EXTERNAL FUNDING SOURCE

NEI Grant EY029823

IACUC NUMBER

IACUC-2019-0036

Relationship between Inflammatory Markers (IL-6, IL-10, TNF-alpha, CRP), Physical Performance Measures and Ethnic Differences

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Neuroscience

ABSTRACT

Background: Hispanics remain highly underrepresented in Alzheimer's Disease (AD) research. This study explores the possible relationship between the inflammatory markers commonly studied in AD and Physical Performance Tests for gait and mobility in patients self-identified as Mexican American and Non-Hispanic White. In addition, this study will elaborate on the variations found in this biomarker-functional measure relationship among different ethnic groups.

Methods: Publicly available data were analyzed on n=1705 participants (n=890 Mexican Americans; n=815 Non-Hispanic Whites) from the Health and Aging Brain Study- Health Disparities (HABS-HD). Participants completed a full study protocol including a clinical interview, cognitive testing, blood work, and functional exam. Targeted proteomics were analyzed on a Meso Scale Discovery Platform using ECL techniques and included markers of inflammation (CRP, IL6, IL10, TNF α). The functional testing included the following measures: Tug Time Test, Balance Test, Gait Speed Test, and Chair Stand Test. Linear regression models were run with select inflammatory markers (CRP, IL6, IL10, and TNF α) as the independent variables and the different musculoskeletal functional tests as the dependent variables. The analyses were conducted in a split method to compare the output by ethnic group (Hispanic and Non-Hispanic White).

Results: This study showed that physical performance measures had a more direct relationship with the inflammatory markers in the Mexican American group as compared to the Non-Hispanic White group. Among Mexican Americans, all physical performance measures were found to be significantly related to IL-6 and TNF α while Gait speed was found to be significantly related to CRP, IL-6, IL-10 and TNF α . Although non-significant, there was a trend for the relationship between IL-10 with both Tug Time and Total Balance Test. Among Non-Hispanic Whites, IL-10 was found to be significantly related to the functional measure of Total Balance while TNF α was significantly related to the Chair Standing Test. IL-6 was found to be significantly related to all physical performance measures. CRP was not found to be related to any of the functional/physical performance tests.

Discussion: The results demonstrate differences in the relationship between inflammatory markers and physical performance measures across ethnic groups. Our findings support the research community's need to focus more on differences among ethnic groups. Surprisingly, CRP was not found to be related to physical performance measures (in the Non-Hispanic White group) despite being a widely used inflammatory marker in clinical settings. To examine the potential utility for understanding the impact of inflammatory markers on functional abilities and the potential application for clinical use, future work is planned to look at this relationship among those with AD.

IRB NUMBER

2016-128

Probable genetic vulnerabilities that can account for the pathophysiology of cerebral palsy

PRESENTER

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COLLEGE/SCHOOL

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ABSTRACT TOPIC

Neuroscience

ABSTRACT

Purpose: Cerebral palsy (CP) is a nonprogressive brain and movement disorder that manifests as abnormal muscle tone. Despite the increase in cesarean sections, the rates of CP have remained constant. Research has shown that 14% of CP cases of cases have a likely causative single gene mutation and up to 31% have several genetic variations. However, no single gene has been found to explain all the symptoms of CP. The aim of the present study was to use patient's genetic reports to determine what percentage of patients had a causative/putative gene to explain symptoms and to identify the role of those genes. The pathogenic alleles identified may warrant screenings to assess for secondary risks.

Methods: Using Invitae CP spectrum disorders panel, we analyzed the positive CP genetic reports of the 31 patients tested from November 2020 and July 2022 from a single pediatric neurology practice. We collected information about patient demographics, pathogenic alleles, and variants of uncertain significance (VUS).

Results: Of the 31 positive genetic reports, 30 patients (97%) had at least one pathogenic allele found; Twenty-nine pathogenic alleles were identified: four (13.8%) with autosomal dominant (AD) diseases, and seven (24.1%) with both AD and recessive (AR) diseases. Some of the pathogenic alleles found were CACNA1A (n=2), CREBBP (n=1), CTNNB1 (n=1), ATM (n=1).

Conclusion: Many of the genes identified were associated with a movement disorder that shares features of CP, including spasticity or dystonia. The incidence of genetic findings and the high yield of dominant disorders and potential secondary risks suggest the need for both patient management and family counseling.

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2022-016

Identification of New Allosteric Modulators for the mGlu2 Receptor by using a Ligand-based Drug Discovery Approach

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ABSTRACT TOPIC

Pharmaceutical Sciences

ABSTRACT

Purpose: The human mGlu receptors are G protein-coupled receptors located within the central nervous system. These receptors normally bind to glutamate, which is the primary excitatory neurotransmitter in the body. The receptors can then assist in modulating the transmission of excitatory signals within the brain. These characteristics help to make the mGlu2 receptor a potential, novel target for future drug development, particularly for the treatment of certain neurologic or neuropsychiatric disorders, such as schizophrenia or depression. However, most allosteric ligands bind non-selectively on both mGlu2 and mGlu3 receptors. A pharmacological tool that assists with distinguishing ligands specific to mGlu2 and mGlu3 receptor subtypes will be pivotal to speed-up the drug discovery process. Our purpose in this study is to find novel ligands of potential allosteric modulators for the mGlu2 receptor by using already identified modulators through a ligand-based drug designing approach.

Methods: The potential allosteric ligands for the mGlu2 receptor were obtained by performing similarity searches on the online databases, ZINC and Drugbank. The original compounds used as the basis for the similarity searches came from a previously compiled list of Top 39 ZINC mGlu2 ligands (from the Liu Lab). Once the ligands were downloaded, they were converted into the appropriate file formats for molecular docking. Due to time constraints, it was decided that we would only dock the compounds whose original ligands had <10 results obtained from similar searching through ZINC. The selected ligands were then docked using Autodock Vina and visualized using Pymol. The Top 3 ligands were then determined based on their presence within the mGlu2 allosteric binding pocket and their predicted binding affinity for the receptor. Additionally, these ligands were also analyzed using a previously developed machine learning model. Specifically, the machine learning model would predict mGlu2 ligand likeness and binding affinity for each of the obtained ligands.

Results: A total of 1507 allosteric ligands were obtained for the mGlu2 receptor through the similarity searches. Machine learning model analysis of the similar ligands deemed that 88.89% of them were more likely to be mGlu2 ligands. Additionally, 83.50% of the ligands were deemed to have a high predicted binding affinity for the mGlu2 receptor. A total of 46 compounds were docked to the mGlu2 receptor using Autodock Vina, and their predicted binding affinities were obtained. The Top 3 similar ligands for the mGlu2 receptor, listed in order, exhibited binding affinities of -12.5 kcal/mol, -12.3 kcal/mol and -11.0 kcal/mol.

Conclusion: We were able to identify 1507 potential ligands for the mGlu2 receptor through similarity searches. Through further molecular docking of 46 of the similar ligands, we have determined three specific allosteric ligands for the mGlu2 receptor that are comparable or slightly better to their original counterparts. However, we believe additional research and investigation is required for validation of their potential efficacy. Future studies should involve analysis of the specific protein-ligand interactions that exist between the mGlu2 receptor and the three similar allosteric ligands, followed by comparison with the interactions present in their original counterparts.

Depression in opioid-dependent chronic pain patients in rural Texas: a complex relationship

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Community Medicine

ABSTRACT

Purpose: Chronic pain and depression are frequently cited as two of the most common causes for seeing a primary care provider. The link between pain, depression, and opioid use has an interdependent relationship that has measurable effects on patient care. Rural patients are often more susceptible to the challenges of managing chronic pain and depression. The goal of this study is to evaluate multiple factors of depression and treatment in chronic pain patients using long term opioids amongst three different rural Texas populations.

Methods: Participants were recruited at local clinics in Graham, Athens, and Andrews, Texas. Patients included in the study were adults aged 18+ who have used opioid pain medication for greater than three months. A survey and Patient Health Questionnaire-9 scoring (PHQ9) questionnaire were self-completed by each participant. The survey gathered information on participant demographics, description of pain and medication use, limited medical history, and alternative pain therapy.

Results: In total, 107 people enrolled in the study. After reviewing data, 27 (25.2%) incomplete surveys were excluded, leaving a total of 80 surveys for analysis. Of the remaining participants, 28 (35%) were from Graham, 48 (60%) from Athens, and 4 (5%) from Andrews. Forty-seven respondents (58.8%) were female and 33 (41.3%) were male. Average age of respondents was 64.74 years (SD=13.05). Depression, as diagnosed by PHQ9, was identified in 45 (56.3%) of participants. Significant risk factors for clinical depression among study participants included family history of substance abuse (OR=23.67, $p=0.008$), personal history of depression (OR=6.86, $p<0.001$) and previous session with a counselor or therapist (OR=2.76, $p=0.035$). The severity of depression in study participants was significantly associated with a prescription for Naloxone ($p=0.015$), family history of substance abuse ($p<0.001$), personal history of depression ($p<0.001$), current use of an SSRI ($p<0.001$), and the use of physical therapy ($p=0.036$). Additionally, there was a statistically significant difference in mean pain scale scores ($p=0.022$), length of opioid use ($p=0.011$), and PHQ9 scores ($p=0.02$) between participants from Graham and Athens.

Conclusions: The results of this study suggests a high burden of depression among study participants and enhances our understanding of the risk factors for depression among chronic pain patients in these communities. The data further emphasizes the need for proper depression screening and treatment for individuals with chronic pain and opioid use. Further research should explore effects of rural physician beliefs about prescribing opioids with antidepressants, rural vs urban opioid prescribing practices, and the relationship between opioid use and other common mental health conditions.

EXTERNAL FUNDING SOURCE

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IRB NUMBER

2018-081, Title "Outcomes of WE HAIL Geriatric Workforce Enhancement Program"

Association of the Patient-Physician Relationship with Racial Disparities in Chronic Pain Outcomes

PRESENTER

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ABSTRACT TOPIC

Health Disparities

ABSTRACT

Purpose: Racial disparities involving health outcomes in the United States have been widely investigated. However, the role of the patient-physician relationship in these disparities remains unclear. Of interest, Black patients may experience different treatment and outcomes relating to pain management. This research aims to determine if the patient-physician relationship mediates the association between race and pain outcomes among patients with chronic low back pain.

Methods: Participants in this study were selected from the Pain Registry for Epidemiological, Clinical, and Interventional Studies and Innovation (PRECISION Pain Research Registry) from April 2016 through December 2021. All participants were 21 to 79 years of age, had chronic low back pain according to criteria established by the National Institutes of Health, and had a physician who regularly treated their low back pain. Primary outcomes included low back pain intensity measured with a numerical rating scale and physical function measured with the Roland-Morris Disability Questionnaire. The patient-physician relationship variables were derived from the Communication Behavior Questionnaire, Consultation and Relational Empathy Measure, and Patient Satisfaction Questionnaire. Mediation analyses were performed with the PROCESS v4 software, using multiple mediation models and 95% bootstrap confidence intervals.

Results: A total of 1177 participants were studied, including 217 and 960 Black and White participants, respectively. Black participants reported worse outcomes for pain intensity (mean, 7.1; 95% CI, 6.8-7.3 vs. mean, 5.8 95% CI, 5.7-6.0; $P < 0.001$) and back-related disability (mean, 15.8; 95% CI, 15.1-16.6 vs. mean, 14.1; 95% CI, 13.8-14.5; $P < 0.001$). The differences in the patient-physician relationship between Black and White participants were not significant, with the exception that Black participants experienced more open and effective communication with their physicians than White participants (mean, 72.1; 95% CI, 68.8-75.4 vs. mean, 67.9; 95% CI, 66.2-69.6; $P = 0.03$). In the mediation analyses, virtually none of the association between race and each outcome was mediated by the individual or combined effects of physician communication, physician empathy, and patient satisfaction.

Conclusions: These findings suggest that factors other than the patient-physician relationship are important drivers of pain disparities experienced by Black patients in the United States. Additional research on system factors, such as access to high-quality medical care, may be helpful in identifying more promising approaches to mitigating racial pain disparities.

EXTERNAL FUNDING SOURCE

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Case Study on the Effect of Osteopathic Manipulation on Gallbladder Ejection Fraction

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Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Physical Medicine / OMM

ABSTRACT

Background: There is minimal research regarding the effects of osteopathic manipulative treatment (OMT) upon biliary emptying. Despite the limited research, OMT has been used to treat gallbladder dysfunctions in clinical practice.

Case Information: The purpose of this case study was to examine the effects of OMT on gallbladder ejection fraction (EF) as measured by ultrasound and to determine if there was sufficient evidence of OMT-influenced biliary emptying to base a larger study. OMT was performed by a neuromusculoskeletal medicine board certified osteopathic physician on a medical student, who was acalculous and asymptomatic of any biliary disorder. Interventions included OMT targeting sympathetic and parasympathetic innervation levels, Chapman points, visceral myofascial release, and Sphincter of Oddi release. Results included gallbladder EF as measured by ultrasound. Blinded analysis demonstrated a 8.88% increase in average gallbladder EF following OMT, with a statistically significant difference in mean ejection fraction between OMT (M=46.95, SD=19.83) and no OMT (M=38.07, SD=19.13) conditions (paired $t(4)=2.828$, $p=0.047$).

Conclusions: A limitation in the design of this study is that the comparison EF was measured 15 days after the OMT intervention. In future studies, we would first measure the EF and then perform OMT and measure the EF at least 4 weeks later. The results of this case study provide an enhanced understanding of OMT's effect on gallbladder EF. Future studies should apply the biliary OMT protocol to a diverse clinical population with and without functional gallbladder disorder to determine if OMT could be used as an alternative treatment.

Cranial Bone Ossification Trajectories in a Mouse Model of Osteogenesis Imperfecta

PRESENTER

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COLLEGE/SCHOOL

School of Biomedical Sciences

ABSTRACT TOPIC

Structural Anatomy

ABSTRACT

Purpose: Osteogenesis imperfecta (OI) is a genetic disorder that affects the production of type I collagen. Altered collagen production results in delayed or impaired skeletal formation and biomineralization. It also results in the defining characteristics of OI: brittle bones and high rates of fractures. Investigations of skeletal growth in OI have primarily focused on the postcranial skeleton, where interrupted, atypical, and disorganized ossification is seen at long bone growth plates. However, few studies have investigated changes in craniofacial growth in OI and there are currently few early interventions to improve growth trajectories in this region. The current medication prescribed for children with OI to improve skeletal growth, such as bisphosphonates, have major side effects and are not suitable for long-term use. A better understanding of craniofacial development in OI can help with targeting specific developmental stages when new treatments can be administered to provide the best results. The aim of this study is to examine cranial ossification from birth to weaning to determine where and when differences in growth occur in OI. We hypothesize that starting at birth mice with OI will have delayed craniofacial growth due to the poor collagen formation.

Methods: To test our hypothesis, we collected cranial bone volumes from micro-CT scans of the homozygous recessive OI murine model (OIM or B6C3Fe a/a-Col1a2^{oim/oim}) and compared them to their wild type (WT) littermates. The OIM model has a COL1A2 mutation that has been found to express a similar skeletal phenotype to the severe form (type III) of OI in humans. Bone volumes were collected from birth (P0) and weaning (P21) from the nasal, frontal, parietal, interparietal, and occipital bones (n=2/genotype/timepoint).

Results: At birth, OIM and WT bone volumes were similar. By weaning, bone volume was lower in OIM mice compared to WT mice. Our results demonstrate that OIM mice have reduced rates of bone ossification between birth and weaning, and these differences are most profound in the facial and occipital regions. Additionally, OIM skulls are characterized by low bone volume and potential delays in the closure of cranial sutures and fontanelles.

Conclusions: This study suggests that the divergence in cranial ossification rates related to COL1A2 mutations occurs postnatally. Interventions to recover craniofacial bone growth in this experimental model should focus on the critical growth period between birth and weaning. Results from this research have the potential to assist in developing treatments and highlight the importance of early life development of the craniofacial bones in human patients with OI.

EXTERNAL FUNDING SOURCE

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IACUC NUMBER

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Novel functions of the Glutaredoxin (Grx) System in the Lens

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School of Biomedical Sciences

ABSTRACT TOPIC

Eye / Vision

ABSTRACT

Purpose: The purpose of this study is to evaluate the function and therapeutic potential of the glutaredoxin (Grx) system, both glutaredoxin 1 (Grx1) and glutaredoxin 2 (Grx2), using Grx1/Grx2 double knockout (DKO) mice as a model.

Methods: We isolated primary LECs from wild-type (WT) and DKO mice for in vitro studies including cell proliferation assays, cell cycle distribution analysis via flow cytometry, cell apoptosis via western blot and ELISA kit, mitochondrial function evaluation via ATP bioluminescence assay, expression levels of mitochondrial complexes I-V, and seahorse mito stress test, cell cytoskeleton visualization using a fluorescence microscope.

Results: We found that DKO cells displayed a much slower proliferation rate compared to WT cells. The population of DKO cells in the G2/M phase was two-fold higher than that of WT cells. On the other hand, the population of DKO cells in the S phase was 50% less than that of WT cells. Additionally, DKO cells are pro-apoptotic under non-stressed condition as indicated by higher levels of Bax and cytochrome C. For the mitochondrial function, lower ATP production, less expression of mitochondrial complex III subunit UQCRC2 and complex IV subunit MTCO1 (CIV-MTCO1), lower coupling efficiency, and higher proton leak were presented in DKO cells as compared to WT cells, indicating multi-dimensional mitochondrial dysfunction in DKO cells. As for the cell cytoskeletal organization, we found that DKO cells had microtubule polarization because of the higher levels of vimentin expression which is an indicator of nuclei degeneration inhibition during the lens cell differentiation.

Conclusion: Overall, we found slow cell proliferation, cell cycle arrest, and mitochondrial dysfunction in the LECs from DKO mice. Our data indicate Grx system plays an important role in maintaining the normal function of mLECs, and Grx system activation might serve as a new therapeutic strategy for cataract prevention.

EXTERNAL FUNDING SOURCE

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Incorporating ultrasound imaging in graduate gross anatomy labs improves learning

PRESENTER

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ABSTRACT TOPIC

Education

ABSTRACT

Purpose: Teaching ultrasound imaging is on the rise in both undergraduate and medical anatomy education. Despite the vast literature surrounding these areas, there is little research exploring the use of ultrasound in preparatory graduate programs, which emphasize credential enhancement for professional school applications. The purpose of this study is to identify the effects of ultrasound imaging inclusion in a graduate gross anatomy course.

Methods: Students in the Master of Medical Sciences program enrolled in the gross anatomy course, a prosection-based cadaver lab that included pinned cadaver stations and an ultrasound station. Using ultrasound, teaching assistants imaged live human volunteers to demonstrate anatomical structures that students previously learned at the cadaver stations. To assess learning, students were given one ultrasound image question on each lab practical exam. Students also completed a pre- and post-course survey regarding perceptions of ultrasound inclusion in the course. Student lab practical scores and final course grades from the 2019 cohort were used as a historical control. Students in the 2022 cohort's lab practical grades, final course grades, and survey data were used in statistical analysis. Classes disrupted by Covid-19 were excluded (2020 & 2021 cohorts).

Results: 205 students from the 2019 cohort and 167 students from the 2022 cohort participated in this study, with 29 students from the 2022 cohort responding to the surveys. Students in the 2022 cohort had significantly higher lab practical scores in practicals 2 ($p < .001$, $d = .361$), 3 ($p < .001$, $d = 1.038$), 4 ($p < .001$, $d = .487$) and 5 ($p < .001$, $d = .412$). Survey data revealed that there was a significant increase ($p < .001$, $d = 1.203$) in learning outcome achievement from pre-survey to post-survey. Students who correctly answered the ultrasound question performed significantly better on practicals 3 ($p = .005$) and 4 ($p = .005$) than those who missed the ultrasound question.

Conclusion: These findings suggest that ultrasound imaging in a gross cadaver lab is beneficial to masters' students' learning and understanding of gross anatomy and structural relationships. The utilization of ultrasound during cadaveric anatomy courses improves learning and outcome achievement in these graduate students. This hands-on instructional procedure would likely have the same effect on other cadaveric anatomy courses such as those in health sciences and medical curricula.

IRB NUMBER

1825433-3

Investigating Associations Between Asthma and Nasal Abnormalities: A Computed Tomography (CT) Approach

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Structural Anatomy

ABSTRACT

Purpose: Asthma affects over 300 million people worldwide and 3,500 people suffer asthma related deaths each year. Although there is no clear cause of asthma, approximately 90% of asthmatics suffer from cold/exercise induced bronchoconstriction, a symptom triggered by the inhalation of cold and/or dry air. As the nasal passages account for most of the heat and moisture transferred to inspired air during respiration, anatomical variation in nasal morphology may contribute to asthma development. While the existence of nasal anatomical variants is well documented, little is known about the prevalence of such variants among asthmatics.

Methods: Accordingly, this study sought to investigate potential associations between asthma and three common nasal anatomical variants: septal deviations, concha bullosa, and paradoxical turbinate. This study analyzed Computer Topography (CT) scans of a diverse, mixed sex sample (n=242) from the New Mexico Decedent Image Database (NMDID). The asthmatic individuals (n= 120) were identified through associated medical records and compared to a control sample of non-asthmatics (n = 122). CT scans were analyzed using Avizo permitting qualitative coding of each anatomical variant for presence and type. Chi-square tests of independence were then used to test for differences in variant prevalence between the asthmatic and control samples.

Results: The results of our study show significantly higher prevalence of concha bullosa in asthmatics compared to control individuals ($\chi^2= 5.87$, $p=0.015$), with 70.0% asthmatics exhibiting at least one pneumatized turbinate compared to only 54.9% of control individuals.

Conclusions: This result suggests a potential relationship between the presence of conchae bullosa and asthma, possibly due to this variant negatively influencing intranasal air-conditioning capabilities. Future work employing computational fluid dynamics (CFD) analyses may be able to further elucidate the influence concha bullosa have on nasal passage air flow and conditioning. Such work could provide important insights into the role nasal anatomy may play in asthma prevalence and severity. This project was supported by Texas Center for Health Disparities grants RF00241 & RI40241

EXTERNAL FUNDING SOURCE

Texas Center for Health Disparities grants RF00241 & RI40241"

The Effects of Low Dose Naltrexone in Children with Chronic Pain

PRESENTER

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Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Background: Naltrexone is an FDA-approved opioid antagonist. At one-tenth the usual dosage, it is thought to have antinociceptive effects mediated through microglial cell inactivation, which can be helpful for chronic pain states, such as fibromyalgia, in adults.[1,2] The percentage of youth that are affected from chronic pain conditions is estimated to be at 15-35%.[3] The present study is the first to examine the efficacy of low-dose naltrexone (LDN) in treating chronic pain in pediatric patients.

Methods: A retrospective chart review was conducted on pediatric patients who were prescribed LDN between 2019 and 2022 for a chronic pain condition. At the start of LDN treatment and for each pain-clinic visit in the subsequent year, pain scores and functional disability inventory (FDI) scores were collected. Multilevel cumulative logit models and multilevel linear models were used to determine the effect of time of LDN on pain and FDI scores, respectively.

Results: There were 168 patients who met inclusion criteria. As compared to visits without LDN, there was no statistically significant difference in pain scores for visits in which the patient had been on LDN for 0-2 months ($p=0.88$) or for ≥ 2 months ($p=0.25$). As compared to visits without LDN, FDI scores significantly decreased after taking LDN for ≥ 2 months ($p< 0.001$) but not for 0-2 months ($p=0.12$).

Conclusion: Children who took LDN had a significant improvement in daily function as compared to before taking LDN.

Citations:

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3. King, S., Chambers, C. T., Huguet, A., MacNevin, R. C., McGrath, P. J., Parker, L., & MacDonald, A. J. (2011). The epidemiology of chronic pain in children and adolescents revisited: A systematic review. *Pain*, 152(12), 2729–2738.

IRB NUMBER

2022-011

SPHARM, a New Computational Approach for Locomotor Signal Identification in 15 MYA fossil primates from Maboko Island, Kenya

PRESENTER

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ABSTRACT TOPIC

Structural Anatomy

ABSTRACT

Purpose: Maboko Island, western Kenya preserves a diverse collection of seven catarrhine proximal humeri from the middle Miocene (~15 Ma). Proximal humeri are extremely rare in the Miocene (25-5 mya), limited to only four specimens outside of Maboko. Identified taxa include cercopithecoids (*Victoriapithecus*), nyanzapithecines (*Mabokopithecus*), small-bodied “apes” (“*Micropithecus*”), and large-bodied hominoids (*Kenyapithecus*), all of which provide important insight into diversity of locomotor patterns among middle Miocene catarrhines.

Methods: This project uses weighted spherical harmonics analysis (SPHARM), a landmark-free automated method to explore locomotor signals in the Maboko sample. Meshes of five intact humeri were compared to a sample of 94 extant catarrhines and platyrrhines, spanning a range of locomotor modes (suspensory arborealism, terrestrial quadrupedalism, arboreal quadrupedalism, and knuckle walking). Principal components analyses (PCA) were run on the associated SPHARM coefficients to explore differences among these locomotor groups.

Results: Preliminary assessment shows extant suspensory arboreal primates clustering away from both knuckle-walking and quadrupedal group along PC1 and PC2. Along PC2, further separation was observed between arboreal and terrestrial quadrupeds. The Maboko specimens show distinctions between all five of the fossil primates, particularly between two taxa previously suggested to be arboreal (*Mabokopithecus* and “*Micropithecus*”) and two taxa documented as terrestrial quadrupeds (*Victoriapithecus* and *Kenyapithecus*).

Conclusion: Though preliminary, this analysis provides insight into the diversity of catarrhine locomotor behavior during the middle Miocene, reinforcing previous descriptions of locomotor partitioning among the Maboko specimens. Future research that includes early and late Miocene taxa may shed light into diversity of catarrhine locomotor behaviors that spanned the Miocene epoch.

Sexually Transmitted Infections: Does knowledge impact perceived susceptibility?

PRESENTER

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ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Introduction: Young adults (18-24) have high rates of sexually transmitted infections (STIs), including bacterial infections such as chlamydia and gonorrhea. STI research commonly focuses on disease prevention through reducing the associated risk behaviors, such as condomless sexual activity, but limited research exists on risk perceptions related to STIs. Perceived susceptibility, a Health Belief Model construct, describes perceived risk of acquiring a disease. This study assessed perceived susceptibility to chlamydia and gonorrhea and the relationship with STI knowledge.

Methods: An online survey panel was used to recruit sexually active young adults aged 18-24 (n=375). STI knowledge was assessed using the Sexually Transmitted Disease Knowledge Questionnaire, a 27-item validated scale. The participants responded to each statement with either true, false, or don't know. Correct responses were given one point and the scores were averaged to calculate a knowledge score, with a perfect score being 27. Perceived susceptibility to chlamydia and gonorrhea infection was measured using three categories (strongly disagree/disagree, neutral, agree/strongly agree). Demographics including gender, race, sexual orientation, and education status were collected. Participants also reported on prior gonorrhea and/or chlamydia diagnoses as well as current sex practices and risk behaviors. Descriptive and bivariate analyses were conducted in SPSS. This study was approved by the university's Institutional Review Board.

Results: The average knowledge score among participants was 8.3 (standard deviation=5.4, range 0-22). Most respondents perceived that they were not at risk (strongly disagreed/disagreed) for acquiring chlamydia (54%) or gonorrhea (50%). The average knowledge score did not significantly differ by participants perceived susceptibility to chlamydia ($p=.087$). However, those who agreed/strongly agreed that they were at risk of contracting gonorrhea had a significantly higher knowledge score (mean of 9.9) than those who were neutral (mean knowledge score of 7.7; $p=.016$) or strongly disagreed/disagreed (mean knowledge score of 8.0; $p=.021$).

Conclusion: The results from this study indicate a significant relationship between STI knowledge and perceived susceptibility to contracting gonorrhea, leading to the conclusion that individuals with more knowledge about STIs can more accurately assess their potential risk of infection. However, this relationship was not noted with perceived susceptibility of contracting chlamydia. Further exploring the difference in overall STI knowledge scores based on susceptibility of disease may provide insight into specific areas of STI knowledge to improve. Future aims should be broadly directed towards STI education among sexually active young adults to increase perceived susceptibility to these infections and improve preventative behaviors, such as increasing condom use.

EXTERNAL FUNDING SOURCE

American Sexually Transmitted Diseases Association

IRB NUMBER

1798874

Application of Structural Retinal Biomarkers to Detect Cognitive Impairment in a Primary Care Setting

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Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Aging / Alzheimer

ABSTRACT

Introduction

Alzheimer's Disease (AD) is the most prevalent form of dementia and a leading cause of death in the elderly. The detection of AD remains poor in primary care despite the advancement of neurodiagnostic procedures. There are no rapid and cost-effective tools available to primary care providers to conduct cognitive examinations to diagnose AD. The goal of this study is to determine the predictive ability of structural retinal biomarkers to identify cognitive impairment in a primary care setting.

Methods

Participants were recruited from Alzheimer's Disease in Primary Care (ADPC) study. As part of the ADPC Retinal Biomarker Study (ADPC RBS), visual acuity, an ocular history questionnaire, eye pressure, optical coherence tomography (OCT) imaging and fundus imaging was performed. Exclusion criteria included high intraocular pressure defines as greater than or equal to 30 mmHg in either eye, history of adverse effects with pupillary relation, known hypersensitivity to tropicamide or any ingredient in the formulation, active ocular infection or inflammation, history of angle closure glaucoma, or having undergone ocular surgery within the last 6 months. Cognitive diagnoses were assigned algorithmically and verified at consensus review by an expert in the field of dementia.

Results

Data were examined on a total of 91 participants (59 cognitively unimpaired, 32 cognitively impaired (26 mild cognitive impairment (MCI), 6 AD)). The top biomarkers for predicting cognitive impairment included the inferior quadrant of the outer retinal layers, all four quadrants of the peripapillary retinal nerve fiber layer (pRNFL), and the inferior quadrant of the macular retinal nerve fiber layer. While all four quadrants of the pRNFL are highly important biomarkers for identifying those with cognitive impairment, the inferior and superior quadrants displayed higher relative importance compared to the temporal and nasal quadrants.

Conclusion

This study was the first to examine the utility of retinal biomarkers in diagnosis cognitive impairment in a primary care setting with models reflecting how it could be employed as a screening tool in practice. The current data provides strong support for continued investigation into structural retinal biomarkers, particularly the retinal nerve fiber layer, as screening tools for AD. In prior studies, preferential thinning of the inner retinal layers is found in AD compared to healthy controls. This study can help distinguish those with cognitive impairment from those cognitively unimpaired. The availability of such a biomarker could increase access to disease modifying treatments once available.

IRB NUMBER

2020-032

Population-specific mtDNA indices of mitochondrial stress associated with Alzheimer's disease in Mexican Americans and Non-Hispanic Whites

PRESENTER

AUTHOR(S)

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School of Biomedical Sciences

ABSTRACT TOPIC

Molecular Genetics

ABSTRACT

Purpose: Alzheimer's disease (AD) is the most prevalent form of dementia and is one of America's leading causes of death. Age is known to be the biggest risk factor for AD, and Mexican Americans are one of the fastest-aging populations in America. Mitochondrial stress and dysfunction are key players in the progression of AD and are also known to be impacted by lifestyle and environmental exposures/stressors. Mitochondrial dysfunction can cause the release of mitochondrial DNA (mtDNA) extracellularly, which can be detected in the peripheral blood (i.e., plasma). MtDNA copy number within the cell can also serve as an indicator of overall mitochondrial health, biogenesis, and/or mitophagy. This project hopes to identify population-specific differences in mitochondrial stress and dysfunction detectable in the blood and identify any relationship between AD risk factors and cognitive impairment. This data may help to further elucidate the role that mtDNA may be playing in population-specific Alzheimer's disease pathogenesis.

Methods: DNA was extracted from 200uL of participant plasma and buffy coat using the Mag-Bind® Blood & Tissue DNA HDQ 96 kit (Omega Bio-tek) according to the manufacturer's specifications. mtDNA and nuDNA copy number was assessed through absolute quantitative PCR (qPCR), targeting the mitochondrial minor arc (MinArc), and the nuclear-encoded beta-2-microglobulin gene (B2M). Data was stratified by population and sample type and linear regressions were performed to adjust for batch effects and identify factors that may influence this phenotype of mitochondrial dysfunction.

Results: Population-specific differences in factors contributing to the mtDNA phenotype were observed at the $p < 0.05$ level. In the Mexican American cohort, there was a significant relationship between cellular mtDNA:nuDNA ratio (quantified from buffy coat) and BMI, Clinical Dementia Rating Sum of Boxes score (CDRSum), and education. Further, there was a relationship between cell-free mtDNA copy number (quantified from participant plasma), education, and CDRSum. In the non-Hispanic white cohort, there was a significant relationship between cellular mtDNA:nuDNA ratio (from buffy coat) and both age and CDRSum. Age was associated with cell-free mtDNA in the non-Hispanic white cohort.

Conclusions: Evidence supports that there are population-based differences in which factors may be predictive of this blood-based phenotype of mitochondrial dysfunction. Mexican American populations seem to be more heavily influenced by environmental factors (BMI and education) whereas the non-Hispanic white population seems to be more heavily influenced by non-environmental factors (age). There also seems to be an indication of a relationship between these indicators of mitochondrial dysfunction and AD-related cognitive impairment (when measured through the CDR sum of boxes score).

EXTERNAL FUNDING SOURCE

Texas Alzheimer's Research and Care Consortium (TARCC) award #RS00049

IRB NUMBER

#1330309-1

The Role of Pregnancy Intention in the Choice of Contraception Among U.S. Women of Reproductive Age: 2017-2019 National Survey of Family Growth

PRESENTER

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COLLEGE/SCHOOL

School of Public Health

ABSTRACT TOPIC

General Public Health

ABSTRACT

Purpose: Contraceptive use is an important aspect of women's reproductive health. Long-acting reversible contraceptives (LARCs) such as the intrauterine device and hormonal implant, are known to be highly-effective methods to prevent an unintended pregnancy. Pregnancy intention may contribute to contraception use, and women who do not intend to get pregnant may opt for effective contraception methods. However, pregnancy intention is a behavioral factor that is subject to change based on circumstances. This study describes contraception use by pregnancy intention among a nationally representative sample of U.S. women aged 15-49 years.

Methods: The study sample included women aged 15-49 years from the 2017-2019 National Survey of Family Growth (n=3025). The dependent variable was current contraception method at the time of interview, operationalized into four categories: LARCs (reference category), pill/ring/patch/injectable, barrier methods, and no contraception. Pregnancy intention (in the future or after a current pregnancy) was operationalized as intending, not intending, and don't know/refused. The relationship between pregnancy intention and current contraception method was examined using weighted, multinomial logistic regression analyses, adjusting for race, age group, and type of current health insurance coverage.

Results: The mean age of the women was 29.6 years (SD=8.4 years), and women identified as White (67.6%), Black (24.2%), and Other (8.2%). Less than a third (29.6%) of the women had a bachelor's degree or higher, and a majority (58.4%) of women had private insurance. Overall, 22.1% were currently using LARCs and 15.7% were using no contraception. Compared to women intending to get pregnant, women not intending to get pregnant had lower odds of using pill/ring/patch/injectable (aOR=0.57; 95%CI=0.41, 0.80), barrier methods (aOR=0.54; 95%CI=0.40, 0.73), and no contraception (aOR=0.40; 95%CI=0.25, 0.64) versus LARCs. Women aged 20-29 years had lower odds of using pill/ring/patch/injectable (aOR=0.41; 95%CI=0.25, 0.67) and no contraception (aOR=0.43; 95%CI=0.24, 0.79) versus LARCs, compared with women aged 15-19 years. Older women within the age group 40-49 had higher odds of using barrier methods (aOR=1.98; 95%CI=1.05, 3.73) and significantly lower odds of using pill/ring/patch/injectable (aOR=0.32; 95%CI=0.18, 0.57) versus LARCs, compared with women aged 15-19 years. Compared to women with private insurance, women with public insurance (Medicaid/Children's Health Insurance Program) had lower odds of using pill/ring/patch/injectable (aOR=0.50; 95%CI=0.35, 0.72) versus LARCs.

Conclusions: Overall, women not intending to get pregnant were less likely to use pill/ring/patch/injectable and barrier methods compared to LARCs. As such, women who desire to prevent unintended pregnancy may opt for LARCs. Findings also show that a proportion of women not intending to get pregnant were not using any method of contraception, which highlights the need to examine reasons for no contraceptive use among this group of women. Given that pregnancy intention can be dynamic, preconception care should be accessible to women to support them in making informed decisions about their reproductive health. Moreover, there is need to examine factors that impact decision-making on contraception methods while accounting for pregnancy intention.

It's not a GIST: A Histopathological Investigation of a Rare Gastric Schwannoma

PRESENTER

AUTHOR(S)

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Structural Anatomy

ABSTRACT

Background: Gastric schwannomas are rare gastrointestinal mesenchymal tumors, accounting for <0.2% of all gastric neoplasms. Gastric schwannomas are benign, arise from the gastrointestinal nerve plexus, and are often misdiagnosed as gastrointestinal stromal tumors (GISTs). Gastric schwannomas are typically incidental findings on conventional imaging studies, surgery, or autopsy. Reported patients are usually asymptomatic. Gastric schwannomas can be differentiated from GIST and other mesenchymal gastrointestinal tumors through the use of immuno-histochemical markers such as S100, Vimentin, and glial fibrillary acidic protein (GFAP).

Case Information: During routine dissection of a 78-year-old female, a 1.5 x 1.2 x 1.0 cm tan, firm nodule protruding from the anterior stomach wall was identified. The nodule was located 11 cm from the gastroesophageal junction, 7 cm from the incisura angularis, and 6 cm from the pyloric sphincter. Sectioning revealed white, whorled, and rubbery cut surfaces. No hemorrhage, necrosis, or cystic spaces were grossly appreciated. Subsequently, the tissue underwent routine fixation, processing, paraffin embedding, sectioning, and hematoxylin and eosin (H&E) staining. Using light microscopy, histopathologic findings included a well-circumscribed area containing mostly eosinophilic spindle cells with nuclear palisading, foci of lymphoid infiltration, and a micro-trabecular pattern noted centrally. Additionally, a peripheral lymphoid cuff was present. No mitotic figures were identified. Based on our histopathology findings, we hypothesized the presented nodule to be a gastric schwannoma. This diagnosis was corroborated by immunohistochemistry to demonstrate positive S100b protein expression. Common differential diagnoses include gastrointestinal stromal tumors (GISTs), leiomyomas, and solitary fibrous tumors, all of which lack S100 protein reactivity.

Conclusion: This case aims to contribute an additional report about gastric schwannomas to better enhance our collective understanding of this rare lesion.

Unilateral Levator Scapulae Anatomical Variants

PRESENTER

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ABSTRACT TOPIC

Structural Anatomy

ABSTRACT

Background: Neck pain constitutes 13.8% of chief complaints. Causes of neck pain, including Levator Scapulae Syndrome (LPS), have become increasingly important and warrant discussion of contributing factors, such as anatomical variations. We present two discovered anatomical variants of the levator scapulae (LS) muscle. Awareness of the variation in LS accessory muscles may be relevant in differentiating between normal and pathological diagnoses, while remaining a possible target of therapy in pain syndromes, such as LPS.

Case Information: Routine cadaveric dissection of a 41-year-old female and a 50-year-old male donor was performed. Upon dissection of the superficial back of both cadavers, we discovered accessory muscle variants. Dissection of the deep upper back of the female cadaver, we noted a L sided, unilateral, accessory LS muscle slip that casually attached to the serratus posterior superior aponeurosis and tracked with the main body of the LS muscle superiorly. The caudal aspect of the accessory slip inserted perpendicularly onto the broad aponeurotic fibers of the serratus posterior superior muscle around T3. The insertion tracked anterolaterally and superiorly, combining with the muscle belly of the LS around C7-T1 and traveling deep to the right sternocleidomastoid (SCM) to insert on the C1-C4 cervical vertebrae. Following a superior reflection of the R-sided trapezius muscle in the male cadaver, we noted an unilateral accessory muscle band that was attached to the midline spine caudally and tracked with the main body of the LS superiorly. The caudal attachment originated from the T3-T4 spinous process, deep to the rhomboid major muscle and superficial to the posterior serratus superior muscles. The insertion of the accessory runs anteriorly and superiorly, deep to the right SCM, and tracks in a parallel fashion to the main body of the LS.

Conclusions: This case series presents two unilateral LS anatomical variants discovered separately during routine cadaveric dissections.

Assessment of the Pediatric Mental Health Calls Program during the COVID-19 Pandemic and Stress Findings Among Teens and Adolescents.

PRESENTER

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ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Purpose: The Pediatric Mental Health Calls Program was created in March 2020 as a response to the dramatically reduced in-person medical visits and increased virtual visits at the UNTHSC Pediatrics Clinic in Fort Worth following the COVID-19 pandemic. The program was initially used as a tool to support pediatric patients and caregivers while following up on their mental health status. However, considering the potential for the PMHC program in monitoring the long-term and enduring effects of the pandemic on the mental health of teens and adolescents, the program was assessed for data summary and project growth. Methods: The Pediatric Mental Health Calls were previously performed by trained medical and PA student volunteers who used call scripts to standardize the conversation with patients and their caretakers. In a retrospective review, data collected by REDCap electronic data capture tools was then stratified into three main groups: Infant, Toddler and Teens from 2020-2022. Data was then screened and summarized based on yes or no questions as answered by the patient's caregivers regarding stress levels and mental health. Interview questions were also assessed for areas of improvement. A Chi-squared test of independence analysis was used, and significance was set at $p < 0.05$. Results: When surveying parents of teens and adolescents age 10-19, there was a higher percentage that reported yes to increased stress due to COVID-19 in 2021 (53%) compared to 2020 (39%), with a statistical significance of $p < 0.015$. Of the teens and adolescents who had online schooling for six months to one year or greater at the time of surveying in 2021, the percentage of increased stress was even higher at 61%. In addition, problems with discipline, motivation and/or socialization in teens and adolescents were higher in students who reported increased stress due to the pandemic in 2021 than in students who reported no stress. Conclusions: Due to the relatively inexpensive and flexible nature of home calling by volunteers, the PMHC program is a viable way to monitor stress and its effect on mental health amongst the pediatric population alongside changes in the COVID-19 pandemic, especially with the lift of quarantine mandates and return to in-person schooling. Future health calls may be improved by incorporating more of the teen/adolescent answers alongside parents to gauge correspondence between answers as well as providing scaled answer choices for further quantitative analysis.

EXTERNAL FUNDING SOURCE

N/A

Active suppression of adaptive immunity by *Borrelia burgdorferi* in the murine host

PRESENTER

AUTHOR(S)

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School of Biomedical Sciences

ABSTRACT TOPIC

Immunology

ABSTRACT

Purpose: *Borrelia burgdorferi* (*Bb*), the spirochetal agent of Lyme disease, utilizes a variety of tactics to evade and suppress the host immune response which enable it to persist chronically. These tactics can include complement inhibition, antigenic variation, extracellular matrix degradation, and adaptive immune suppression. Adaptive immune suppression by *Bb* is still not well understood. Previous studies have shown that lymph node (LN) germinal centers generated in response to *Bb* collapse one-month post-infection. The resulting humoral immune response is characterized by unusually strong and persistent IgM production and lack of long-lived immunity. Here we aimed to better characterize how *Bb* manipulates the host humoral immune response, ultimately resulting in failure to clear the infection. Methods: Mice were infected with *Bb* and concomitantly immunized with recombinant SARS-CoV-2 spike protein to measure the antibody response to the immunization and how it may be dampened by infection with *Bb*. We also immunized mice at 2-, 4-, and 6-weeks post-infection to test how long this humoral immune suppression lasts. Using RT-qPCR, we also examined changes to gene expression in murine LNs 15 days post-infection to better characterize what may be causing this observed immune dysfunction. Results: Suppression of host antibody production against the rSARS-CoV-2 spike protein peaked at 2 weeks post-infection but continued for all timepoints measured. We also found that live *Bb*, but not heat-killed (HK) *Bb*, broadly suppressed many genes related to T cell homing and function. Genes which play a critical role in the establishment and maintenance of T cell zones within the LNs, *Ccl19* and *Ccr7*, were significantly downregulated. This was interesting considering previous studies have provided evidence of disorganization of LN architecture and the disruption of T cell zones beginning around 10 days post-infection. In addition, both *Il2* and *Il2ra* were significantly downregulated, which is typically observed during the resolution of infection and indicates a lack of antigenic restimulation. Conclusion: These data suggest potential T cell disruption by *Bb*, which may play a role in the failure to mount an appropriate humoral immune response to the infection.

EXTERNAL FUNDING SOURCE

State of Texas

IACUC NUMBER

2020-0033 and 2021-0021

Targeting Sp1 in Ewing Sarcoma: A multi-approach method for the utilization of Mithramycin

PRESENTER

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COLLEGE/SCHOOL

School of Biomedical Sciences

ABSTRACT TOPIC

Cancer

ABSTRACT

Purpose: Ewing Sarcoma (ES) is a bone and soft tissue cancer affecting young adults and children. ES mostly occurs in the bones or soft tissue of the arms, legs, and pelvis. Localized ES presents with 5-year survival rate of 70%, but metastatic 5-year survival rate is between 15% and 30%. Our laboratory is interested in combination treatments using less toxic agents to induce sensitization to chemotherapy in ES. The anti-cancer activity of an antineoplastic antibiotic, Mithramycin, against ES cells has been shown. Mithramycin inhibits Specificity protein 1 (Sp1) a marker associated with aggressive cancer cell growth and resistance to chemo/radiation therapies. However, its mechanistic effects on other oncogenic proteins have yet to be elucidated in ES. The purpose of this study is to evaluate the effectiveness of Mithramycin and various combinations with other chemotherapeutic agents, Etoposide and Vincristine, to inhibit ES cell growth and assess the effect on key cancer related proteins regulated by Sp1. Future studies will include expanding upon Mithramycin's mechanism of action in Ewing Sarcoma utilizing RNA sequencing and various computational methods.

Methods: Cell lines were obtained from Children's Oncology Group (COG). Anti-proliferative activity of Mithramycin and/or Vincristine and Etoposide against ES cell lines, TC205 and CHLA10, was evaluated using CellTiterGlo kit. Dose curves were plotted and IC50 values were determined by Sigma-Plot software. The expression of Sp1 and survivin was determined by Western blot analysis. The specific type of effect (additive/antagonistic/ synergistic) of the combination treatments were determined by analyzing the combination index obtained via Calcsyn software. Nude mice were injected with TC205 cells and treated over two weeks with either Mithramycin (1mg/kg per week) and/or Etoposide (5mg/kg per week) and tumor volume was compared. Protein models were obtained from RCSB PDB and homology tests were performed using the Swiss-model workspace.

Results: Mithramycin, etoposide, and vincristine decreased ES cell line viability in TC205 and CHLA10 cells as monotherapies, but more effectively in combination. Tumor volume was greatly attenuated upon Mithramycin and/or etoposide introduction, but more significantly when used in combination. Mithramycin showed the ability to reduce the expression of Sp1 and offer differing effects on survivin expression, indicative of anti-apoptotic mechanisms being implemented in the ES cell lines. Decreases in viability upon chemotherapeutic and Mithramycin introduction were drastically increased when used in combination and this effect was mirrored in further decreases in Sp1 expression. Synergistic drug responses were shown in the combination of Mithramycin with both Vincristine and Etoposide (CI <1). Sp1 and survivin protein models were established and homology verification using Ramachandran plots and QMEAN Z-scores indicated quality protein models for further computational studies.

Conclusions: Mithramycin may effectively sensitize ES cells and improve the response of chemotherapy while lowering necessary effective dosages. Studies to understand the mechanism of action of Mithramycin on Sp1, survivin, and other proteins involved in Ewing Sarcoma are underway.

EXTERNAL FUNDING SOURCE

Cancer Prevention and Research Institute of Texas (Award#: RP210046)

IACUC NUMBER
IACUC-2016-0047

Pituitary Apoplexy in an Adult Male

PRESENTER

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Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Neuroscience

ABSTRACT

Background: The pituitary gland is a major regulator of endocrine function, located at the base of the skull behind the eyes and inferior to the optic chiasm. Pituitary adenomas are noncancerous growths of pituitary tissue. Most pituitary adenomas will arise from the anterior lobe of the pituitary, due in part to the anterior lobe accounting for most of the pituitary's size. Most are small microadenomas, measuring <1 cm in diameter. Lesions larger than 1 cm are called macroadenomas. Despite popular belief, pituitary adenomas are perhaps not as rare as previously thought, and it is estimated that one in ten people will develop a pituitary adenoma in their life. Because of the pituitary's endocrine function, some of these growths will produce hormones or hormone precursors. The most common functioning adenoma secretes prolactin and is known as a prolactinoma. Pituitary adenomas which do not produce hormones are termed nonfunctioning adenomas. Pituitary apoplexy is the occurrence of a sudden onset of symptoms due to spontaneous hemorrhage or infarction of the pituitary, usually precipitated by the presence of an adenoma.

Case Study: A 35-year-old male presented to the emergency department, reporting two days of severe headache and nausea. Neurological examination revealed diminished right sided peripheral vision. An abnormally prominent sella turcica was noted on CT scan, which led to follow up magnetic resonance imaging. This revealed moderate pituitary enlargement and heterogeneously hyperintense T1W signal characteristic for hemorrhagic pituitary apoplexy. The patient was observed for several days before a transsphenoidal hypophysectomy was successfully performed. Endocrinology assays done, both preceding and following the surgery, indicated that the adenoma that bled was nonfunctioning. The patient reports a history of an asymptomatic pituitary mass that was incidentally discovered in childhood. The patient was given instructions at that time to follow up with a physician concerning this mass should symptoms arise.

Conclusion: This case presents an example of a benign, nonfunctioning pituitary adenoma with apoplexy to the literature, with endocrinological, histological and radiographic contributions. Given the high prevalence of pituitary adenomas, there should be a strong emphasis on educating physicians about pituitary apoplexy and about adenoma detection methods in patients with endocrinological imbalances related to the pituitary. Raising awareness can result in early detection to promote noninvasive treatments that would avoid potential complications of surgery and the toll of the disease.

P1-CPP promotes Foxo1 and Creb signaling and reduces apoptosis in Neurotrophic Factor-Deprived Primary Retinal Ganglion Cells

PRESENTER

AUTHOR(S)

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School of Biomedical Sciences

ABSTRACT TOPIC

Eye / Vision

ABSTRACT

Purpose: To elucidate the intracellular mechanisms underlying neuroprotective effects of the core peptide of a-B crystallin, peptain-1 (P1) conjugated to a cell-permeable peptide CPP (P1-CPP) in primary retinal ganglion cells (RGCs). Targets of the investigation were limited to Creb1, Bak1/Bad, and Foxo1, based upon RNA sequencing data obtained from RGCs of IOP-elevated rats treated with P1-CPP in comparison with the vehicle.

Methods: Primary RGCs isolated from Sprague Dawley rat pups were deprived of neurotrophic factors (NT) namely, BDNF, CNTF, and Forskolin for 48 hours, either in the presence or absence of P1-CPP (4 μ M). After the treatments, RNA isolation was carried out using Trizol reagent. Subsequently, cDNA synthesis and qPCR analysis of the target genes expression, including Creb1 (n=2), Foxo1 (n=3), and Bak1 (n=3), was performed. Another set of RGCs subjected to the same treatments was fixed with 4% paraformaldehyde for 20 minutes and used for immunocytochemical analyses of p-CREB (n=3), FOXO1 (n=3), and BAD (n=3) protein expression. Immunostaining with an RBPMS antibody was used as an RGC marker. N indicates experimental repeats.

Results: Following NT deprivation, there was an increase in mRNA expression of Creb1 (2-fold) in RGCs treated with P1-CPP, compared to the vehicle-treated RGCs. Moreover, the phosphorylated (active) form, p-CREB, was increased (by 102%; p=0.04) in primary RGCs treated with P1-CPP, compared to the vehicle-treated group. Pro-apoptotic Bak1 mRNA expression was not changed in the P1-CPP-treated RGCs compared to the vehicle-treated group. Primary RGCs stained for BAD protein showed a decrease (by 62%; p=0.08) in the P1-CPP treated group compared to the vehicle-treated RGCs. Foxo1 mRNA levels were increased by more than 2-fold in the P1-CPP treated RGCs, compared to the vehicle-treated RGCs. FOXO1 protein was also elevated in primary RGCs treated with P1-CPP compared to the vehicle group (by 59%).

Conclusions: P1-CPP is neuroprotective against neurotrophic factor deprivation through multiple mechanisms, including early changes in the expression of mitochondrial homeostasis regulator Foxo1, activation of the pro-survival CREB pathway, and inhibition of pro-apoptotic members of the BCL-2 family of proteins.

EXTERNAL FUNDING SOURCE

T32 AG020494; NEI R01 DLS

Title: Understanding Type II Diabetes Insulin Management During The COVID-19 Pandemic: Findings from a Hospital and a Clinic

PRESENTER

AUTHOR(S)

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COLLEGE/SCHOOL

HSC College of Pharmacy

ABSTRACT TOPIC

Patient Safety

ABSTRACT

Purpose: COVID-19 disrupted the care of people with diabetes. It is not clear how the disrupted care impacted medication safety and diabetic control outcomes. During the pandemic, questions emerged regarding whether patients experienced changes in care that led to higher glucose levels, inappropriate medication changes and poorer health outcomes. The role of strategies to control glucose, such as the use of antidiabetic drugs has been established. We examined safety issues related to the association between insulin use and diabetic control among diabetic patients during COVID-19. Results: After examining 42 patient cases, it is noted that most (55%) patients had controlled A1C (pre-Covid vs Covid-era). (55%) of patients whose A1C was < 8% (pre-Covid vs Covid era) were prescribed insulin compared to (45%) of patients who had an A1C >8% (pre-Covid vs Covid era). The cease in insulin prescribing (pre-Covid vs Covid era) increased the A1C levels for uncontrollable patients. Conclusion: During the COVID pandemic, gaps in insulin prescriptions were associated with occurrences of diabetic control status changing to uncontrolled status, indicating patient safety issues. Monitoring insulin prescribing among diabetic patients during the pandemic may identify care gaps and help to improve patient care outcomes.

IRB NUMBER

2019-163

Sleep Duration and Social Determinants of Health Predict Osteoporosis in Adults 50 Years of Age and Older After Controlling for Vitamin D, Demographic Characteristics, and Physical Activity.

PRESENTER

AUTHOR(S)

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Diabetes

ABSTRACT

Purpose:

Osteoporosis is a bone disease that develops when bone density and mass decreases, or when the quality or structure of bone changes. There are many causes of osteoporosis, with some etiologies being more understood than others. Prevention is critical in the treatment of osteoporosis, due to its serious complications, including life altering hip and spine fractures. Despite prevention and treatment, osteoporosis in most cases is inevitable, but the onset and severity is what can be helped. Finding other ways to slow or even prevent osteoporosis is an active area of study, with sleep being one of the many variables of interest due to its role in homeostasis. The literature demonstrates contradictory findings for the relationship between sleep and osteoporosis. Many of the studies lack a recent and/or big enough sample size, and there is a need for further research on the subject. Additionally, recent literature has not included variables representative of social determinants of health, such as income and education. The purpose of this study was to further investigate the association that between sleep and osteoporosis in individuals 50 and older using the NHANES Database while controlling for potential covariates such as social determinants of health.

Methods:

Data from the National Health and Nutrition Examination Survey (NHANES), 2017-2020 were analyzed to determine the association between sleep duration and osteoporosis in adults 50 and older. Multivariate logistic regression was performed controlling for race/ethnicity, age (≥ 50 years), gender, highest household education, physical activity, poverty, vitamin D, and BMI. Analyses were considered statistically significant at $p < 0.05$.

Results:

Analyses included 4963 adults over the age of 50, with 51% (2507) being female. A total of 12.3% (611) of the cohort had a diagnosis of osteoporosis, with 87% of the osteoporotic group being female (530). Mean age was 65.2 years ($sd=9.3$) for the total sample, 64.5 ($sd=9.2$) for non-osteoporotic individuals, and 70.0 ($sd=8.8$) for osteoporotic individuals. In the adjusted analyses, we found no statistically significant association between sleep duration and osteoporosis. There is a statistically significant association between family monthly poverty level and osteoporosis ([OR:0.93; 95%CI(0.87-0.99) $p=0.047$]. BMI, Age, and Gender were also significantly associated with osteoporosis. Other social determinants of health such as race, physical activity, and education were not statistically significant. Vitamin D was also not associated with osteoporosis.

Conclusion:

The purpose of this study was to further investigate the association between sleep and osteoporosis in individuals 50 and older while controlling for covariates, particularly social determinants of health. We looked at specifically sleep duration, and a previous diagnosis of osteoporosis. We theorized that lower sleep durations may have an association with osteoporosis; however, our results did not support this. The association between family poverty index and osteoporosis highlights the importance of exploring socioeconomic differences in

sleep and osteoporosis research in the future, respectively. Finally, this study is limited by a lack of a quantitative measure of osteoporosis. Future work with additional socioeconomic variables and more consistent data collecting modalities should shed more light on the subject

IRB NUMBER

1944684-1

Impacts of Whole School, Whole Community, Whole Child Interventions on K-12 Mental Health

PRESENTER

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Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Health Disparities

ABSTRACT

Purpose: Youth mental health is a growing problem, with one third of high school students reporting persistent feelings of sadness or hopelessness in 2019. In 2014, the Association for Supervision and Curriculum Development (ASCD) and Centers for Disease Control and Prevention (CDC) introduced the Whole School, Whole Community, Whole Child (WSCC) model, which emphasizes collaborative networks between educational, community, and health sectors to integrate education, health promotion, and disease prevention. Although the WSCC model has since gained popularity, there remains little data on its impact on K-12 mental health outcomes. This rapid review describes: (1) the current body of research on the WSCC model on mental and behavioral health of students, (2) common practical applications of the model, and (3) future research opportunities.

Methods: We conducted a systematic, rapid review of literature on WSCC interventions. Peer-reviewed systematic reviews or primary studies since 2012 that targeted K-12 mental, behavioral, or emotional wellness within the United States were included. A three-person research team reviewed the studies and categorized findings by emerging themes.

Results: 460 articles were screened, and 14 were included for review. The results show positive impacts of WSCC interventions on K-12 mental health, particularly: enhancing preventative efforts by facilitating health-education partnerships and strengthening student-educator relationships by incorporating comprehensive wellness into education initiatives. Common challenges include competing priorities and garnering cohesive resources and support for interventions. The professional development of educators and tailoring to high risk groups including LGBTQ students, students of color, and military-connected youth were identified as key components to success.

Conclusions: Identifying available evidence and knowledge gaps may inform the implementation of future WSCC initiatives. More discussion and research on its impacts, best use cases, and practical applications are needed, but the WSCC model offers a promising framework for promoting mental and behavioral wellness in the K-12 setting.

Evaluation of Create-Your-Own-Adventure Activities on Student Knowledge and Critical Thinking Skills in Second-Year Student Pharmacists

PRESENTER

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HSC College of Pharmacy

ABSTRACT TOPIC

Education

ABSTRACT

Purpose: Create-your-own-adventure (CYOA) activities are educational innovations where students choose the “best pathway” of treatment. Current literature suggests increased student perception of knowledge and critical thinking skills with use of CYOA activities; however, evidence that such skills ultimately improve is lacking. The primary objective of this study is to assess changes in knowledge and critical thinking after completing a CYOA activity. Methods: Seventy-five second-year pharmacy students completed a CYOA activity on venous thromboembolism, with a six-question quiz immediately before and after. Questions were mapped to pre-set learning objectives with slight alterations to questions on each assessment. Four questions were then mapped to the final exam which occurred approximately three weeks after the activity. Friedman’s two-way analysis and Cochran’s Q test were used to evaluate differences in scores. Descriptive statistics were used to describe student perceptions and scores on a modified Need for Cognition scale. Results: There was a significant decrease in mean scores for each assessment (68.1% vs. 64.9%, vs. 40.0%; $p < 0.001$). Similar results were found when stratifying scores by question. Of the 48 survey responses, 94% preferred the CYOA activity and perceived increased critical thinking skills. All Need for Cognition items scored > 3.5 , indicating satisfaction in critical thinking. Conclusions: Although we hypothesized an increase in scores with use of CYOA activities, there was a negative association between the activity and scores. Possible limitations include mapped questions that were too dissimilar, VTE management being too multivariate, and lower student retention of cumulative material on finals. These limitations will be addressed in future CYOA activities.

IRB NUMBER

2016-086

Higher expression of Annexin A2 in bladder urothelial carcinoma promotes migration and invasion.

PRESENTER

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ABSTRACT TOPIC

Cancer

ABSTRACT

Purpose: Bladder cancer is a prevalent and often aggressive malignancy, precipitating high morbidity and mortality rates in the US. The paucity of non-invasive and low-cost methods for detection necessitates investigation into improved surveillance assays for bladder urothelial carcinoma (BLCA). Annexin A2 (AnxA2) is a phospholipid-binding protein involved in malignant processes in several cancers but has yet to be studied in association with bladder carcinoma. This study aims to investigate the association of AnxA2 in BLCA and establish its role in the metastasis of bladder cancer cells.

Results: The Cancer Genome Atlas Data analysis demonstrated that AnxA2 mRNA expression was significantly increased in BLCA tumor tissue compared to normal bladder tissue. Higher AnxA2 mRNA expression was significantly associated with high pathological grades, stages, and non-papillary tumor histology and poor overall survival, progression-free survival, and disease-specific survival. Similarly, we found that AnxA2 expression was higher in bladder cancer cells derived from high-grade metastatic carcinoma than in cells derived from low-grade urothelial carcinoma. In addition, expression of AnxA2 was significantly mobilized to the surface of bladder cancer cells that were highly metastatic versus cancer cells derived from low-grade tumors. This expression was also associated with high plasmin generation and AnxA2 secretion. Downregulation of AnxA2 cells significantly inhibited proliferation, migration, and invasion in bladder cancer and decreased expression of proangiogenic growth factors and cytokines.

Conclusion: Results of this study show that higher expression of AnxA2 is involved in proliferation, migration, and invasion in bladder cancer and is associated with poor prognosis of patients with BLCA. These findings demonstrate the potential for AnxA2 as a prognostic marker and therapeutic target for BLCA.

EXTERNAL FUNDING SOURCE

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Animal model of kidney disease induced by high folic acid

PRESENTER

AUTHOR(S)

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COLLEGE/SCHOOL

HSC College of Pharmacy

ABSTRACT TOPIC

Pharmaceutical Sciences

ABSTRACT

Purpose: The kidney is a vital organ that helps the body eliminate waste and toxic substances and return nutrients and vital substances back into the bloodstream. Kidney disease can be categorized into acute kidney injury (AKI) or chronic kidney disease (CKD). This may be caused by numerous risk factors such as ischemia, sepsis, drug toxicity and drug overdose, exposure to heavy metals, and diabetes. However, the exact prognosis from an AKI to CKD is not fully understood. In addition, approximately 37 million individuals in the United States population currently suffer from CKD. Despite the high prevalence of CKD, information is lacking on our understanding of the pathogenesis of AKI and CKD and there are still no available therapeutics that can be used to combat kidney disease effectively. This highlights an urgent need to further study the pathological mechanisms underlying AKI, CKD, and AKI progression to CKD. In this regard, animal models of kidney disease are imperative.

Methods: This presentation reviews a widely used animal model of kidney disease, which is induced in mice with folic acid (FA). While a low dose of FA is nutritionally favorable, a high dose of FA is toxic to the kidneys. A high dose of FA is injected intra-peritoneally in the mice. Following a brief description of the procedure for disease induction by FA, major mechanisms of FA-induced kidney injury are then reviewed. This includes observing oxidative stress levels, mitochondrial abnormalities such as impaired bioenergetics and mitophagy, ferroptosis, pyroptosis, and increased expression of fibroblast growth factor 23 (FGF23). This is completed to explore possible pathological mechanisms of kidney disease and thereby the efficacy of a variety of therapeutic approaches may be evaluated. These procedural methods required Institutional Animal Care and Use Committee (IACUC) clearance and proper laboratory training to ensure ethical laboratory practices. The presentation will also highlight an overview of how to obtain IACUC clearance and ethical practice certification.

Results: This animal model of inducing high doses of FA can induce both AKI and CKD in mice and therefore can be used to further study AKI to CKD progression.

Conclusion: Given that the animal model is reproducible and can recapitulate human kidney disease phenotypes, it should be useful for both studying the pathological mechanisms of kidney disease and identifying effective therapeutic targets to fight kidney disease.

EXTERNAL FUNDING SOURCE

This presentation is supported by PDRT at UNTHSC

IACUC NUMBER

IACUC-2022-0011

Peripheral Vascular Function is Not Correlated to Subjective Sleep Quality in Young Healthy Humans

PRESENTER

AUTHOR(S)

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Cardiovascular

ABSTRACT

Background: Peripheral vascular dysfunction (including endothelial dysfunction) may be an early biomarker of cardiovascular disease. Prior studies have shown a relationship between poor sleep quality and impaired vascular function, indexed by flow-mediated dilation (FMD) of the brachial artery. However, these investigations did not allometrically scale for baseline artery diameter, nor control for shear stress, which both affect the magnitude of flow-mediated vasodilation. Without scaling for baseline artery diameter, FMD may overestimate the magnitude of dilation in individuals with small baseline diameters. Additionally, greater shear stress will elicit a greater magnitude of vasodilation via release of vasoactive mediators from the endothelium, such as nitric oxide. With the quality of sleep declining in the United States, and cardiovascular disease remaining a leading cause of mortality, we sought to further explore the relationship between sleep quality and peripheral vascular function corrected for both baseline artery diameter and the magnitude of shear stress. Hypothesis: Poor sleep quality is associated with impaired peripheral vascular function indexed by “corrected” brachial artery FMD. Methods: Thirteen young and healthy human participants (7M, 6F) completed the Pittsburgh Sleep Quality Index (PSQI) survey prior to assessment of brachial artery FMD. PSQI scores range from 0-21, with higher scores indicating worse sleep quality. Brachial artery diameter and blood velocity were then obtained via duplex Doppler ultrasound during a 2-min baseline, a 5-min occlusion of the brachial artery, and a 3-min reactive hyperemia period. FMD of the brachial artery was calculated as the percent change from baseline diameter to the maximum diameter induced by reactive hyperemia. Shear stress was estimated as shear rate, calculated as eight times the ratio of brachial artery blood velocity to diameter. FMD was corrected for baseline diameter, and the shear stress area under the curve up to maximum diameter via ANCOVA (i.e., “corrected FMD”). Pearson correlations were calculated between PSQI score and uncorrected FMD, and between PSQI score and ANCOVA corrected FMD. Results: The mean PSQI score was 5.3 ± 4.5 (range, 0-17), and mean FMD was 5.0 ± 2.2 % (range, 2.7-9.4 %). While an unexpected modest positive correlation was observed between uncorrected FMD and PSQI score ($r=0.51$, $p=0.08$), corrected FMD and PSQI score were not correlated ($r=0.38$, $p=0.25$). Conclusion: There was no relationship between subjective sleep quality and peripheral vascular function as measured by corrected FMD in this cohort of young and healthy participants. These findings likely reflect the multivariate nature of vascular function in young healthy adults with lower cardiovascular risk, and the subsequent narrow range of both flow-mediated dilation and subjective sleep quality.

EXTERNAL FUNDING SOURCE

American Heart Association Transformational Project Award (19TPA34910743)

IRB NUMBER

2021-067

Anti-proliferative effects of a copper(II) complex with a thiosemicarbazone ligand against selected human cancer cells

PRESENTER

AUTHOR(S)

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COLLEGE/SCHOOL

School of Biomedical Sciences

ABSTRACT TOPIC

Cancer

ABSTRACT

Purpose: The frequent relapse and drug resistance associated with the current cancer chemotherapy treatments necessitate the development of alternative strategies. Thiosemicarbazones are a class of metal chelators that have been explored to treat diverse human diseases, including cancer. Copper, a crucial structural component for many significant enzymes and a key catalytic co-factor in redox processes, is being explored for several medical applications. Additionally, the anti-cancer activity of certain chemotherapeutic agents can be enhanced by the use of copper-containing complexes. This study aimed to evaluate the antiproliferative effects of a copper(II) complex with a thiosemicarbazone ligand (Cu-acetylethTSC or [Cu(acetylethTSC)Cl]Cl·0.25C₂H₅OH (where acetylethTSC = (E)-N-ethyl-2-[1-(thiazol-2-yl)ethylidene]hydrazinecarbothioamide)) against human cancer cell lines, viz., medulloblastoma (DAOY, D283), glioblastoma (LN-229), Ewing sarcoma (TC205, CHLA10), and acute lymphoblastic leukemia (CCRF-CEM, SUP-B15). **Methods:** These selected cell lines were cultured using standard protocols. Cell viability was measured using a Cell Titer-Glo kit at 48 h after treatment with various concentrations of Cu-acetylethTSC. Each treatment group and the controls were read in triplicates and the data were plotted as percentage cell viability versus concentration of the complex. Dose-response curves were generated based on the cell viability data obtained, and IC₅₀ values were calculated. Cardiomyocytes (H9C2) were also cultured and used to test cytotoxicity in non-malignant cells. **Results:** Cell viability was inhibited in a dose-dependent manner in all the selected cancer cell lines while that of H9C2 was not significantly affected. **Conclusion:** This indicates that Cu-acetylethTSC was selective for malignant cells. Further studies are underway to understand the efficacy, protein targets, and underlying mechanisms of the role of Cu-acetylethTSC.

EXTERNAL FUNDING SOURCE

Grant from the Cancer Prevention and Research Institute of Texas.

Outcomes of a Team-Based Chronic Care Management Service in a Dual-Eligible Medicare and Medicaid Population with Diabetes Mellitus

PRESENTER

AUTHOR(S)

Angel Nguyenly, Ashlyn Aguiniga, Emmanuel Rodriguez, Didi Ebert-Blackburn, Megan Wesling

COLLEGE/SCHOOL

HSC College of Pharmacy

ABSTRACT TOPIC

Other

ABSTRACT

Purpose: Patients receiving Medicare and Medicaid benefits (dual-eligible) have a higher prevalence of multiple comorbidities, including diabetes mellitus. This same population is less likely to have routine preventative measures completed and a higher incidence of disease-related complications. The purpose of this study is to evaluate the effectiveness of a team-based Chronic Care Management (CCM) program in achieving health outcomes in dual-eligible patients with type 2 diabetes (T2D) and the financial sustainability of a CCM program.

Methods: Dual-eligible patients with T2D meeting CCM enrollment criteria were evaluated in a retrospective, pre-/post- intervention, observational chart review study from March 2019 to August 2021. Statistical analyses using non-parametric tests evaluated clinical outcomes (e.g., hemoglobin A1c), preventative measures and clinical staff encounters. Preliminary financials are reported descriptively. *Results:* Twenty-six patients were included in the analysis. There was a significant reduction in mean A1c levels (8.15% to 7.34%, $p = 0.035$). Changes in preventative metrics included a statically significant increase in statin prescriptions ($p=0.039$) while a non-significant increase in pneumococcal and influenza vaccine rates and depression screenings is noted. \$14,721.00 was billed to insurers for the service with a reimbursement rate of 39.6%.

Conclusion: This study shows that team-based patient care in a CCM program improves A1c levels and supports achievement of preventative measures. Full realization of intervention impact limited by the lack of in-person access to healthcare services due to shutdowns in response to the global pandemic.

IRB NUMBER

#2021-115

Diabetes-Related Outcomes of an Interprofessional Chronic Care Management (CCM) Service in Medicare Beneficiaries

PRESENTER

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COLLEGE/SCHOOL

HSC College of Pharmacy

ABSTRACT TOPIC

Diabetes

ABSTRACT

Purpose: Patients with type 2 diabetes (T2D) often have coexisting conditions requiring consistent monitoring and preventative measures. Chronic Care Management (CCM) is a Medicare program that aims to improve chronic disease state management, however literature on clinical outcomes is lacking. The purpose of this study is to evaluate the diabetes-related outcomes of an interprofessionally-delivered CCM program in patients where Medicare is the singular payer and secondarily, its financial impact.

Methods: Adult Medicare patients with T2D enrolled in CCM between February 2020 and August 2021 were included in this retrospective chart review. Participants were evaluated pre- and post-CCM enrollment using non-parametric tests on 1) clinical measures such as A1C; 2) preventative measures; and 3) involvement of clinical staff such as pharmacists and social workers. Descriptive statistics were used to describe financials.

Results: Thirty-three patients were included in the study. Changes in clinical measures included a significant reduction in mean A1C from 8.4% to 7.4% ($p=0.012$), and a nonsignificant reduction in blood pressure and body mass index. There was also a significant increase in pharmacist and social worker involvement, but no significant changes to preventative measures. A total of \$26,673.00 was billed to Medicare, with a reimbursement rate of 44%.

Conclusion: The CCM service demonstrated a significant reduction in A1C and a significant increase in pharmacist and social worker access. There were no significant changes in preventative measures, likely due to the overlapping study period and COVID-19 pandemic. Future studies outside of pandemic conditions are needed to further assess these nonsignificant outcomes.

IRB NUMBER

2021-115

Barriers to in-Person Focus Group Participation during the Third-Year of COVID-19 Pandemic: A Case Study of Colorectal Cancer (CRC) Screening in Underrepresented Groups

PRESENTER

AUTHOR(S)

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COLLEGE/SCHOOL

HSC College of Pharmacy

ABSTRACT TOPIC

Cancer

ABSTRACT

PURPOSE:

In the process of conducting research to understand barriers to colorectal cancer (CRC) screening in underrepresented groups such as Blacks and Hispanics, it became evident that there were also barriers to recruitment in this population. This study assesses the challenges faced in recruitment of focus group participants regarding CRC screening practices among underrepresented groups. Since the COVID-19 pandemic, qualitative research participants have primarily been interviewed through online video or audio interactions. However, as restrictions on in-person interactions have been lifted, in-person focus groups are being increasingly considered.

METHODS:

The study investigators began recruitment through community health workers in August 2022, when COVID-19 vaccines were available for all adults (age>18 years). Eligible individuals were: age 45-75, Black or Hispanic, with Medicaid or no insurance, and no family history of CRC or diagnosis of certain colon-related diseases. We combined in-person and virtual recruitment strategies, including posting flyers in communities, advertising our study at health fairs, and on social media. Participants would receive a \$50 gift card.

RESULTS:

Fifty-five met the eligibility criteria among 144 respondents, and 45 subjects (29 women and 16 men) agreed to be contacted. An average of 2.5 attempts were made per eligible subject. Unfortunately, we were able to recruit only four women (3 Hispanic and one non-Hispanic black). Traveling to the research site was a barrier to participation. Many subjects (49%) requested virtual participation (online video or audio interactions); some declined because the topic was too sensitive (considered taboo), and eligible men were reluctant to participate in-person.

CONCLUSIONS:

The requirement of in-person participation affected our recruitment goals, suggesting that COVID-19 has shifted the preferences of research participants to virtual interaction. In response to the eligible participant preferences, the study protocol has been revised to re-contact patients and schedule virtual FG sessions.

EXTERNAL FUNDING SOURCE

Exact Sciences

IRB NUMBER

1859167-7

Program Director Survey Determining Effects of Single Accreditation and Pass/Fail Licensing Exams on Osteopathic Medical Students Applying for Surgical Residency

PRESENTER

AUTHOR(S)

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Education

ABSTRACT

Purpose

Prior to the single accreditation system (SAS), some residency programs were accredited by the American Osteopathic Association (AOA), rather than the Accredited Council for Graduate Medical Education (ACGME) and trained osteopathic (DO) graduates only. Recently, United States Medical Licensing Examination (USMLE) Step 1 and Comprehensive Osteopathic Medical Licensing Examination (COMLEX) Level-1 transitioned from numeric scores and pass/fail outcomes to pass/fail only. The purpose of this survey was to examine the effects of these changes on DO students applying for surgical residency.

Methods

A voluntary, anonymous survey was distributed five times over 9.5 weeks to 1539 surgical program director (PD) emails collected from the Fellowship and Residency Electronic Interactive Database (FREIDA). 302 responses were received (response rate 19.6%) and 244 survey responses were included in statistical analyses. 58 responses were excluded because of incompleteness, the respondent was not a PD, or the respondent disqualified DO students from matching.

Results

For DO applicants, most former-AOA programs recommend Step 1 while most non-AOA programs require it. The majority of both program types require Step 2 CK. When deciding whom to interview, former-AOA programs significantly preferred Level-2 scores and completion of an acting-internship at the program while non-AOA programs significantly preferred the Medical Student Performance Evaluation and clerkship grades/evaluations. Both program types highly valued Step 2 CK scores and letters of recommendation.

Conclusion

Based on this study, DO applicants should almost certainly take both Step 1 and Step 2 CK (in addition to Level-1 and Level-2) to be considered competitive. Additionally, the results underscore the importance of identifying surgical residency programs as former-AOA or non-AOA— particularly when prioritizing where to complete acting-internships. Despite the SAS, former-AOA and non-AOA surgical residency programs differ in their preferred medical licensure examination and metrics for determining competitiveness. DO students should consider these differences to improve osteopathic surgical match rates.

Deep Profunda Femoris variant found within the Sciatic Sheath supplying the posterior compartment of the leg

PRESENTER

Austin Driskill

AUTHOR(S)

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Structural Anatomy

ABSTRACT

The lower extremity has well documented arterial variations; however, finding an artery within the sciatic sheathing and providing muscular branches to the proximal leg is abnormal. During the dissection of a 64-year-old male cadaver, a branch of the deep femoral artery was found within the sciatic sheath of the lower right extremity in the posterior compartment. Knowledge of the branches of the femoral and deep femoral arteries is clinically relevant in radiology nerve blocking treatment and surgically relevant in knee and femoral surgeries. The deep femoral artery branches off the femoral artery on the proximal portion of the anteriomedial side of the thigh. Deep to the rectus femoris muscle and between the vastus medialis muscle and adductor magnus muscle, the deep femoral artery provides perforating branches that give off cutaneous, anastomotic, and muscular branches to the flexor aspect of the thigh. The variant artery in this cadaver was found as an enlarged perforating branch of the profunda femoris artery, piercing through the adductor magnus muscle and supplying the posterior compartment of the thigh. Perforating branches commonly terminate in the posterior thigh, but this variant continues through the posterior leg and popliteal fossa within the sciatic sheath. The variant blood vessel terminates distal to the knee as muscular branches for both heads of the gastrocnemius and soleus muscles.

LABEL-FREE QUANTITATIVE PROTEOMICS REVEAL PROTEIN NETWORKS AND ASSOCIATED BIOLOGICAL PROCESSES IN ANDROGEN DEPRIVED MOUSE SEMINAL VESICLES IN RESPONSE TO 17- β -ESTRADIOL (E2) TREATMENT

PRESENTER

Ammar Kapic

AUTHOR(S)

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COLLEGE/SCHOOL

School of Biomedical Sciences

ABSTRACT TOPIC

Proteomics

ABSTRACT

Purpose: Androgen deprivation therapy (ADT) remains the primary treatment strategy for inhibiting prostate cancer progression. However, systemic ablation of androgen-mediated signaling induces various metabolic disorders, cognitive decline, and osteoporosis. Therefore, like in menopausal women, 17- β -estradiol (E2) supplementation has been suggested as a treatment to reduce side effects associated with ADT. A recent clinical trial utilizing transdermal estrogen patches reported reduced osteoporosis markers and hot flashes. Estrogen receptors (ER) are expressed in the male reproductive system and play a role alongside androgens in maintaining function and growth. Under normal physiological conditions, increased E2 concentrations induce an inhibitory effect on the size of the male reproductive organs, including the seminal vesicles (SV); however, under androgen depletion, E2 supplementation has been reported to reduce the atrophy of the SV in mice. In this study, we report for the first time a discovery-driven proteomic analysis of E2's effects on the SV in mice under the conditions of surgical castration to model patients undergoing ADT.

Methods: Surgically castrated mice (n=4) were subcutaneously injected with E2 (treated group) or vehicle (control) daily for five days and sacrificed to obtain SV. Proteins were extracted, reduced, alkylated, and digested with trypsin for analyses using data-dependent microflow liquid chromatography–electrospray ionization tandem mass spectrometry (LC–ESI-MS/MS) on LTQ Orbitrap Velos Pro™ (Thermo Fisher Scientific). MS/MS data was searched against the UniProt Mouse protein database using Sequest in Proteome Discoverer (Thermo Fisher Scientific) and MaxQuant (Max Planck Institute). Validation of protein and label-free quantification (LFQ), combining spectral counting and total TIC, were performed using Scaffold (Proteome Software) to identify significantly affected proteins. Post-hoc t-test was performed to identify differences in protein abundances between groups. Regulated proteins were mapped to protein interaction networks and biological functions employing Ingenuity Pathway Analysis® (IPA®, Qiagen). Targeted proteomics-based validation of significant candidate proteins is ongoing, and data will be analyzed using Skyline™ (MacCoss Lab, University of Washington).

Results: Our discovery-driven LC–ESI-MS/MS analyses identified 7000 proteins with high confidence from the SV of E2-treated and control mice. IPA®-based bioinformatics of the E2-regulated proteins showed molecular and cellular functions-associated enrichment of carbohydrate metabolism, DNA replication, recombination, and repair, as well as free radical scavenging. The topmost regulated protein interaction network represented cell cycle, cell signaling, and small molecule biochemistry. Enhanced activation of the estrogen receptor β (ESR2) was implicated by the molecule activity predictor (MAP) tool of IPA®. Additionally, MAP predicted that the protein interaction represented within this network might impact disease and physiological processes associated with the proliferation of prostate cancer and regulation of gonadal cells. Furthermore, we were able to screen several preclinical biomarkers that participate in androgen receptor activity, modulating ER-mediated

transcription and reproductive system development and function. Targeted proteomics-based validation of these biomarkers is ongoing.

Conclusion: Our study aims to provide an in-depth account of the alterations occurring at the protein level in the SVs in response to E2 supplementation during ADT and to select and validate preclinical biomarkers for prognostic and therapeutic applications.

EXTERNAL FUNDING SOURCE

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IACUC NUMBER

IACUC-2018-0066

Prevalence and Factors Associated with SSRI Use Among Adults with Depressive and Thyroid Disorders in the United States

PRESENTER

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AUTHOR(S)

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COLLEGE/SCHOOL

HSC College of Pharmacy

ABSTRACT TOPIC

Health Disparities

ABSTRACT

Background: Patients with hypothyroidism and hyperthyroidism are at high risk for developing anxiety and depression. Sixty percent of adults in the United States with thyroid disorders have depression. Selective serotonin reuptake inhibitors (SSRIs) are used to treat depression. However, SSRIs reduce thyroid function during treatment suggesting SSRIs may not be used in treating depression among adults with thyroid disorders. Few studies have investigated the prevalence and factors associated with SSRI use in adults with diagnosed depression and thyroid disorders.

Objective: This study estimated the prevalence of SSRI use in adults with diagnosed thyroid and depressive disorders in the United States and examined the factors associated with SSRI use.

Methods: The study used a cross-sectional design using pooled data from multiple years (2018-2020) of the Medical Expenditure Panel Survey (MEPS), a nationally representative survey of the civilian non-institutionalized population in the US, to gain an adequate sample size. The study was restricted to adults with diagnosed thyroid and depressive disorders with health insurance. The final sample was (Unweighted N=729; Weighted N= 3,090,551). SSRI use was identified from prescription drug files using Multum drug classifications. Rao-Scott Chi-square tests were used to examine the unadjusted group differences in SSRI use. Multivariable logistic regression was used to analyze factors associated with SSRI use. The logistic regressions adjusted for age, sex, race and ethnicity, education, income, insurance coverage, prescription drug coverage, polypharmacy (>6 drug classes excluding antidepressants and thyroid hormones), perceived physical and mental health rating, pain, and thyroid hormones.

Results: A majority (61.6%) of adults diagnosed with thyroid and depression used SSRIs. A lower percentage of African Americans (28.5%vs.61.9%; $p<.05$) used SSRIs compared to NHWs; Only 47.0% of those reporting poor health used SSRI compared to those reporting excellent physical health (73.8%) ($p<0.01$). A lower percentage of adults with extreme pain (49.5%vs.65.8%) used SSRIs compared to those with mild or no pain ($p<.05$). A lower percentage of adults with moderate to vigorous physical activity of 5 days/week used SSRIs compared to adults with no exercise. (54.2%vs.65.3%; $p<.05$). A lower percentage of adults with polypharmacy (53.0%vs.67.5%; $p<0.01$) used SSRI compared to those without polypharmacy. In multivariable logistic regression, African Americans had lower odds of SSRI use (AOR=0.28; 95% CI=0.09, 0.88) compared to NHWs. Lower ratings of physical health were associated with SSRI use. Adults with polypharmacy had lower odds of SSRI use (AOR=0.65; 95% CI=0.44, 0.96).

Conclusion: 6 in 10 adults with thyroid and depressive disorders used SSRIs. Racial disparities in SSRI use were observed. We speculate that SSRI use rates may be lower in those with polypharmacy and poor health to reduce the risk of drug-drug interactions and drug-disease interactions.

Strengths and Limitations: Limitations include cross-sectional study design, self-reported data, no distinction between hyperthyroidism and hypothyroidism, and a small sample size despite pooling multiple years.

Nevertheless, the study used nationally representative data adjusted for a comprehensive list of clinical, demographic, and psychosocial factors.

Prediction of Protospacer Adjacent Motif (PAM) dependencies in CRISPR-Cas9 systems and design of novel Cas9 with broad PAM compatibility

PRESENTER

AUTHOR(S)

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COLLEGE/SCHOOL

School of Biomedical Sciences

ABSTRACT TOPIC

Pharmaceutical Sciences

ABSTRACT

Purpose: CRISPR-Cas9 gene editing capabilities has experienced many limiting factors and biological constraints preventing its rapid adoption and mass utilization. Of interest is the Cas9 protein's ability and necessity to recognize unique Protospacer Adjacent Motif (PAM) DNA sequences prior to its gene editing functionality. This recognition constraint has limited the scope of targetable regions of DNA, and thus prevents access to extensive sections of DNA by the Cas9 protein. Given the multitude of Cas9 species, it has become a challenge to fully comprehend the wide variations in this relationship. Machine learning (ML) applications have increasingly been developed to discern obscure patterns and relationships to aid in the analysis and design of the next generation of proteins. In this project, we hypothesize that the relationship between PAM-I domain sequences and its corresponding PAM DNA sequence can be computationally understood to predict new PAM DNA sequences and novel PAM-interacting (PAM-I) protein domain sequences. Specifically, our model attempts to directly associate such a relationship with a sequence-based approach between amino acid and DNA. The implementation of computational technologies into understanding biological function can facilitate the advancements in overcoming the innate constraints in the CRISPR-Cas9 system and provide a pipeline toward modern protein engineering.

Method: Protein and DNA sequence data were extracted from public database sources. From EMBL-Uniprot queries, Cas9 protein sequences were obtained for various species. From NCBI-GenBank, protein CRISPR sequences were obtained from each protein's respective genomic DNA matched by accession. Collection of PAM DNA sequences were gathered from predictive alignments utilizing NCBI-BLAST. Construction of our model utilizes a transformer architecture implementing text embedding on the sequence data.

Results: The final construction of our database contains a total of 795 unique Cas9 protein sequences, from which their corresponding PAM-I domains were extracted. From their respective genomic DNA, a total of 18,445 CRISPR sequences were found. From which, we have aligned and collected a large set of PAM DNA targets for each protein species. With our collection of Cas9 protein domain sequences and their associated PAM DNA sequences, we have trained and tested a novel ML model to discern and classify the relationship between the two associated sequences. To further expand the relationship, a similar transformer ML model will be developed to methodically generate unique protein domain sequences capable of recognizing PAM DNA sequence targets. Final accuracy results from our prediction and generation models remain in progress and are pending, with the expectation of reaching at least 50% for both models.

Conclusion: Given its absence and public availability, a unique database of protein PAM-I domains and their associated PAM DNA sequences has been successfully developed and curated to facilitate the development and testing of our novel ML models. The results and outcomes of this project can create an opportunity to directly integrate into a modern protein engineering pipeline to build and test new libraries of Cas9 proteins.

Aggressive Fibromatosis of the Quadratus Lumborum in A 28-Year-Old-Female: A Case Report

PRESENTER

Tejashwini Gattu ([ORCID iD](#))

AUTHOR(S)

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

General Medicine

ABSTRACT

Background: Desmoid tumors (aggressive fibromatosis/desmoid-like tumors) are rare neoplasms that consist of proliferations of clonal fibroblastic proliferation that are aggressive and locally invasive. While the exact cause of desmoid tumors is unknown, they are associated with hereditary conditions such as Gardner's syndrome and familial adenomatous polyposis both of which arise due to inactivating mutations of the APC gene. On the other hand, fibromatosis that arise sporadically generally has an activating mutation of the CTNNB1 gene which encodes beta-catenin. A history of trauma such as injuries and previous surgeries has also been associated with the development of desmoid tumors. Desmoid tumors are rare with an estimated incidence of 2-4 per million people per year and make up 0.03% of all neoplasms. Early diagnosis and treatment of desmoid tumors are crucial in minimizing morbidity and mortality. Fibromatosis primarily arise in the extra-abdominal setting which comprises approximately 58% of all cases. Among this, most arise in the shoulder or pelvic girdle region. Here, we report an uncommon site of origin for desmoid tumors.

Case Presentation: A 28-year-old female with no previous history of trauma presented with lower back pain with radiculopathy radiating to her right hip. An MRI of the lumbar spine revealed a mass in the right iliac fossa and an abdominal and pelvic MRI showed a large circumscribed posterolateral right intra-abdominal wall mass extending up from the right iliac fossa with low signal bands on T1W and T2W imaging. There were intermediate signal areas elsewhere with islands of enhancement. Subsequent abdominal and pelvis CT showed a right posterior pelvic mass measuring 19x13x10 cm concerning for a neoplasm with fibrotic components. The mass originated from the right quadratus lumborum muscle. It involved the posterior distal transversus abdominis and internal oblique abdominal muscle anteriorly. Distally, it involved the iliacus muscle. Differential diagnoses were abdominal wall aggressive fibromatosis/desmoid tumor, solitary fibroid tumor, sarcoma, unusual GIST tumor, neuroectodermal tumor versus nerve sheath tumor, metastasis, lymphoma. A biopsy was performed and results were consistent with aggressive fibromatosis.

Conclusion: Desmoid tumors are rare tumors with a locally aggressive and variable course and high risk of local recurrence. The diagnostic workup often includes imaging with MRI and CT and which allows for determining the origin and involvement of adjacent structures to guide possible interventions. Diagnosis can only be confirmed through biopsy which will reveal a monoclonal proliferation of fibroblasts. Treatment ranges from observation, radiotherapy, surgery, and various medications. Because this case presents a desmoid tumor originating from an uncommon site of origin in the quadratus lumborum region, we hope to provide a better clinical picture for the screening and diagnosis of similar aggressive fibromatosis.

Assessing Incontinence Reporting by Women at a Rural Texas Clinic

PRESENTER

AUTHOR(S)

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Health Disparities

ABSTRACT

Urinary incontinence is estimated to affect between 20-45% of women in the US; a potential reason that estimates vary is due to underreporting of symptoms. In Eagle Lake, Texas, family physicians are the main source of health education concerning uro-gynecologic issues in women. No local Ob-Gyn or urology specialists practice in Eagle Lake. The two most established family physicians in Eagle Lake are male and they recently discontinued obstetric care. The goal of this project was to assess the prevalence of incontinence and reporting of symptoms by female patients in Eagle Lake, in lieu of a local Ob-Gyn or urologist. The goal of this project was to assess the prevalence of incontinence and reporting of symptoms by female patients in an Eagle Lake Family Medicine clinic, where factors exist which might present barriers to reporting.

Methods

A paper survey was created the Questionnaire for female Urinary Incontinence Diagnosis was used to screen for incontinence in female patients 55 years and older. Questions concerning willingness to discuss symptoms and use of UI medications were asked in multiple-choice format. Data was collected for 10 weeks, and percentages were calculated in Microsoft Excel.

Results

Out of 51 total participants, 50.9% screened positive for incontinence and 17.86% take bladder control medications. Out of women with incontinence, 60.71% indicated they have not brought up symptoms to a physician. Out of those who have not brought up symptoms, 13.89% indicated they would not see a physician for bladder symptoms, 13.89% indicated they would see a female physician only, and 69.44% indicated they would see either a female or male physician. Out of women with incontinence who have brought up symptoms with a physician, 27.27% reported symptoms to a female physician, 54.54% have reported symptoms to a male physician, and 18.18% reported symptoms to both a male and a female physician.

Conclusions

This data demonstrates that more than half of female patients 55 years and older at Rice Medical Associates are incontinent, that more than half of the incontinent women have not discussed their symptoms with a physician, and that less than twenty percent of the incontinent women are on medication for it. Some reasons for underreporting may include insufficient screening in clinic, lack of health literacy on when to seek care, and patient avoidance of discussions concerning "delicate" uro-gynecologic matters. The data shows that some women choose only to discuss bladder symptoms with a female physician, while some choose not to discuss their symptoms at all. Additionally, there were two patients who refused to complete the survey because they were uncomfortable with the topic. Due to research bias from sampling patients in a male family practitioner's clinic, further studies should survey women outside of a healthcare setting and clarify whether reporting would be different at an Ob-Gyn office. This study indicates the need for purposeful screening for incontinence by rural family physicians, to compensate for underreporting of uro-gynecologic issues by women in areas with limited healthcare options.

IRB NUMBER
2018-081

Changes in Blood Pressure and Abundance of Kidney Sodium Channels in Postpartum Preeclamptic Rats

PRESENTER

AUTHOR(S)

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COLLEGE/SCHOOL

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ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Purpose: Postpartum (PP) preeclamptic (PE) women have an increased risk of developing hypertension (HTN) and chronic kidney disease. However, the mechanisms of these diseases in PP PE women are not fully understood. Results from our previous studies show 10-week PP PE rats have HTN (PMID: 34727994). One factor that could cause elevated blood pressure is an increase in sodium transport in the kidneys of PP PE rats. Our current study will examine the BP as well as the amount of Sodium Potassium Chloride Cotransporters (NKCC), Sodium Hydrogen Exchanger-1 (NHE1) and α -subunit of the Epithelial Sodium Channel (ENaC) within the kidney of PE rats 6 weeks postpartum (PP6). We hypothesize that PP6 PE rats will have an increase in BP as well as increased amounts of NKCC, NHE1 and α -ENaC proteins. Methods: Pregnant Sprague Dawley rats were divided into 2 group: control (CON) normal pregnant rats and PE rats (derived from the surgically induced placental ischemic model of PE). All rats gave birth and were weaned for 3 weeks. At PP6, BP was measured via carotid catheterization. Kidney cortex (KC) and medulla (KM) tissue were collected to measure for NKCC, NHE1 and α -ENaC amounts via Western Blots.

Results: BP was significantly elevated in PP6 vs CON rats (128 ± 6 vs 106 ± 4 mmHg, $p < 0.05$). The amount of NKCC channels within the KC was significantly increased in PP6 vs CON rats (107.82 ± 5.64 vs 100 ± 1.48 IU/Protein/CON%, $p < 0.05$). The amount of α -ENaC proteins within the KC was also increased in PP6 vs CON rats (123.4 ± 4.67 vs 116.5 ± 33.03 IU/Protein/CON%, $p = 0.06$). NHE1 channels within the KC were slightly decreased in PP6 vs CON rats (77.31 ± 15.28 vs 100 ± 16.61 IU/Protein/CON%, N.s). No changes were observed in α -ENaC proteins within the KM in PP6 vs CON rats.

Conclusion: PP6 PE rats have HTN as well as increased NKCC and α -ENaC sodium transport proteins in the kidney cortex. These results confirm our hypothesis that increased sodium transporters in the kidney, which could elevate sodium and water reabsorption, correlates with an increase in blood pressure. This study is clinically relevant because it informs clinicians on the pathophysiology of HTN and renal disease/dysfunction in PP PE women. It also highlights novel approaches to providing potential therapies to manage blood pressure in PP PE women. Future studies will investigate the cause-and-effect relationship between blood pressure and sodium handling in the kidney of PP PE rats.

IACUC NUMBER

IACUC-2021-0037

Preliminary Results from the DFW Viet-American Health Pilot Study

PRESENTER

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ABSTRACT TOPIC

Health Disparities

ABSTRACT

Introduction

Arthritis is a chronic condition that can cause pain, physical disability, and reduced quality of life (QOL). The prevalence, severity, symptoms, and management of osteoarthritis (OA) are known to differ by race and ethnicity. Studies on racial differences focused mostly on Black or Hispanic populations with little attention on Asian Americans, such as socioeconomically marginalized, medically under-served, and hard-to-reach Vietnamese-Americans (VietAmericans). This pilot study investigated the occurrence, symptoms, knowledge, and management of arthritis among Viet-Americans.

Methods

From 7/1/22-8/31/22 and with help from community leaders of faith-based community organizations, we recruited people of Vietnamese descent of age ≥ 45 years and living in the Dallas-Fort Worth (DFW) metroplex. We translated and adapted a linguistically and culturally appropriate questionnaire from English to Vietnamese using the Translation, Review, Adjudication, Pretesting, and Documentation (TRAPD) Model. Participants completed the survey which asked about their demographics, height, weight, chronic conditions, the 12-item Knee Injury and Osteoarthritis Outcome Survey (KOOS), the Veterans RAND 12-item Health Survey (VR12), and awareness of knee osteoarthritis (OA). We then calculated the body mass index and summary scores for KOOS pain, function, and QOL.

Results

Of 272 participants who completed the questionnaire (82% enrollment rate), 53% were women and 54% were ≥ 65 years old. The average stay in the US was 30 years (± 12.8). The results indicated a low prevalence of overweight (21%) and obesity (6%). Knee OA occurred in 20% of men and 25% of women. Of note, 13% of men and 22% of women said they have rheumatoid arthritis (RA). Only 41% of participants knew that an optimal weight could prevent knee OA. About a third of men and women reported knee pain (KOOS QOL pain score < 70). Additionally, 25% of men, 35% of women, and 36% of those ≥ 65 years reported experiencing pain weekly, daily, or constantly. Furthermore, 40% of men, 53% of women, and 56% of those ≥ 65 years reported having fair or poor general health. Compared to a year ago, 50% of men and women rated their physical health as slightly or much worse. Although 95% of patients had medical insurance, most of the participants (84%) used alternative pain management such as massages, herbal medicines, and acupuncture.

Conclusion

Participants reported a high prevalence of both OA and RA despite a low prevalence of overweight or obesity. Many people were unaware of risk factors related to OA and how weight management is crucial in the prevention of this disease. The results may be limited by the participants' knowledge of medical conditions such as OA and RA. The next phase of the study will investigate and examine the reliability and validity of the translated instruments, the accuracy of self-reported OA and RA, and factors associated with poor health, including arthritis-related pain.

EXTERNAL FUNDING SOURCE

National Institute on Minority Health and Health Disparities

IRB NUMBER

2020-064

Analysis of Key Cellular Changes of Triple Negative Breast Cancer Cells in Response to Kinase-Inhibiting BI2536 and Associated Derivatives

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ABSTRACT TOPIC

Cancer

ABSTRACT

Purpose: Triple Negative Breast Cancer (TNBC) is a subtype of breast cancer that grows quickly and has higher rates of metastasis and reoccurrence relative to other Breast Cancer subtypes that make it, in general, a much more dangerous subtype of breast cancer. The Kinase Chemogenomic Set (KCGS) is a collection of 187 kinase-inhibiting compounds with broad activity across 215 different kinases. We hypothesize that this plate contains compounds with the potential to inhibit TNBC and that exploring the transcriptomic and proteomic changes in TNBC cells may give insights into novel treatment targets.

Methods: To test this hypothesis, we have utilized two main cell lines, the MDA-MB-231 line and a patient-derived xenograft line, the TuX-BxC-4IC cell line. Measurements have been taken at various time points up until 72 hours at various concentrations of a compound of interest, BI2536, between 1nM and 1uM. Primarily, data will be collected using qRT-PCR to gain insight into the transcriptomic changes during the potential EMT changes. Additionally, various other experiments related to migration, staining, and other essential markers will be conducted on the compound of interest and derivatives of the compound.

Results: Initial results and prior work indicate that the compound of interest has moderate success in slowing cancer cell growth. Additionally, initial findings indicate that the compound may succeed in halting and potentially even reversing the EMT process.

Conclusion: With this primary data set, we believe that the kinases targeted by the compound may hold potential key targets for the treatment of TNBC.

EXTERNAL FUNDING SOURCE

UNTHSC

Opportunities to Enhance Primary Care Management of Osteoporosis: A Mixed Methods Study

PRESENTER

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COLLEGE/SCHOOL

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ABSTRACT TOPIC

Other

ABSTRACT

Purpose: The incidence of osteoporotic fractures is greater than that of heart attack, stroke, and breast cancer combined. However, healthcare providers often focus on other comorbidities at the expense of bone health management. Primary healthcare is poised to play a significant role in protecting bone health, yet osteoporosis (OP) care is often delayed until after the initial fracture. This research aimed to determine potential gaps in primary care management of osteoporosis and to attain insight from multiple stakeholders' experiences to understand care expectations and opportunities to enhance services.

Methods: This research was performed within a geriatric practice setting using a convergent, mixed methods study design. This study included geriatric practice specialists from multiple disciplines (n=9) and patients selected to represent both male and female genders, diverse age groups, and varying bone health diagnoses (n=9). Quantitative data was attained through a 3-year (October 2018-2020) retrospective chart review to collect patient demographics, health-related measures, and outcomes. A physician survey provided further quantitative data on practice patterns and preferences. Qualitative data was attained through physician interviews and focus groups by engaging clinicians and patients on five key topics related to care decisions, screening, intervention, care expectations, and improvement opportunities. Quantitative descriptive data was used to attain varying distribution points on demographics and alignment with performance measures and clinical practice guidelines. Additional quantitative data was evaluated for consensus through responses from a Qualtrics physician survey regarding practice patterns and preferences. Qualitative data from focus groups and physician interviews were processed in distinct stages using Ritchie and Spencer's framework analysis. Integration of quantitative and qualitative results was achieved during analysis and interpretation.

Results: The chart review consisted predominantly of female patients, 95.9% (375/391). A diagnosis of osteopenia with and without fracture was 7.4% (29/391) and 22.3% (87/391); osteoporosis was 23.5% (92/391) and 46.8% (183/391), respectively. In the presence of osteoporosis or fracture, 44.7% (123/275) and 38.8% (47/121) were prescribed OP medication, respectively. 39.9% (156/391) presented with health conditions that could attribute the bone loss to secondary osteoporosis. 69.2% (259/372) of women \geq 65 y.o. age and 33.3% (5/15) of men \geq 70 y.o. age had a documented dual-energy X-ray absorptiometry (DXA). Per quality metrics, 73.8% (48/65) of women aged 67-85 received a DXA and/or 43.1% (28/65) received OP medications within 6 months of fracture. Physician surveys revealed consistent practice patterns between physicians except for drug monitoring practices and comfort with using anabolic therapies. The US Preventive Services Task Force guideline was the predominant resource for OP management guidance. The focus group and interviews yielded four main themes: 1) condition awareness and fracture risk; 2) pharmacotherapy hesitancy and intervention preferences; 3) expectations of care; and 4) opportunities to enhance care.

Conclusions: The findings identified gaps and opportunities to enhance primary care osteoporosis management, reflecting all stakeholder input. The data provides insight into pragmatic approaches for future quality improvement implementation to enhance primary care management of osteoporosis.

IRB NUMBER
1849825-2

Optogenetic Activation of PVN-projecting MnPO Neurons Induces Changes in Type I PVN Neurons

PRESENTER

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ABSTRACT TOPIC

Neuroscience

ABSTRACT

The paraventricular nucleus of the hypothalamus (PVN) is an important autonomic control center that receives afferent inputs from the median preoptic nucleus (MnPO). The link between the MnPO and the PVN is essential in generating chronic intermittent hypoxia hypertension. An optogenetic intersectional viral approach was used to gain more insight into the contribution of MnPO inputs to changes in PVN function that could contribute to hypertension. Adult male Sprague-Dawley rats were anesthetized with isoflurane and injected with 100 nL of AAV9.hSyn.HI.eGFP-cre.WPRE.SV40 in the PVN bilaterally and AAV1-Ef1a-DIO-hChR2(H134R)-mCherry-WPRE-HGHpA in the MnPO. This method induced a CRE-dependent expression of channel rhodopsin in PVN-projecting MnPO neurons. Three weeks after the injections, the rats were sacrificed and oblique brain slices containing PVN were made. Postsynaptic currents (PSCs) were recorded from PVN neurons ($V_{\text{Hold}} = -70$ mV) with an aCSF (2-3 ml/min) bath solution. MnPO axon terminals in the PVN were stimulated with 15 Hz LED-generated blue light (470nm) pulses of 20-ms duration for a total of 1 min with an optical fiber directed at PVN. The stimulation train was repeated 5 times at 5 minutes intervals. PSCs were recorded for 40 minutes, including 5 min baseline periods before stimuli and 10 min post-stimulation period. Intrinsic excitability was assessed before the first baseline and after the last stimulation. Cells were characterized as type I, type II, or type III PVN neurons based on the presence of transient outward rectification. Amplitude and frequency data were analyzed offline using Easy Electrophysiology v2.5.0 software from a total of 17 Type I PVN neurons. Optogenetic stimulation evoked EPSC or mixed EPSC/IPSCs in 13 Type I neurons. From the 13 photo-evoked neurons, 10 neurons showed a significant increase in EPSC frequency following intermittent stimulation as compared to the preceding baseline (1st: 6.149 ± 1.438 Hz vs 27.377 ± 5.474 Hz, $p=0.0187$; 2nd 7.532 ± 1.670 Hz vs 27.562 ± 5.514 Hz, $p=0.0161$; 3rd 7.395 ± 1.659 Hz vs 25.415 ± 5.028 Hz, $p=0.0170$; 4th 7.343 ± 1.466 Hz vs 24.225 ± 4.750 Hz, $p=0.0183$; 5th 6.709 ± 1.375 Hz vs 21.837 ± 4.464 Hz, $p=0.0220$). In the same neurons, spontaneous EPSC frequency in the first minute after stimulation trains 1 to 4 also was significantly higher than the first pre-stimulus baseline but the effect gradually decreased over time (baseline 6.149 ± 1.438 Hz vs 14.615 ± 3.260 Hz, $p=0.0236$; vs 12.055 ± 2.519 Hz, $p=0.0213$; vs 10.904 ± 2.340 Hz, $p=0.0247$; vs 9.801 ± 2.027 Hz, $p=0.0331$). There were no changes in EPSC amplitude. More type I neurons with photo-evoked PSCs showed increased excitability after the last stimulus (4 out of 7) than those which did not respond to the optogenetic light (2 out of 6). Repetitive optogenetic stimulation of MnPO inputs to Type I PVN neurons increased EPSC frequency and intrinsic excitability in a time-dependent manner. Additional experiments will be needed to specify the mechanism behind the increase in frequency and whether this phenomenon occurs in other PVN cell types.

EXTERNAL FUNDING SOURCE

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Sex differences in the activation of central autonomic control regions and neuroinflammation in chronic intermittent hypoxia

PRESENTER

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COLLEGE/SCHOOL

School of Biomedical Sciences

ABSTRACT TOPIC

Integrative Physiology

ABSTRACT

Purpose: Obstructive sleep apnea (OSA) is an independent risk factor for hypertension. Chronic intermittent hypoxia (CIH), which models episodic hypoxemia of OSA, produces daytime hypertension, oxidative stress, and activation of central autonomic regions that regulate mean arterial pressure (MAP) in male Sprague Dawley (SD) rats. Unlike gonadally intact females, gonadectomized females and males develop CIH hypertension. Lesioning of median preoptic nucleus (MnPO) in males prevents CIH hypertension. We hypothesize that the sex difference observed in CIH hypertension is due sex differences in neuroinflammation and activation of central autonomic regions that support MAP in CIH.

Methods: Gonadally intact adult male and female SD rats (250-300g) were continuously exposed to normoxia (CON) or CIH (10% O₂ every 3mins cycling 21% O₂ every 3mins, 8h/day) for 7 days. Radiotelemetry transmitters were implanted in rats to record MAP and heart rate (HR). After one week of baseline recording, the rats were exposed to either continuous normoxia or CIH and were euthanized (inactin 100 mg/kg ip) on the 8th day for immunohistochemistry and blood analysis. All forebrain sections were stained for FosB/ Δ FosB and either neuronal nitric oxide synthase (NOS1) or IBA1 to identify active microglia.

Results: CIH males exhibited significantly increased hematocrit indicating erythropoiesis compared to control males (CON 42.1% \pm 0.6, n=10; CIH 44.6% \pm 0.7, n = 10. P = 0.0173). CIH males exhibited an increase in the average number of FosB positive neurons (CON male 20 \pm 2 cells/section, CIH male 35 \pm 3; CON female 11 \pm 1, CIH female 12 \pm 2,) and colocalization of FosB and NOS1 (CON male 10 \pm 1 cells/section, CIH male 18 \pm 4; CON female 5 \pm 1, CIH female 6 \pm 1) in the MnPO. CIH females showed a trend for an increase in the average number of IBA1 immunoreactive microglial cells in MnPO (CON 187 \pm 16, n = 2; CIH 218 \pm 18, n = 4).

Conclusion: CIH is associated with increased FosB staining in the MnPO of male rats as opposed to female rats which is consistent with our working hypothesis. In addition, FosB positive MnPO neurons also contained NOS1. In female rats, CIH is associated with a trend for an increase in the numbers of IBA1 positive microglia, indicating increased neuroinflammation in females that is independent of hypertension. CIH was associated with increased FosB staining in NOS1 positive MnPO neurons suggesting that they may be contributing to the sustained hypertension reported in male rats.

EXTERNAL FUNDING SOURCE

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IACUC NUMBER

IACUC-2021-0012

Ligand Identification for the Orthosteric site of Sigma 1 Receptor using Computational Molecular Docking and Virtual Screening Methods

PRESENTER

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ABSTRACT TOPIC

Pharmaceutical Sciences

ABSTRACT

Purpose: The σ 1 Receptor (Sig-1R) is a ligand operated membrane protein resides in the mitochondria-associated-membranes of the endoplasmic reticulum (ER). At the molecular level, Sig-1R has several important roles in cellular homeostasis, including Ca^{2+} regulation, and helping chaperone the unfolded protein response. This ER stress has been found to be one of the factors leading to cytokine storm and clinical deterioration in patients with a coronavirus infection, leading to an interest in drugs which modulate the response of the Sig-1R for treatment of COVID-19.

These receptors are found throughout the CNS as well as the periphery, explaining its wide range of effects throughout the body. At the organ level, studies conducted on the Sig-1R have implicated its involvement in neurodegenerative diseases such as Parkinson's and Alzheimer's Disease, cardiac diseases such as heart failure and cardiovascular disease (CVD), and major depressive disorder. This implication in a wide variety of disease states means it has a large potential as a drug target. Our study's purpose is to identify novel potential drug candidates at the orthosteric binding site of Sig-1R with high binding affinity, specificity, and favorable PK parameters using a structure-based drug design approach.

Method: Prior work in this lab found a list of the top 1000 orthosteric ligands by docking Sig-1R against libraries containing 9,270 small drug-like molecules using the TACC drug discovery tool. These libraries were extracted from the ZINC database. From this list of 1000 compounds, we selected the top 130 compounds (binding affinity cut-off ≥ -11.0 kcal/mol) and re-docked against the Sig-1R using the efficient docking suite Glide in Maestro. Also, we analyzed the pharmacokinetic/ADME parameters of these compounds using SwissADME, identifying possible candidates to use as our scaffold to try and design a ligand with even stronger binding affinity to the orthosteric site of Sig1R. Furthermore, we docked 130 compounds with the Dopamine Receptor D2 (D2R) to analyze their specificity for the Sig-1R.

Results: Using an extra precision molecular docking in Glide, we found that our molecule 106 (-12.88 kcal/mol), molecule 105 (-12.83 kcal/mol), and molecule 100 (-12.29 kcal/mol) all had very high binding affinity for the Sig-1R. Both Molecules 105 and 100 had favorable PK parameters, as both were estimated to be BBB permeable, as well as not breaking any aspects of Lipinski's Rule of Five. Molecule 100 was also found to have relatively low binding affinity (-7.6 kcal/mol) for the D2R.

Conclusion: Using our computational molecular docking methods, we have identified molecule 100 as a ligand with strong affinity and specificity for the Sig1R, as well as favorable PK parameters. This could be a strong candidate to use as a chemical scaffold to develop a ligand with even stronger binding affinity for Sig-1R, which can eventually go on to in-vitro assays to confirm activity.

EXTERNAL FUNDING SOURCE

Summerfield G. Roberts Foundation

The Correlation Between Menopause and Quiet Standing Variable Changes

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Purpose: During menopause, individuals experience hormonal changes that can affect body systems contributing to balance. It has been established that balance declines with increasing age, but cohort studies have shown that there is a significant increase in falls during the perimenopausal phase of an individual's life. A previous study has also been able to relate kyphosis and osteoporosis, postmenopausal changes often associated with estrogen deficiency, to altered standing balance specifically an increase in velocity of the center of pressure (COP) displacement compared to premenopausal females, though this study had a relatively small sample size. The purpose of our study is to measure sway to determine if there are meaningful balance changes that occur during the menopausal transition. This could indicate intervention strategies and decrease risk for falls in postmenopausal females.

Methods: Data was obtained from ongoing quiet standing project at the University of North Texas Health Science Center (UNTHSC). Patients visiting the osteopathic manipulative medicine (OMM) and geriatric clinic were asked to quietly stand on a Bertec force plate (Bertec, Columbus, Ohio) for 30 seconds with their eyes open and eyes closed. A total of 475 females were stratified into two groups those less than 48 years old were considered premenopausal (total = 188) and those 48 and older were considered perimenopausal or postmenopausal (total = 287).

Results: When comparing the menopausal group to the pre-menopausal group with eyes open, 13 out of 20 sway variables showed a statistically significant difference, similarly with eyes closed, 17 out of 20 variables showed statistical significance. The most significant changes in variables in participants with their eyes open were found for the range of the COP in the anterior posterior direction (AP) and velocity. For the premenopausal group, the average range of COP AP direction was 13.09 mm, while the average range of COP AP in the postmenopausal group was 16.45 mm. The velocity showed a similar change in that the premenopausal group showed an average velocity of 7.84 mm/s², while the menopausal group had an average velocity of 10.76 mm/s².

Conclusion: The increase in the average range of COP AP and average velocity between the two groups leads us to hypothesize that the menopausal group may have a decline in postural control due to hormonal changes. With the significant difference in the majority of the SWAY variables, it appears the menopausal group has increased movement during quiet standing at an increased velocity. Suggesting that this group is having increased difficulty in modulating the position of their body, which could lead to increased likelihood of fall. We also hypothesize that the menopausal group likely relies on vision more for stability because of age related changes in proprioception and strength. Further studies would be required to determine if these changes are related to age or menopause. In the future, identifying balance changes associated with menopause should be studied. This will lead to better monitoring and early preventative measures to prevent falls.

IRB NUMBER

1455048-11

Design of Man-made Miniature CRISPR-Cas Proteins Using Computational and Artificial Intelligence Technologies

PRESENTER

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COLLEGE/SCHOOL

Postdoctoral Fellow

ABSTRACT TOPIC

Other

ABSTRACT

Purpose: The CRISPR/Cas system is a popular genome editing technique that uses a guide RNA and specific proteins known as Cas proteins for its function. A major challenge in harnessing CRISPR-Cas technology for applications in living organisms is the lack of an efficient delivery system. Due to the larger size of available Cas proteins used in this tool, it is challenging to encapsulate the CRISPR components into a single vehicle for delivery. To address this issue, we have used computational and Artificial Intelligence (AI) tools on designing compact-size Cas proteins that have a similar function and are more efficient than available Cas proteins.

Methods: The available crystal structures of the smallest CRISPR-Cas systems were utilized and further reduced. A novel method termed the “Blocks and Gaps approach” was employed to design new mini-Cas proteins with a size range of 450-500 amino acids in length. The generated protein sequences (1 million) were subsequently used in machine learning-based two classification models to filter out the non-Cas proteins from it. The resultant Cas protein sequences were used in homology-modeling-based (Swiss-Model) and AI-based (AlphaFold2) protein structure prediction methods to obtain their 3D structures. Further, the global and local structural features as well as the solubility of these proteins were analyzed, and top candidates were subjected to molecular dynamics (MD) simulations including substrate DNA and gRNA.

Results/Conclusions: A library of man-made miniature Cas proteins was generated, and these proteins are less than half the size of the widely used CRISPR-Cas such as Cas9 or Cas12a. 50% of these were predicted as Cas proteins by both the machine learning-based classification models used. And 90% of them show similar 3D structures as their original counterparts. 10% of these passed through the final validations. Experimental testing of the activity of these designed proteins is to be investigated at this point of the study.

Oral Health Disparities among LGB and Non-LGB Individuals in the United States, 2007-2016

PRESENTER

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School of Public Health

ABSTRACT TOPIC

Health Disparities

ABSTRACT

Purpose: Although oral health in America has generally improved over recent decades, health disparities in the field have remained an issue for several marginalized groups, one such being lesbian, gay, and bisexual (LGB) individuals. Few studies have investigated oral health outcomes in LGB individuals in comparison with their heterosexual counterparts. As such, the aim of this study was to examine potential oral health disparities among a national sample of American adults and investigate sex-differences in the association between sexual orientation and poor oral health.

Methods: We used pooled data (2007-2016) from the National Health and Nutrition Examination Survey (NHANES) for men and women aged 18-59. Multiple imputation methods were used to impute missing data. Multiple logistic regression models were used to examine the association between sexual orientation and self-reported oral health, both overall and separately for men and women.

Results: A total of 20,298 responses were included in this analysis. Compared with heterosexuals, LGB individuals had higher odds of reporting poor oral health than heterosexuals in both the unadjusted (OR = 1.20 95% CI = 1.04-1.38) and adjusted (OR= 1.21 95% CI 1.04-1.40), combined analyses. In the unadjusted sex-stratified analyses, sexual orientation was found to have a statistically significant association with poor oral health in females (OR= 1.51 95% CI = 1.26-1.79). After adjusting for covariates, women who were LGB had a 38% statistically significant increased odds of having poor oral health compared with their heterosexual counterparts (OR= 1.38 95% CI 1.14-1.67). Sexual orientation was not associated with poor oral health in males, with adjusted odds close to null comparing LBG men with their heterosexual counterparts (OR = 0.98, 95% CI = 0.74 - 1.29).

Conclusion: This study explored oral health disparities among a large national sample of LGB Americans. Widening disparities continue to persist among minority populations, despite recent progress made in oral health settings. The findings in this study add to the information base of disparities prevalent in the field of oral health and may inform future interventions and public health frameworks.

Cannabis and its effect on health outcomes and behaviors of UNTHSC graduate students

PRESENTER

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COLLEGE/SCHOOL

School of Public Health

ABSTRACT TOPIC

General Public Health

ABSTRACT

Purpose: The rate of cannabis usage is high among graduate students. According to the reference data of the National College Health Assessment survey of Spring 2022, 42.4% of graduate students reported cannabis use sometime in their life. Cannabis use is often linked with the use of alcohol, tobacco, and other drugs but there is limited research on its relationship to mental health outcomes such as anxiety, depression, and stress among graduate students. There is also limited information about the effect of cannabis use on academic success, which is often a significant concern among graduate students. The purpose of this study was to assess the associations of cannabis use with health outcomes and behaviors among graduate students.

Method: The National College Health Assessment (NCHA) survey data collected by the Office of Care and Civility of UNTHSC were analyzed after approval from the Institutional Review Board. Variables included were cannabis use (ever used or never used), anxiety (ever diagnosed or never diagnosed), depression (ever diagnosed or never diagnosed), tobacco use (ever used and never used), alcohol consumption (ever consumed or never consumed), stress (no, low, moderate, high), and if cannabis use has affected academic performance in the past years (yes or no). A descriptive analysis using Chi-square tests and Fisher's Exact tests were conducted using RStudio, with a p-value of <0.05 being considered significant.

Results: In total, 32.2% of graduate students on the UNTHSC Campus reported non-medicinal use of cannabis sometime in their life. A total of 29% of cisgender men, 33% of cisgender women, and 50% of transgender/gender non-conforming graduate students on campus reported using cannabis ever in their life. Statistically significant associations were found between the use of cannabis and anxiety ($p=0.0003$), cannabis use and depression ($p=0.006$), cannabis use and alcohol use ($p<0.0001$), and cannabis use and tobacco use ($p<0.0001$). No significant associations were noted between cannabis use and stress ($p=0.76$) and the influence of cannabis use on academics ($p=0.27$).

Conclusion: We noted that cannabis use was associated with mental health outcomes and other substance use among this sample of graduate students. The results from this analysis will guide the Office of Care and Civility to develop future health programming on campus with a more holistic approach. Moreover, mental health outcome numbers are high among graduate students on the UNTHSC campus, and programming or awareness campaigns for cannabis might be effective in addressing mental health outcomes as well. However, since this study is a cross-sectional study, we cannot comment on causation, but future work may benefit from further exploring these relationships to determine causality.

Enhancing the translational relevance of the nicotine drug discrimination paradigm in rat model

PRESENTER

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COLLEGE/SCHOOL

School of Biomedical Sciences

ABSTRACT TOPIC

Neuroscience

ABSTRACT

Purpose: Drug discrimination has over the past 50 years been used as a tool for understanding mechanisms of drug addiction. As an operant conditioning-based technique, it is largely influenced by the specific rat training conditions such as training dose and pre-treatment time (PT). A nicotine training dose of 0.4 mg/kg at a PT of 15 min is widely used in nicotine discrimination studies. This dose in rats, however, produces a peak plasma concentration that comparatively exceeds the peak plasma concentration in tobacco smokers. Pharmacokinetic studies have shown that smaller doses of nicotine in rats produce peak plasma concentrations that closely resemble that in human cases. The question that remains is whether rats can be trained to discriminate these smaller doses of nicotine. Our goal was therefore to re-evaluate nicotine training conditions in rats and find that which is trainable and produces a translatable pharmacokinetic profile.

Methods: Using a two-bar drug discrimination operant chamber, six rats trained to discriminate 0.4 mg/kg of nicotine tartrate at a PT of 15 min were tested at a fixed dose (0.4 mg/kg) of nicotine tartrate, but at different intervals after injection (0, 5, 15, 30, 60, 120, 240 min). This test was repeated but at a fixed dose of 0.1 mg/kg. Subsequently, a nicotine dose effect (0.01, 0.025, 0.05, 0.1, 0.2, 0.4 mg/kg) was conducted at a fixed pre-treatment time (5 min). Percentage of drug lever responses were recorded in all studies to measure substitution and analyzed using repeated measures ANOVA.

Results: The time course study conducted with 0.4 mg/kg showed full substitution (100% nicotine lever response) at a PT of 5 min, with 240 min as the longest duration of action. The dose effect study at a fixed PT of 5 min showed full substitution at 0.1 mg/kg. At that, the discriminative effects of nicotine faded within 15 min.

Conclusion: These findings show even at lower doses and shorter PTs, rats can perceive nicotine, and therefore can be trained using a lower nicotine dose of 0.1 mg/kg and at a shorter PT of 5 min (an onset that more closely resembles the onset in humans after smoking a cigarette compared to 15 min PT) Using these training conditions in place of the high training dose (0.4 mg/kg) and the long PT (15 min) provides a nicotine discrimination model of higher translational relevance to nicotine smoking studies in humans.

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IACUC NUMBER

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Use of the General Movement Assessment as an Early Marker of CP

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ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Purpose: Cerebral palsy (CP) is the most common physical disability in children affecting 1 in 500 live births. The average national standard of detecting CP occurs after 2 years of age by analysis of neurological signs. Since December 2014, the NICU Early Support and care Transition (N.E.S.T.) Clinic at Cook Children's Medical Center has provided multidisciplinary comprehensive follow-up to high-risk NICU survivors. Cook Children's Medical Center implemented an Early CP detection program in 2019 using the General Movement Assessment (GMA) in the NICU and NEST Clinic. There has been emerging evidence that evaluation of general movements in early infancy (writhing and fidgety periods) is predictive of a future CP diagnosis in an infant. This early diagnosis is key for better neurodevelopmental outcomes.

Methods: Infants who met inclusion criteria had GMA videos captured shortly after birth during the NICU stay. Infants with abnormal GMA videos had further evaluation at 3-4 months corrected gestational age, during their NEST clinic visit. The data from the NEST clinic were then compiled to include high-risk variables. Retrospective review and analysis of data previously collected for the Early CP detection program was performed under the direction of Dr. Yvette Johnson and her Early Detection Team. Univariate Cox regression analyses were performed to determine which variables were predictive of CP diagnosis.

Results: There were 471 patients who met inclusion criteria, including 292 (62%) very low birth weight (VLBW), 131 (28%) hypoxic-ischemic encephalopathy (HIE), 15 (3%) congenital diaphragmatic hernia (CDH), 8 (2%) extracorporeal membrane oxygenation (ECMO), and 25 (5%) congenital heart disease (CHD) infants. Four hundred ten (87%) had GMA's in the writhing phase and 205 (44%) had GMA's in the fidgety phase. The median (range) age of CP diagnosis was 1.07 (0.34-1.93) years, and 91% had been diagnosed by 1.50 years. The infants with HIE had a statistically significant increased risk of CP diagnosis compared to those in the VLBW category (10% vs. 6%, HR=2.50, p=0.014). The infants with an absent or abnormal fidgety GMA interpretation during the fidgety period had a statistically significant increased risk of CP diagnosis compared to those with other interpretations (46% vs. 3%, HR=15.69, p<0.0001).

Conclusion: The results showed that having an abnormal or absent fidgety general movements during the fidgety phase was a significantly strong predictor of CP outcomes. These data can be extrapolated in clinical settings to provide early and evidence-based interventions that can improve long-term functional motor outcomes.

IRB NUMBER

2022-020

Characterization of Bilingual Mexican Americans among a Community Dwelling Cohort: An HABS-HD Study

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ABSTRACT TOPIC

Aging / Alzheimer

ABSTRACT

Introduction: Bilingualism has been increasingly studied in the context of neuroprotection particularly as it relates to cognitive decline. Despite higher rates of English/Spanish bilingualism, Mexican Americans also experience a higher risk of cognitive decline related to Alzheimer's disease (AD) and Alzheimer's Disease Related Dementias (ADRDs) as compared to Non-Hispanic Whites. Few studies to date have broadly examined the link between bilingualism and specific demographic, cognitive, and biomarkers among this ethnic group. The aim of this study is to examine the relationship between language status (monolingual/bilingual) on select demographic, cognitive, and AD specific blood biomarkers among this racial/ethnic group.

Methods: Data were analyzed on n=890 Mexican Americans from the The Health & Aging Brain Study - Health Disparities (HABS-HD) study. Participants completed a clinical interview, which includes a self-report of language status (monolingual/bilingual) as well as various neuropsychological tests and an informant interview in order for clinicians to determine cognitive and functional status. Plasma amyloid (A), tau (T), and neurofilament light chain [NfL](N) blood biomarkers were assayed using the ultra-sensitive Single molecule array (Simoa) technology. Demographic characteristics were generated utilizing independent t-tests or chi square analyses for continuous and/or categorical variables. ANCOVAs were conducted with covariates of age, sex, and education for cognitive test performance and A/T/(N) blood biomarkers split by language status (monolingual, bilingual) as well as by cognitive status (cognitively unimpaired, cognitively impaired).

Results: Of the n=890 Mexican Americans, n=393 self reported as monolingual and n=497 as bilingual. Among monolinguals, 70% were diagnosed as cognitively unimpaired, 20% with mild cognitive impairment (MCI), and 10% with Dementia while among bilinguals, 78% received a diagnosis of cognitively unimpaired, 17% with MCI, and 5% with Dementia. Regarding neuropsychological testing, bilingual individuals performed significantly better across measures of global cognition, attention, and processing speed ($p < 0.001$). While examining blood biased biomarkers, a trending significance of higher total tau was found among bilinguals compared to monolinguals. When separated by cognitive status, total tau was higher among bilingual Mexican Americans who were cognitively unimpaired ($p = 0.044$). Higher A β 40 levels were found to be significantly associated with reduced performance on measures of attention, processing speed, and executive functioning among bilinguals who were cognitively unimpaired ($p < 0.001$). Among bilinguals with cognitive impairment, higher total tau levels were associated with lower performance on a measure of working memory ($p = 0.001$) and higher NfL levels were associated with lower performance on measures of global cognitive screening measure and working memory ($p = 0.001$).

Discussion: As rates of AD and ADRDs increase in Mexican Americans, their bilingualism may be advantageous in delaying this pathology. Bilingualism is differentially related to cognitive and AD biomarkers. Better understanding the relationship between bilingualism and these markers might be informative regarding potential protective effects for this at risk group.

IRB NUMBER

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Characteristics and Outcomes of Patients With Hepatocellular Carcinoma Diagnosed at John Peter Smith Hospital

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ABSTRACT TOPIC

Cancer

ABSTRACT

Purpose: The incidence of hepatocellular carcinoma (HCC) is increasing in the US, particularly in individuals infected with hepatitis C (HCV). Although early detection is crucial for better outcomes, at present, there is conflicting evidence regarding HCC screening and its reduction on cancer-related mortality. This study aimed to determine overall survival, prognostic factors influencing survival, and the effects of screening at-risk patients on HCC-related mortality.

Methods: A retrospective chart review of patients diagnosed with HCC from 1/1/2018 to 6/4/2021 for the one-year survival analysis and 6/4/2019 for the three-year analysis. Person-time was calculated as the days from the date of diagnosis until the last known encounter or death. The primary exposure of interest was screening within two years prior to the diagnosis date via ultrasound, MRI, and/or CT. Potential covariates were age at diagnosis, race/ethnicity, gender, insurance status, alcohol use disorder, HCV, HBV, and cirrhosis. Kaplan Meier, log rank test, and Cox proportional hazards (CPH) model were used to assess survival curves, survival distributions across screening status, and the effects of additional covariates on prognosis at one and three years, respectively. A backwards stepwise regression was used on the covariates identified via a pre-univariate filtering to construct a multivariable model.

Results: There were 165 and 71 patients who met the one- and three- year inclusion criteria, respectively. Survival at one and three years was 38% and 14%, respectively. Median survival for the 165 patients was 265 days (95% CI: 166, 337). Overall, 36% (n=59/163; 2 missing) and 27% (n=19/70; 1 missing) were screened prior to diagnosis. The CPH model showed a statistically significant difference in hazard ratio of death in the first year for those without screening compared to patients with screening (HR: 1.9; 95% CI: 1.2, 3.0; p-value: 0.005). After adjusting for race/ethnicity and insurance type, the CPH model yielded similar results (HR: 2.2; 95% CI: 1.3, 3.6; p-value: 0.002). The CPH model showed a statistically significant difference in hazard ratio of death in three years for those without screening compared to patients with screening (HR: 3.4; 95% CI: 1.7, 7.1; p-value: 0.001). After adjusting for gender, HBV, and race/ethnicity, the CPH model yielded similar results (HR: 2.2; 95% CI: 1.2, 4.0; p-value: 0.009).

Conclusion: Overall survival in patients diagnosed with HCC at JPS, a safety-net hospital, is similar to national statistics. Screening in patients at-risk for HCC shows improved survival at one and three years. Further evaluation based on the extent of disease at the time of diagnosis, treatment decisions, and type/timing of screening could be beneficial in determining the outcomes in HCC patients.

IRB NUMBER

2022-052 EXEMPT

The Impact of the Social Determinants of Health on a Patient with Renal Cell Cancer: A Case Report

PRESENTER

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Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Health Disparities

ABSTRACT

Background: Renal cancer is the seventh most common cancer and 90% of cases are renal cell carcinoma (RCC). Symptoms of RCC may include hematuria, abdominal/flank pain, or fatigue, but over half of those with RCC are asymptomatic and diagnosed incidentally by an unrelated abdominal imaging study. Renal tumor size provides the greatest insight into a patient's chance of survival. For every 1 cm increase in tumor size there is a 16% increase in malignant potential and masses greater than 7 cm have only a 7% chance of being benign. RCC has a 40% mortality rate that disproportionately affects those of low socioeconomic status (SES) who often present with larger and more advanced RCC. This correlation with low SES reflects decreased healthcare access and an increased prevalence of poor prognostic factors including obesity, hypertension, and hyperlipidemia. Additionally, patients without health insurance are 5.6% less likely to survive RCC.

Case Information: A 56-year-old Hispanic male first presented to a community clinic in Fort Worth, Texas in early 2017 for occasional fatigue and right flank pain that began in 2002. In addition to managing his hypertension, diabetes mellitus, and hyperlipidemia, the physician ordered an abdominal and pelvic CT that revealed a 5.4cm cystic and solid-enhancing right renal mass that was highly suspicious for RCC. Further disease progression was suggested with a 2019 ultrasound showing internal blood flow to the solid component of the mass and 2022 laboratory studies that revealed an elevated BUN (21 mg/dL), serum calcium (10.6 mg/dL), and ALT (56U/L). At the end of 2022, the patient brought in his latest CT report that he could not read because it was only provided in English. The CT revealed the 6.4cm x 4.1cm x 3.7cm mass and while medical translators communicated with the patient, differences in language may have impacted his understanding of his condition. For five years imaging and labs were performed repeatedly to monitor the large tumor, but treatment was never initiated because the patient believed he could not afford care without health insurance. The patient was referred to a local charity program for evaluation, but the program had a policy of not providing cancer treatment. The patient was encouraged to seek treatment in the local county health system, but he believed he could not afford treatment there or the expenses to relocate for treatment elsewhere. At this point, no further options exist for the patient.

Conclusions: Surgery would provide the greatest odds of survival for this patient, and ideally, it would have been performed before the mass reached such a concerning size. However, the patient believed he could not afford care without health coverage. With such a dismal prognosis, one can only speculate how the outcome would have changed if prompt medical care had been accessible to the patient. His financial resources, health coverage, language barrier, documentation status, and lifestyle all contributed to the unfavorable disease progression. This case serves as a single example of how social determinants of health continue to alter patient outcomes.

Changes in cardiac oxidative stress, nitric oxide bioavailability, mitochondrial function, and blood pressure in postpartum preeclamptic rats

PRESENTER

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ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Background: Preeclampsia (PE) is characterized by new onset hypertension (HTN) during pregnancy that usually occurs in the third trimester and is associated with decreased nitric oxide (NO) bioavailability, increased oxidative stress (OS), and mitochondrial dysfunction. Postpartum (PP) PE women have an increased risk of developing HTN and cardiovascular diseases (CVD) later in life. The timing and mechanisms of this rise in blood pressure (BP) and cardiovascular dysfunction in PP PE women are unknown. Previous studies in our lab indicate that PP PE rats have HTN, increased OS, and cardiac mitochondrial dysfunction at 10 weeks (PP10) (PMID: 34727994). Our current study examines the relationship between BP and cardiac NO bioavailability, OS, and mitochondrial dysfunction at 6 weeks (PP6), an earlier time point from our previous study. We hypothesize that PP6 PE rats will have HTN, increased cardiac OS, decreased cardiac NO bioavailability, and mitochondrial dysfunction.

Methods: Pregnant Sprague Dawley rats were divided into 2 groups: normal pregnant rats (NP) and PE rats, derived from the surgically induced reduced uterine perfusion pressure model of PE (RUPP). All rats gave birth, and their offspring were weaned for 3 weeks. At PP6, BP was measured via carotid catheterization and heart tissues were collected to measure heat shock protein (HSP-1) (a measure of OS), copper zinc superoxide dismutase (CuZnSOD) (an antioxidant), manganese SOD (MnSOD) (a mitochondrial specific antioxidant), endothelial NOS (eNOS) (a measure of NO producing enzyme), and electron transport chain (ETC) proteins (a measure of mitochondrial function). These quantities were obtained through Western blots.

Results: BP was significantly elevated in PP RUPP vs PP NP rats (128 ± 6 vs 106 ± 4 mmHg, $p < 0.05$). HSP-1 was significantly decreased in PP RUPP vs PP NP rats (88 ± 1.51 vs 100 ± 4.05 IU/Protein/CON%, $p < 0.05$). CuZnSOD showed no change between the two groups while MnSOD was drastically increased in PP RUPP vs PP NP (123 ± 2.91 vs 100 ± 5.30 IU/Protein/CON%, $p < 0.05$). eNOS and ETC proteins were unchanged between PP RUPP and PP NP rats.

Conclusion: Contrary to our hypothesis, PP6 PE rats have HTN with no increase in cardiac OS (due to decreased HSP-1 and increased in MnSOD amount) or decrease in cardiac NO bioavailability and mitochondrial dysfunction. These observations are different from our 10-week PP PE rats and may suggest that the heart is protected at 6 weeks PP despite the increase in blood pressure. Future studies will focus on the time frame in which cardiac dysfunction occurs in PP PE rats. Additionally, studies will explore the antioxidant, NO, and mitochondrial pathways along with other cellular mechanisms that may prevent the heart from damage and/or dysfunction after a PE pregnancy. This study is clinically relevant because it will inform clinicians on the mechanisms of HTN and cardiac dysfunction in women following a PE pregnancy as well as provide insights on therapies that could be used to prevent the development of CVDs later in life for PP PE women.

IACUC NUMBER

IACUC-2021-0037

SARS-CoV-2 induced exacerbation of HbA1c in Type 2 Diabetics

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Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Diabetes

ABSTRACT

Background: The Covid-19 pandemic started when severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was discovered in Wuhan, China. Although the majority of those infected suffer mild symptoms and recover, it is estimated that about 20% of infected patients can develop pneumonia, and some of these patients can develop acute respiratory distress syndrome (ARDS). Diabetes mellitus is a complex disease that affects millions of people worldwide. When it comes to type 2 diabetes mellitus the CDC reports that about 11.3% of the United States population is affected by diabetes.

Case Presentation: A 56-year-old Hispanic male presented to the clinic for his routine 6-month diabetes follow-up. He had a medical history of type 2 diabetes mellitus, morbid obesity, benign hypertension, BPH without urinary obstruction, and unspecified hyperlipidemia. For his diabetes, the patient took 500 mg metformin, 4 mg glimepiride, and 2 mg/dose semaglutide. The patient had been compliant with his medication. His only relevant family history included his mother with a diagnosis of diabetes mellitus. The patient denied constitutional, cardiovascular, respiratory, and neurological ROS questions. There was no change in the patient's medical history except that he had contracted SARS-CoV-2 three months before the visit. The patient described his symptoms, and his infection was classified as a mild version of the disease. The patient's vitals were within normal limits, and he had a BMI of 37.3. His general, cardio, respiratory, and skin PE findings were all normal as well. HbA1c was recorded at 10.2% and his estimated average blood glucose was 242 mg/dl. Both values had increased from 7.1% and 157 mg/dl respectively since his previous visit on July 22, 2022. At this current visit, his (nonfasting) glucose was 324 mg/dl. The patient's semaglutide was stopped and replaced with tirzepatide in hopes of reducing his HbA1c along with helping him lose weight. Unfortunately, the patient could not tolerate a higher dose of metformin.

Discussion: The question remains whether this patient's sudden increase in HbA1c of 3.1% from 7.1% to 10.2% could be attributed to the patient's mild infection of COVID-19. A study published by Joshi & Pozzilli in 2022 in the Diabetes Research and Clinical Practice journal found that SARS-CoV-2 can dysregulate glucose homeostasis even in patients with no previous risk factors for diabetes mellitus. One report that studied the relationship between these two variables found that there was an association between severe COVID-19 and increased blood glucose. They also found that HbA1c was slightly elevated in those with severe COVID-19 compared to mild COVID-19 however, this finding did not reach significance. Physicians taking care of type 2 diabetic patients can caution their patients on the possibility of being infected with COVID-19 and worsening their A1c levels. For those patients battling a severe form of COVID-19, their A1c levels could also be measured after the infection to rule out COVID-19-induced diabetes mellitus. This case report also expands the list of long-term complications from COVID-19.

Machine Learning Based Classification of CRISPR-Cas Proteins Using Complete Protein Spectrum

PRESENTER

AUTHOR(S)

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COLLEGE/SCHOOL

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ABSTRACT TOPIC

Molecular Genetics

ABSTRACT

Purpose: Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) and its associated (Cas) proteins together form the CRISPR-Cas system. The CRISPR-Cas system typically forms the machinery for innate defense mechanism in prokaryotes against foreign genetic elements such as phages and plasmids. The recent development of this mechanism into a gene editing technology holds a promise to correct gene level defects for several genetic diseases. The key element of CRISPR-Cas system is the Cas protein that are nucleases and possess the ability to edit gene of interest. Different types of Cas proteins are involved in different CRISPR-Cas systems. Cas proteins however suffer from inherent limitations like specificity and off-target effects which limits its widespread application as a gene editing tool. In the current study, a novel method has been developed for classifying the Cas9 and Cas12 families. Existing classification tools have a low overall accuracy and are usually built using only a few types of protein features. We also attempt to understand the different protein features governing the Cas9 and Cas12 classes using a multitude of protein features.

Method: We built Random Forest (RF) binary classifiers to classify Cas12 and Cas9 proteins respectively using the complete spectrum of protein features (13,495 features) encoding the physiochemical, constitutional, and evolutionary information. Additionally, we also built multiclass RF classifiers that differentiates between Cas9, Cas12 and non-Cas proteins. The performance of all models was evaluated using a 5-fold cross validation and six evaluation metrics like accuracy, precision, recall, F1-score, AUC score and specificity. We also tested our models on the respective independent datasets that were developed in-house from various public domain databases.

Results: The Cas12 and Cas9 models achieved a high overall accuracy of 0.97 and 0.96 on their independent datasets respectively while the multiclass classifier achieved a high F1 score of 1.0. We observed that amino acid composition, Qasi-sequence-order and Composition-based protein features are particularly important for the Cas12 and Cas9 family of proteins.

Conclusions: We successfully built the classification models for Cas12 and Cas9 protein families and identified the protein features that are unique to each family, which enhance the understanding of the structure and functions of Cas9 and Cas12 proteins and also provide valuable insights into plausible structural modifications in these proteins to achieve enhanced specificity and reduced off-target effects.

Decrease in Mental Health Among Adolescent Students

PRESENTER

AUTHOR(S)

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COLLEGE/SCHOOL

School of Public Health

ABSTRACT TOPIC

General Public Health

ABSTRACT

Background: Persistent feelings of sadness or hopelessness has increased among adolescent high school students over time. Lack of physical activity has been identified as a risk factor for persistent feelings of sadness or hopelessness. The purpose of this study was to understand the epidemiology of persistent feelings of sadness or hopelessness and its association with physical activity among adolescents.

Methods: Data from the Youth Risk Behavior Survey (YRBS), 2019, consisted of N=13,677. The main variable analyzed was '*felt sad or hopeless*' (yes/no) and the association variable was '*were not physically active at least 60 minutes/day on all 7 days of the week*' (yes/no). Demographic variables measured: sex, race/ethnicity, grade, and sexual orientation. Statistical analysis used: logistic regression model, chi-squared test, and t-test using the YRBS data explorer tool.

Results: The current (2019) prevalence of feelings of sadness or hopelessness among adolescents is 36.7%, an increase from previous years. Rates for feelings of sadness and hopelessness were highest among these demographic groups: Females (46.6%), Bisexuals (68.2%), 12th Graders (39%), American Indians (45%), Sex with both sexes (74.4%). There was a significant association between feelings of sadness or hopelessness among adolescents and students who were not physically active at least 60 minutes/day on all 7 days of the week, $p\text{-value} < 0.01$. Adolescent students that were not physically active at least 60 minutes per day on all 7 days of the week were more likely to experience feelings of sadness or hopelessness (39.2%), compared to adolescent students who were physically active at least 60 minutes per day on all 7 days of the week (29%).

Conclusion: There were differences observed in sex, race/ethnicity, grade-level, and sexual orientation among students that experience feelings of sadness or hopelessness. Lack of physical activity is associated with feelings of sadness or hopelessness. Although the role of lack of physical activity cannot be determined in the causation of poor mental health among adolescent students, future research should focus on examining why there are large differences between different demographics and how to combat that issue to improve mental health. In addition, more research should focus on understanding the role physical activity plays in mental health, and specific solutions for how it can be used as a tool to improve mental health among adolescent students.

Outcomes of XEN-45 Gel Stent in Open-Angle Glaucoma using the PoST Technique: 12-month Follow-up

PRESENTER

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COLLEGE/SCHOOL

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ABSTRACT TOPIC

Eye / Vision

ABSTRACT

Purpose: The purpose of this study was to report the 12-month surgical outcomes of the novel PoST technique (Posterior Sweep of Tenon's technique) in eyes undergoing glaucoma surgery with the XEN-45 Gel Stent.

Methods: A retrospective review was performed for patients who underwent ab interno implantation of a XEN-45 Gel Stent using the PoST technique with or without concurrent cataract surgery. The surgery was performed in adults with open-angle glaucoma that was refractory to prior surgical treatment and glaucoma medications.

Results: In total, 87 eyes of 70 patients aged 58 to 91 years were treated with the XEN-45 Gel Stent. 54 eyes (62%) had a prior glaucoma procedure to lower intraocular pressure (IOP), including laser peripheral iridotomy (LPI). 33 eyes (38%) did not have a prior glaucoma procedure.

Across all 87 eyes, the average IOP decrease at 12 months was 6.50 mmHg (28%), from 18.66 mmHg to 12.16 mmHg, with an average decrease of 2.37 (69%) glaucoma medications, from 3.36 to 0.99 anti-glaucoma medications. Patients with a prior glaucoma procedure had an average IOP decrease of 7.84 mmHg (33%) at 12 months with an average decrease of 2.39 (66%) glaucoma medications. In patients without a prior glaucoma procedure, at 12 months, the average IOP decrease was 4.29 mmHg (20%) on an average of 2.33 (74%) fewer medications. An average of 62.76 micrograms of mitomycin C was used during XEN surgery, ranging from 30 to 80 micrograms.

Across all eyes, the mean IOP at 12-month follow-up was significantly reduced compared to preoperative IOP ($P < 0.0001$). The number of glaucoma medications was also significantly decreased from baseline ($P < 0.0001$) at 12 months. The average IOP decrease in patients without concurrent cataract surgery was significantly greater than in patients with combined XEN and cataract surgery (8 vs. 4 mmHg; $P < 0.01$).

Among all study eyes, there were 28 total complications at or after 1 week post-surgery. The most common types of complication were IOP spike > 12 mmHg (55%), followed by blockage of XEN tip in anterior capsule (21%) and blockage of XEN implant (7%). Patients with at least one previous glaucoma procedure were 4.51 times more likely ($OR = 4.51$, $p = 0.0336$) to experience a complication after XEN Gel Stent implantation, compared with patients with no previous glaucoma procedures.

The cumulative proportion of failure was 0.35 for patients with a previous glaucoma procedure and 0.21 for patients without any prior glaucoma procedures, totaling 0.3 for all eyes. Eight patients (9%) required needling after XEN implantation. The cumulative proportion of re-operation was 0.22.

Conclusions: In this study, the XEN-45 Gel Stent was safe and effective in treating 70% to 80% of patients with refractory glaucoma. The use of the PoST technique provided significant IOP and anti-glaucoma medication reduction compared to pre-operative levels. Additionally, the post-operative needling rate is significantly lower than those previously published. The PoST technique should be considered when using the

XEN-45 gel stent in glaucoma patients who have failed previous surgical treatment or are taking multiple glaucoma medications without adequate IOP control.

IRB NUMBER

6262

Impact of Chronic Obstructive Pulmonary Disease Home and Discharge Inhaler Regimens on Exacerbation Severity and Hospital Readmission

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ABSTRACT TOPIC

Pharmacology

ABSTRACT

Purpose: The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines are the standard for diagnosing and treating chronic obstructive pulmonary disease (COPD). According to GOLD, long-acting muscarinic antagonists (LAMA) should be the backbone of COPD management. Studies have shown patients with COPD who are treated with a LAMA experience a reduction in COPD exacerbations. The purpose of this study is to identify the impact of home inhalers for COPD on inpatient (non-critically ill) exacerbation severity and to analyze changes in COPD regimens following an exacerbation and the subsequent impact on hospital readmission.

Methods: This study was a retrospective, observational, cohort study conducted at a community teaching hospital. Adult patients were included if they were admitted for a COPD exacerbation from 2018 to 2021. Patients were excluded if they had other respiratory disorders, infiltrates on chest X-ray, were on vasopressors, mechanical ventilation, or pregnant. Patients' home, inpatient, and discharge medications for COPD (i.e. inhalers), readmission rates, and time to hospital readmission were extracted from the electronic medical record along with other baseline characteristics and laboratory values. Each patient was evaluated on their at-home medication regimen and placed into an inhaler treatment category (e.g. LAMA only, LAMA + LABA, etc.). The primary outcome of the study was to determine the rate of severe COPD exacerbations as stratified by at-home COPD inhaler regimen. Secondary outcomes include the readmission rate, time to readmission, and the percentage of patients with guideline directed LAMA added to therapy. The chi-square test was used to measure outcomes of categorical data, including association of medication regimen and COPD severity. An unpaired t-test was used to compare the impact of discharge inhaler regimens on time to hospital readmission. A two-way loglinear analysis was completed to analyze the association of home inhalers on severity of COPD exacerbation as well as the association of discharge inhaler on hospital readmission.

Results: A total of 288 patients were included in the study. No association was found between home inhaler regimen and patients admitted with severe versus non-severe COPD exacerbation. There was also no association identified between discharge medications and hospital readmission rates, with the exception of the LAMA only group, which did show there was a significant decrease in readmission rate compared to other groups (18.2% vs. 81.8%) ($p=0.05$). Finally, there was no association between the categories of home inhalers on severity of COPD exacerbation or time to readmission. A total 21 patients were previously not on a LAMA and had a LAMA added to their therapy at discharge (9.9%).

Conclusion: No association was found between the majority of home or discharge inhaler regimens and defined outcomes, with the exception of patients discharging on a LAMA only had a lower readmission rate. There was also an increase in patients with a LAMA containing regimen at discharge, which is consistent with the GOLD guideline recommendations.

IRB NUMBER

Exempt from IRB

Evaluating student responses to incorporate Vulnerable Patient Population centered content into the curriculum

PRESENTER

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COLLEGE/SCHOOL

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ABSTRACT TOPIC

Education

ABSTRACT

Purpose: Vulnerable patient populations are considered groups of people who cannot access healthcare resources or services due to social barriers. Despite advances in the healthcare system and medical education, providers still report feeling less comfortable caring for these patients, and medical students around the country report not feeling this topic is adequately addressed in their curricula. The goal of this project was to evaluate students' responses to introducing an optional curriculum dedicated to discussing four vulnerable populations (Transgender Patients, Incarcerated Patients, Housing Insecure Patients, and Intellectually and Developmentally Disabled Patients). Our expectation is that students will feel more comfortable being a part of these patient's healthcare teams, and determine the value of providing students with a manageable curriculum focused on these topics.

Methods: The tested curriculum consists of four modules, with each dedicated to one of the populations. Each module consists of a pre-recorded video lecture, a supplemental article, and an optional 30 minute interactive session with a content expert who is currently a healthcare provider focused on each population. Texas College of Osteopathic Medicine students voluntarily participated in this evaluation activity. A literature review was performed to create the content outline and objectives. This information was presented in a short pre-recorded video lecture taught by peers. Supplemental articles were chosen to pair with each video. After completing the modules, participants had the option to a virtual interactive meeting where a content expert that works with each of these patient populations had 30 minutes to talk about their experiences and answer questions. The students then consented to an anonymous post-survey to evaluate if they feel that taking this course has benefited their educational experience and if they feel more prepared to be a part of a healthcare team for these patients. All content and materials were reviewed by content experts.

Results: 26 students signed up to take the course, and 20 students completed the modules and attended the optional content expert session. Of those 20 students, 90% completed the post-course survey. The survey showed that students feel vulnerable patient populations are important to learn about, that each population has specific healthcare considerations that should be taught, and that a course similar to this is beneficial to their education. Participants reported feeling more informed about caring for these patients and have taken away information that will be valuable in their future practice.

Conclusion: Medical students feel that vulnerable patient populations and their barriers to healthcare are important topics that should be discussed in medical school curriculums. Students recognize that each population has specific healthcare needs that should be individualized to them, and that incorporating a course that discusses this would be beneficial to their classroom and clinical training. The participating students reported that they gained new, useful knowledge that will help them be more supportive for these patients, and wish to see similar content incorporated into the curriculum and expanded on in the future. In conclusion these results are interesting and suggest conducting a research study in the future.

Symptomatic Carrier Frequency of Familial Mediterranean Fever

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ABSTRACT TOPIC

Molecular Genetics

ABSTRACT

Purpose: Familial Mediterranean Fever (FMF) is a genetic disorder that is characterized by recurrent episodes of fever and inflammation of the serous membrane affecting mainly Mediterranean and Middle Eastern populations. Five founder mutations of the Mediterranean fever (*MEFV*) gene, M694V, M694I, V726A, M680I, and E148Q, account for the majority of FMF cases. The disease is considered an autosomal recessive disorder; however, cases of carriers of one *MEFV* mutation have been reported to have FMF-like symptoms. The purpose of this review is to investigate the common symptoms of manifesting carriers and determine the symptomatic carrier frequencies for FMF.

Methods: A comprehensive literature search was carried out utilizing three electronic databases (PubMed, ClinVar, and OMIM). The study included published case reports and cohort studies that evaluated FMF carriers. All the included studies underwent assessment and data extraction and analysis.

Results: Data and clinical presentations from 7 studies that met the inclusion criteria were identified. A range of symptomatic carrier frequencies was determined for different FMF-causing mutations, with M694V being the most common at 0.82%, followed by E148Q at 0.37%, V726A at 0.17%, and M680I at 0.16%. The most common symptoms found were abdominal pain, fever, chest pain, and arthritis, with arthritis being the most prevalent symptom among the carriers. None of the carriers developed amyloidosis, a serious complication associated with FMF.

Conclusions: The results data highlight the existence of a substantial group of FMF patients who possess only one *MEFV* mutation. These findings have important implications for the medical practice and genetic counseling for FMF patients, especially those from classically affected populations. The results also suggest that detection of a single mutation in conjunction with clinical symptoms appears to be adequate and colchicine treatment should be considered.

Developing a nanoparticle platform for selective delivery of the anti-cancer drug MIH 2.4BI to breast cancer cells

PRESENTER

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COLLEGE/SCHOOL

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ABSTRACT TOPIC

Cancer

ABSTRACT

Based on data from the World Health Organization, breast cancer is the most common cancer among women, accounting for about 15% of all cancer-related deaths. Thus, new treatment options are urgently needed to decrease this mortality rate. In recent years, mesoionic compounds have shown promising potential as anti-cancer agents due to their unique structure and reaction properties. We reported that a 1,3-thiazolium-5-thiolate mesoionic compound (MIH 2.4BI) inhibited the growth of most of the breast cancer cell lines tested compared with normal human mammary epithelial cells. Treatment of MCF-7 breast cancer cells with MIH 2.4BI resulted in alterations in cell cycle distribution with an increased proportion of cells in the G2/M phase compared with untreated cells. MCF-7 cells treated with MIH 2.4BI also showed morphological changes consistent with apoptotic cell death. In addition, treating MCF-7 cells with MIH 2.4BI resulted in a significant reduction in all mitochondrial respiratory parameters compared with the control cells, indicative of an overall decrease in mitochondrial membrane potential. These findings suggest that MIH 2.4BI is a promising candidate for treating breast cancer. However, cancer therapy's primary challenge is the selective destruction of malignant cells while sparing normal cells to preserve tissue integrity. The development and use of drug delivery systems is a recognized approach to improving the efficacy of chemotherapy agents. However, drug delivery systems have been unexplored in mesoionic compounds. The reconstituted high-density lipoprotein (rHDL) nanoparticles have several advantages, including enhanced safety, efficacy, and biocompatibility. The payload, which is contained in the core of the HDL particle, is taken up by SR-B1 receptors, making this method particularly useful for targeted cancer chemotherapy. The upregulation of the SR-B1 receptor by tumor cells and tissues might be helpful in cancer treatment by specifically delivering drug-loaded nanoparticles to the tumors. In this preliminary work, we present an improved delivery strategy of a newly developed formulation of MIH 2.4BI compound with rHDL nanoparticles as the delivery agent. Initial synthesis, optimization, physicochemical characterization, drug loading, and drug release assessment of the nanoparticles were performed. These studies support the potential therapeutic use of MIH 2.4BI in treating breast cancer. To advance potential translational studies for monitoring in vitro drug delivery and colocalization of the drug in the cells, we have begun studies of the fluorescence properties of MIH 2.4BI, using steady-state and time-resolved fluorescence techniques. The fluorescence characteristics of free MIH 2.4BI was evaluated using UV/VIS and fluorescence spectroscopy. The steady-state and time-resolved measurements were designed to understand the optical properties of MIH 2.4BI in solution for monitoring in vitro drug delivery and cellular colocalization. All samples, dissolved in various solvents, exhibited maximum absorbance between 440 and 480 nm; excitation at 440 nm elicited the highest emission at approximately 580 nm in methanol. These results may allow future detection and localization of MIH 2.4BI in vitro and in vivo. Follow-up studies utilizing fluorescence confocal microscopy are anticipated to reveal drug accumulation's site(s) in situ and how cytotoxicity is induced in cancer cells.

Tibial Plateau Fracture Treated with ORIF and Tibia Strut in a 37-year-old Male: A Case Report

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

General Medicine

ABSTRACT

Tibial plateau fractures (TPFs) are orthopedic challenges that have multiple injury modalities and clinical presentations. These fractures can be caused by high energy or low energy trauma. Epidemiological studies estimate peak incidence in the third and sixth decade of life for males and between the fourth and fifth decade for females. TPFs are often classified using the Schatzker classification system which can dictate management.

Case presentation: this is a 37-year-old male who complained of right knee pain after sustaining a fall from a truck ramp. The patient heard a pop and had severe, sharp pain in his right knee. In the emergency room, CT imaging demonstrated a comminuted tibial plateau fracture involving the medial and lateral tibial plateau as well as the metaphysis. The lateral tibial plateau was depressed by 5 mm. The patient was placed in a knee immobilizer, made non-weight bearing, and scheduled for surgical planning in 2 weeks. Unfortunately, the patient never followed up and opted for non-operative management. 6 months later, he came to our clinic because of significant pain and instability in the knee. X-rays demonstrated a chronic, incompletely healed fracture of the medial tibial metaphysis extending to the tibial eminence. Chronic fracture deformities of the medial femoral condyle and lateral tibial plateau were also observed. The patient agreed to surgery at our clinic.

The surgical technique was a proximal tibial osteotomy. An incision was made centered over the medial aspect of the gastrocnemius. The medial soft tissue sleeve was elevated off the proximal tibia in subperiosteal fashion while maintaining the MCL insertions. Next, a sagittal saw was used to make an osteotomy. The proximal tibia was elevated to correct for varus deformity. Afterwards, a fibula strut was placed followed by plate and screws. After biplanar x-ray verified adequate reduction and hardware replacement, bone filler was used to fill the void. Post operatively, the patient was made non-weight bearing for 3 months. Range of the motion was encouraged as tolerated.

At the first month follow up, the patient's pain was well controlled and range of motion exercises were done regularly. No paresthesia, numbness, or wound dehiscence were noted. Repeat x-rays demonstrated intact hardware with evidence of healing fracture lines compared to immediate post-operative images. Fragments and the knee were appropriately aligned. No significant soft tissue or joint effusion were appreciated on imaging.

Conclusion: after failing nonoperative treatment, this patient with comminuted bicondylar tibial plateau fracture has received definitive treatment with open reduction and internal fixation. Higher rates of unacceptable results from nonoperative treatment is inline with Schatzker's series in which operative treatment resulted in more acceptable outcomes. Because the fracture in this patient is more consistent with a Schatzker IV or V classification with intra-articular displacement more than 2 mm, the patient's choice for nonoperative treatment was not appropriate. This led to a malunion and non-union that necessitated surgery. Perhaps greater warning should have been given to the patient about the risks of nonoperative treatment at their initial encounter.

Structural optimization of VU0609159 as an activator of Slack potassium channels

PRESENTER

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ABSTRACT TOPIC

Pharmaceutical Sciences

ABSTRACT

Purpose: Slack (Slo2.2) is a sodium-activated potassium channel widely expressed throughout the brain and encoded by the KCNT1 gene. This channel modulates the firing patterns and general excitability of many types of neurons, contributing to neuronal resting membrane potential, action potential repolarization, and afterhyperpolarization. Increasing evidence suggests that channelopathies that alter Slack activity, triggers cognitive dysfunction, as has been found for Fragile X Syndrome (FXS), the most common cause of intellectual disability (ID) and inherited autism. FXS results from the absence of fragile X mental retardation protein (FMRP) which interacts directly with Slack channels to regulate outward currents termed IKNa in neuronal cells. Prior studies involving animal models of FXS demonstrated that lack of FMRP leads to reduced IKNa currents due to diminished Slack activity, affecting neuronal function. We therefore hypothesize that small molecule activators of Slack have potential utility as therapeutics for neurological disorders associated with Slack hypofunction. Thus, the objective of this study is to discover small molecule activators of Slack potassium channels that may be used as in vitro probes to investigate such a hypothesis. A high-throughput screen using a thallium (Tl⁺) flux assay identified the hit compound VU0609159 (VU159) as a moderately potent Slack activator. Here we report our efforts to develop structure-activity relationships (SAR) in the VU159 series through an iterative, systematic optimization plan using parallel library synthesis.

Method: Our approach involved identifying multiple regions of VU159 that could be readily diversified and using short efficient synthetic routes to produce small libraries of analogs. Systematic substitution using a variety of monomers was carried out around the western benzoxazolone ring, the central amide and linker region as well as the eastern aromatic ring. Structure and purity of all analogs were confirmed using spectra obtained from a Bruker Fourier 300HD NMR spectrometer and an Agilent 6230 time-of-flight LC/MS. Cellular activity was then evaluated using a Tl⁺ flux assay in HEK-293 cells that stably express wild-type (WT) Slack channels.

Results: Each region of the VU159 scaffold proved tolerant of modification to some degree. Multiple fused heterocyclic rings proved competent replacements for the benzoxazolone ring with some analogs providing superior potency. Synthesis of alkylated linkers identified preferred enantiomers. Secondary amides were preferred to tertiary amides. Likewise, cyclic linkers were generally less effective than acyclic linkers. Finally, substitution of the eastern aryl ring was allowed with some analogs demonstrating enhanced potency.

Conclusion: Our systematic optimization plan has identified multiple slack activator analogs with improved activity relative to VU159. Multiple regions of the scaffolds are amenable to SAR development, which greatly enhances the probability of reaching our goal of highly optimized in vitro probes. Additional modifications, including preparation of analogs that combine optimal features, could provide additional SAR and analogs with optimal potency for use as an in vitro probe.

EXTERNAL FUNDING SOURCE

We gratefully acknowledge the National Institute of Mental Health (R21MH125257) for their support of our research directed toward the discovery of new small molecule activators of Slack potassium channels.

Looking Beyond Standard Chemotherapy: Peptides in Breast Cancer Treatment

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ABSTRACT TOPIC

Cancer

ABSTRACT

Background: Chemotherapy is the most established method of treatment that kill fast-dividing cancer cells. However, most cancer drugs have very poor cell selectivity and kill normal cells along with cancer cells indiscriminately. Besides, the continuous use of this therapy increases the possibility of drug resistance in the body along with the chances of recurrence. The usage of peptide-based drugs to combat cancer is gaining significance in the pharmaceutical industry. The collateral damage caused to normal cells due to the use of chemotherapy, radiotherapy, etc. has given an impetus to the search for alternative methods of cancer treatment.

Candidate Protein: In the fight against cancer, newer strategies to combat cancer progression are of utmost importance. Peptides derived from naturally occurring proteins are an important strategy to identify lead molecules in the field of cancer therapeutics. Migration and invasion enhancer 1 (MIEN1) is one such candidate protein that is overexpressed in various cancers and plays an important role in cancer cell migration and invasion. Conserved regions of ITAM and prenylation motif in MIEN1 were used as a template to identify anti-cancer peptides.

In vitro Results: The two newly identified bioactive peptides (named LA3IK and RP-7) inhibited genes and proteins responsible for cancer cell migration and invasion in both MDA-MB-231 breast cancer. RNA-seq, qPCR analysis and western blots showed changes in the transcriptome and protein expression after peptide treatment. The mechanism of the action of the peptides involves the inhibition of key pathways like Epithelial-Mesenchymal transition and Epidermal Growth Factor-mediated NF- κ B pathway to exert their anti-cancer activity. Interestingly, the peptides targeted the same signal transduction pathways followed by parental MIEN1 to show their anti-cancer properties. Thus, the two peptides acted as dominant negative effectors of MIEN1 activity.

In vivo results: Additionally, LA3IK and RP-7 peptide treatments induced apoptosis in mice groups bearing tumors derived from MDA-MB-231 cells as evidenced by increased levels of cleaved caspase-3 and PARP proteins in western blots. Intriguingly, the MIEN1 mRNA and protein levels were lowered in the in vivo breast cancer tumor models that remained unchanged in in vitro experiments indicating an improved therapeutic activity in the living system. The peptides did not cause any toxicity in the mice group that received peptides only, at three times the dose used during in vivo assays.

Pharmacokinetic studies: The PK studies along with the half-life determination and plasma-binding studies are underway in collaboration with the Preclinical Pharmacology Core of UT Southwestern Medical Center to identify and improve the drug-like characteristics of the MIEN1-protein derived anti-cancer peptides LA3IK and RP-7.

IP Status: An intellectual property right application has been filed for LA3IK and RP-7 in August 2022. The patent status is pending.

EXTERNAL FUNDING SOURCE

The work was supported by The Texas Center for Health Disparities (TCHD) under the award number: U54MD006882

IACUC NUMBER
IACUC-2021-0008

How did we get here? A historical look at the early clinical trial data investigating Covid-19 monoclonal antibody therapy and implications for the future

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ABSTRACT TOPIC

General Medicine

ABSTRACT

Background: The clinical spectrum of SARS-CoV-2 infection ranges from asymptomatic to mild, moderate, severe, and clinical illness. Current recommendations for the use of monoclonal antibody (mAb) therapy - including Ritonavir-boosted Nirmatrelvir, Remdesivir, and Molnupiravir - for the treatment of SARS-CoV-2 infection include use in patients who are at risk of progressing to severe COVID-19. Given the unprecedented process and speed of research conducted on the use of antibody therapies, beginning with polyclonal antibodies developed from patients recovered from COVID-19 to the development of monoclonal antibodies targeting the spike protein(s) of various COVID-19 variants, it is important to reflect on early data to better understand the early challenges pertaining to mAb and early COVID 19 research.

Methods: Articles published between January 1, 2019 and October 1, 2021 were identified from keyword search of Medline (via PubMed). Clinical trials evaluating the outcomes of monoclonal antibody (MAB) therapy for the treatment of Covid-19 infection were included. This study was IRB-exempt.

Results: Initial search results yielded 493 papers. After title and abstract screen, full articles were read in their entirety. A total of 21 articles were included in this analysis, representing 7833 patients. Eight studies found a statistically significant benefit to MAB use, 12 found no benefit, and one study did not perform formal statistical hypothesis testing. Primary outcomes varied between studies and included mortality rate, ICU admission, mechanical ventilation requirements, Covid-related hospitalization, supplementary oxygen use, clinical composite scores, and viral load.

Discussion: Early clinical trial data was inconclusive but suggested that monoclonal antibody therapy may have reduced hospitalizations and provided a mortality benefit in some populations with COVID-19. However, several important factors may have influenced treatment response. These factors included antibody type, dose, route, therapy initiation relative to symptom onset, and disease severity, varying COVID-19 treatment protocols throughout the pandemic, possible interactions between early vaccinations and mAb, and disease severity-dependent treatment response.

It is important to look back at the early data to understand the progression to current management protocols. Previously, biologics were analyzed for approval independently of other drug applications, and could be given priority as an "orphan drug" with accelerated status for patients with rare diseases needing treatment now, allowing for rapid market mobilization.

The COVID-19 pandemic sped up the process even further. The FDA was able to issue Emergency Use Authorizations (EUA) to companies with promising pharmaceuticals and biologics for direct care of patients with COVID-19, without the confirmatory trials and tests previously required. Although the healthcare system benefited from greater access to approved biologic treatments for COVID-19, many of the biologics were revoked due to concerns about both efficacy and safety. In the end, it remains to be seen if the proper avenues

for the ethical development of pharmaceuticals were neglected in favor of the streamlined approval process by the pharmaceutical companies, and thus should be considered in future international medical events.

Impact of GLUT1 Transporter Knockout in Optic Nerve Head Astrocytes and Retinal Ganglion Cells

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ABSTRACT TOPIC

Eye / Vision

ABSTRACT

Purpose: Astrocytes and axons are the primary constituents of the optic nerve head, the initial site of neurodegeneration in glaucoma. This study was intended to understand the metabolic relationship between astrocytes and RGC axons. We hypothesized that reducing glucose transporter-1 (GLUT1) expression in astrocytes will increase the RGC-associated pathology after ocular hypertension (OHT).

Methods: Mice expressing a GLUT1 gene flanked by loxP sites behind the GFAP promoter ("GFAP-GLUT1") mice were used (n=40) and were divided into 4 groups: GLUT1-knockout+OHT, Control OHT, GLUT1-knockout+No OHT, and Control+No OHT. Baseline and final intra-ocular pressure (IOP), pattern electroretinogram (PERG), and visual evoked potential (VEP) measurements were taken. OHT was induced via magnetic microbead injection into the anterior chamber. Retinas, optic nerves, and brains were collected for retinal ganglion cell (RGC) quantification, anterograde transport analysis, biochemical assays, and protein analysis.

Results: Statistically significant increases were noted in the IOP data between mice subjected to OHT and the No OHT groups. OHT led to statistically significant decreases in RGC number, regardless of GLUT1 status. A statistically significant decrease in PERG amplitude was noted in all groups subjected to OHT. Interestingly, GLUT1 knockout PERG amplitude was significantly lower than Control at the outset, suggesting a negative impact on retinal physiology from loss of the GLUT1 in astrocytes.

Conclusion: Initial observations indicate glial metabolic homeostasis can impact retinal physiology, but GLUT1 knockout did not appear to negatively impact RGC survival. Ongoing analysis will determine if other structures or functions have been compromised by loss of GLUT1 in astrocytes, as well as provide greater insight into the mechanism of physiological change.

IACUC NUMBER

IACUC-2022-0026

A Cross-sectional Study on Healthcare Barriers Experienced by WellMed Patients at the University of North Texas Health Science Center Geriatric Clinic

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ABSTRACT TOPIC

Health Disparities

ABSTRACT

WellMed is Medicare advantage plan geared towards helping aging patients receive high quality healthcare at low cost. WellMed is available to Medicare eligible patients and dual eligible Medicare/Medicaid in Texas or Florida, with the University of North Texas Health Science Center (UNTHSC) geriatric clinic being one of the few centers in the area accepting the insurance. During the pandemic, it has become clear that access to care is a barrier for aging and underinsured patients, and a better understanding of what the barriers these patients face will help facilitate improved quality of care.

A cross-sectional survey using Qualtrics was administered to WellMed patients at the UNTHSC geriatric clinic during regular clinic hours from June-July 2022. A total of 36 in-person surveys were administered and completed. The self-reported survey consisted of 23 multiple choice and fill-in questions that elicited information on wellness and potential healthcare barriers. A comparison between each variable and patient zip code was made.

Looking at the responses to patient perceived healthcare barriers, 59.4% of respondents reported no barriers, 21.2% stated location of clinic, 12.1% lacked transportation, 12.1% found the appointment system difficult to use, and 6.1% had inadequate finances. Of note, incompatible clinical hours and lack of support for languages other than English were not perceived as barriers. For the fill-in "other barriers not listed" option, 5.6% stated the telephone system not being adequate for communication to the staff and doctors, and 2.8% cited problems with the patient portal. A total of 24 different zip codes were collected. When correlating each barrier with zip code, clinic location and lack of transport correlated with areas on the edge of Tarrant County. No particular relationship between zip code and other outcome measures were observed.

Access to care is a social determinant of health that is cited as a cause of decreased health outcomes. In Tarrant County 22% of adults are uninsured and the ratio of primary care physicians to patients is 1:1690. This study elucidates health barriers WellMed patients in the county are facing. Addressing these barriers patients can experience improved quality of healthcare and easier access to necessary care.

Symptomatic Rathke's Cleft Cyst in a Pediatric Patient: A Case Report

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Background: A Rathke's cleft cyst (RCC) is an epithelium-lined intrasellar benign growth believed to originate from remnants of the Rathke's pouch. It is commonly believed that the cleft regresses during embryologic development, and the persistence and enlargement of the cleft lead to the formation of RCC. However, other theories have been proposed to explain their exact origins, such as derivation from the neuroepithelium or endoderm, or metaplastic anterior pituitary cells.¹ Based on autopsies, asymptomatic RCC is relatively common, being detected in 2-26% of individuals. Symptomatic cysts, on the other hand, are rare, with approximately 150 cases reported.¹ Symptoms of RCC arise from cyst enlargement and compression of the optic chiasm, the pituitary gland/stalk, and/or the hypothalamus. According to the Eguchi study, visual symptoms were present in 47% of patients.² Transsphenoidal surgery is the most common approach to treat RCC, in which the cyst is partially excised and drained. This method preserves the pituitary function and has been effective in reducing symptoms.¹ This case report details a child with symptomatic RCC exacerbated by traumatic brain injury (TBI) and discusses the radiographic findings.

Case Information: A 14-year-old female with a past medical history of one prior concussion several years ago and lifelong occasional headaches, presented two weeks following a head injury during a basketball game. The patient fell while playing basketball and hit her head. She denied any loss of consciousness. The patient has had headaches in the past, but since the injury, the headaches have increased in frequency. They now occur multiple times a day with each episode lasting about 15 minutes, and the pain is localized to the retroorbital and bilateral temporal regions. The patient has lifelong vision issues which have also worsened since the injury. She also reports photophobia, fatigue, anxiety, trouble breathing, and difficulty focusing during school. The photophobia is so intense that she must wear sunglasses all the time, even during class. A pertinent physical exam revealed flattening of the right nasolabial fold and protruding tongue deviation to the right, suggesting possible facial (CN VII) and hypoglossal (CN XII) cranial nerve involvement. Magnetic Resonance Imaging (MRI) revealed an RCC and brain capillary telangiectasia versus hemosiderin deposition in the setting of traumatic brain injury. The patient was urgently referred to neurology and neurosurgery following imaging results, as well as optometry and ophthalmology. Despite brain and physical rest for a week, and a new prescription for glasses, her headaches and visual symptoms continued to worsen. Due to severe photophobia, persistent daily headaches, and inability to complete classwork, the patient was removed from in-person school and all sports. Neurology is currently monitoring the patient for further progression of symptoms, and she is awaiting neurosurgery and ophthalmology evaluations.

Conclusion: Given the common occurrence of RCC, symptomatic RCC should always be considered when assessing patients with persistent headaches and visual field defects. Furthermore, it is important to promptly order a brain MRI and refer patients to neurology and neurosurgery to assess the need for transsphenoidal surgery.

Screening for Methylenetetrahydrofolate Reductase (MTHFR) Mutation

PRESENTER

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ABSTRACT TOPIC

Community Medicine

ABSTRACT

Purpose: The C677T and A1298C allele codes for methylenetetrahydrofolate reductase enzyme in the liver that converts folate to L-methylfolate (LMF). L-methylfolate is the version of folate the brain can absorb. Once in the brain L-methyl folate is thought to help stimulate production of essential neurotransmitters. Mutations in this enzyme are strongly linked to depression, however it could also lead to other psychiatric conditions.¹ Studies show that when L-methylfolate supplementation was used alongside antidepressants in 502 participants with depression, they reported improvement in depressive symptoms.² With more people tested for this mutation we can identify people that need on proper L-methylfolate supplement and get them on it. Thus, improving their overall health.

Methods: We implemented a screening tool that comprised of multiple questions including a PHQ-9 and GAD-7. We gave it to all adult patients at the Hendrik Family Medicine Clinic in Abilene, Texas between August 2022 and October 2022. Positive screening results were based on the criteria of history of depression or a five or greater on the screening.

Results: We screened a total of 188 patients with 106 qualifying for the test. Fifty-three patients performed the test, and the other half did not due to cost, loss to follow up, or other reasons. Forty-one, or 77%, of the patients screened tested positive for a mutation in one or both alleles. On average PHQ-9 scores were higher in patient who had a mutation in both alleles. 14 of the 41 positive mutation patients were on additional pain medication (Tylenol-3, Tramadol, or Both).

Conclusion: This study suggests that MTHFR gene mutations is prevalent in people who met criteria through the screening. Even though it was prevalent more research need to be done to know the impact of obtaining screenings and outcomes once starting supplementation. A future goal is to follow up with patients who have the mutation and test if there is any improvement in their symptoms after supplementation.

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IRB NUMBER

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COVID-19 Parainfectious Demyelinating Lesion in a Pediatric Patient

PRESENTER

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COLLEGE/SCHOOL

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ABSTRACT TOPIC

Neuroscience

ABSTRACT

Background: Although COVID-19 primarily causes respiratory symptoms, the virus may affect other organ systems. SARS-CoV-2 neuropathology continues to be defined, but recent studies have indicated that a considerable percentage of COVID-19 patients experience neurological or psychiatric symptoms.

Case Information: A previously healthy 15-year-old female presented to the emergency department with altered mental status and seizures. The patient was intubated for airway protection and transferred to intensive care. The patient was initially COVID negative but later found to be COVID positive. Extensive laboratory workup including inflammatory, infectious, oncologic, and rheumatologic studies were unrevealing. Lumbar puncture demonstrated benign cerebrospinal fluid with no malignant cells. Initial brain magnetic resonance imaging (MRI) demonstrated a diffusely heterogeneously enhancing white matter lesion in the left parietal and temporal lobes. Electroencephalogram demonstrated periodic lateralized epileptiform discharges in the left central and temporal region. Rheumatology, infectious disease, hematology, nephrology, and neuro-oncology were consulted. To control the seizures, intravenous Keppra and Ativan were administered. High-dose steroids and plasma exchange were initiated as treatment for possible demyelinating lesion as demonstrated on MRI. The first MRI after completion of plasma exchange showed expansion of the lesion although the patient clinically improved significantly. Follow-up MRIs indicate that the lesion has continued to demonstrate regression over time. Her clinical symptoms have also shown improvement.

Conclusion: SARS-CoV-2 is a pathogen capable of causing severe illness affecting a variety of different organ systems. There is potential for a variety of neurological complications in patients who are COVID-19 positive, and patients can present with neurologic complications even in the absence of more typical symptoms. Successful treatment in this patient included high dose intravenous steroids and plasma exchange as well as seizure management. Long-term immunotherapy was not necessary for continued improvement.

The Effects of ERAS Protocol on Complex Spine Surgery Complications and Length of Stay: a Single Institution Study

PRESENTER

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ABSTRACT TOPIC

Neuroscience

ABSTRACT

Background: With the goal of improving patient outcomes, the Integrated Spine Center at UT Southwestern Medical Center implemented an Enhanced Recovery After Surgery (ERAS) protocol which includes pre and post surgery guidelines. The goal of this study was to investigate the impact of the ERAS protocol on complication rates in the perioperative period, as well as length of stay in hospital and ICU.

Materials and Methods: A retrospective cohort study was performed on all patients (3,495) who underwent spine surgery between September 2016 and September 2021. Of those, 2,472 met inclusion criteria as complex spine cases, and were divided into non-ERAS (2,147) and ERAS (325) groups. Patients in each group were matched for gender, age range, BMI range, comorbidities, and surgery type. Post-operative complications such as surgical site infection, acute kidney injury, deep vein thrombosis, myocardial infarction, sepsis, pneumonia, pulmonary embolism, stroke, shock, and other complications were recorded, as was length of stay. A two-tailed Fisher's exact test was used to establish significance.

Results: Significant differences between the ERAS and non-ERAS groups were found in complication rates of UTI (7.3% vs. 1.4%, respectively; $P=0.011$), and any complications (30% vs. 19.6%, respectively; $P=0.032$). Length of stay was also significantly different between the ERAS and non-ERAS groups (5.4 ± 3.4 vs. 4.7 ± 3.7 d, respectively; $P=0.018$). There was no significant difference in the rates of other complications, or in length of ICU stay.

Conclusions: Implementation of the ERAS protocol did not decrease complication rates or length of stay, and ERAS patients had significantly higher rates of UTI or any complications, as well as average length of stay. There may have been confounding factors due to the type of cases where ERAS was followed.

Key Words: perioperative protocol, complex spine surgery, complication rates, length of stay

Neonatal Diabetic Ketoacidosis - A Case Report

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Diabetes

ABSTRACT

Background: Neonatal diabetes mellitus (NDM) is a rare condition (1 in 400,000 live births). It generally presents within the first 6 months of life and may be transient or permanent. The transient form is commonly associated with paternal isodisomy and monogenic variants, such as KCNJ11 and ABCC8, located on chromosome 6. The permanent form is also associated with monogenic variants, most commonly KCNJ11 and ABCC8. Diabetic ketoacidosis (DKA), which is common in older children and teens with autoimmune diabetes mellitus (T1D), is rare in NDM and often overlooked.

Case Study: A 1-day-old female with low birthweight (2.520 kg) was referred to Cook Children's Medical Center for tachypnea (78 to 84 bpm) and hyperglycemia. Her blood pH was 7.22 (7.29 – 7.24), pCO₂ <12 (27-40 mmHg), pO₂ 122 (54-95 mmHg), and HCO₃ of 4.1 (19.0-24.0 mmol/L). Blood glucose levels were >200 mg/dL. Due to persistent respiratory symptoms, she was suspected of being septic and was treated with ampicillin and gentamicin. She was on the cutoff for SGA. Within the initial 48 hours of admission, her lab test results were consistent with DKA - blood glucose of 305 mg/dL (50-96 normal), lactic acid of 2.3 mmol/L (0.5-2.0 normal), anion gap of 21 (10-16 normal) and B-hydroxybutyrate of 9 mmol/L (0.4-0.5 normal). Genetic testing showed a variant of unknown significance in HNF1a. Following stabilization, the parents underwent diabetes education, and the infant was discharged on daily insulin therapy for follow-up in the Endocrine clinic. By 5 years-of-age, she continued to require daily injections of insulin for glucose control. This case is unique in that the infant was found to have a variant of unknown significance for HNF1a, a monogenic mutation that is typically seen in maturity-onset diabetes of the young (MODY). In general, MODY is not typically associated with DKA. Therefore, while our finding is intriguing, we cannot state that this variant is causative in the case we presented. Further reports of HNF1 variants are needed to help determine if there is an association with NDM and DKA.

Conclusions: In infants, NDM and DKA are rare and present with nonspecific symptoms, which often delays the diagnosis. Although rare, it is imperative that NDM and DKA be considered in order to avoid adverse consequences, including death.

Visium Spatial Transcriptomics Reveal Sex Differences in Supraoptic Nucleus Gene Expression of Adult Rats Related to Cell Signaling and Ribosomal Pathways

PRESENTER

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COLLEGE/SCHOOL

Dual Degree

ABSTRACT TOPIC

Integrative Physiology

ABSTRACT

Purpose: There are many well-known sexually dimorphic regions of the hypothalamus; however, sex differences in gene expression in the supraoptic nucleus (SON), a region crucial in the regulation of body fluid homeostasis, has been relatively unexplored. Our previous spatial transcriptomics study revealed gene cluster analysis successfully differentiated myelinated fiber tracts from nuclei and identified several distinct neuronal populations in the coronal brain sections from both male and female rats. Our current study aims to interrogate the sex differences in SON gene expression using two unique methods of differential gene expression (DGE), gene ontology, and pathway analyses. The first DGE approach used Loupe Browser, an application developed by 10x Genomics specifically for their transcriptomics workflow, while the second approach used DESeq2, a more traditional DGE analysis method. **Methods:** Gonadally-intact adult male (n=4) and female (n=4) Sprague-Dawley rats were anesthetized with isoflurane (2-3% in 95% O₂) and their brains were removed and flash frozen. Each brain was sectioned at 10µm thickness and sections (~4x4mm) containing the SON and other brain structures were mounted in capture areas on Visium slides containing probes that bind mRNA. All sections underwent the following workflow: 1) sample staining and imaging, 2) cDNA library preparation, 3) sequencing, and 4) analysis/data visualization. Data were analyzed using 10x Genomics' Loupe Browser application and other bioinformatic tools.

Results: Using Loupe Browser, DGE analysis of the SON identified 116 genes (e.g., *Avp* and *Oxt*) common to both sexes, 31 genes unique to the males, and 73 genes unique to the females. DGE analysis using DESeq2 revealed 183 significant differentially expressed genes between the two groups. Gene Ontology (GO) Enrichment and pathway analyses using significant genes identified via Loupe Browser revealed GO terms and pathways related to: 1) neurohypophyseal hormone activity, regulation of peptide hormone secretion, and regulation of ion transport for the significant genes common to both males and females, 2) G_i signaling/G-protein mediated events for the significant genes unique to males, and 3) potassium ion transport/voltage gated potassium channels for the significant genes unique to females, as some examples. In contrast, GO/pathway analyses using significant genes identified via DESeq2 comparing female vs. male groups revealed GO terms/pathways related to ribosomal structure/function.

Conclusions: The two DGE analysis approaches elucidated different aspects of sex differences in SON gene expression. Loupe Browser-based analysis identified genes related more to cell signaling pathways, while DESeq2 identified genes associated with ribosomal structure/function. Future spatial transcriptomic studies will investigate changes in SON gene expression that contribute to sex differences in cellular mechanisms involved in body fluid homeostasis and possibly pathophysiology.

EXTERNAL FUNDING SOURCE

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IACUC NUMBER
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Colloid-Enhanced Flush Limits Initial Edema but Exacerbates Subsequent Edema During Hypothermic Machine Perfusion of Porcine Kidneys

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Integrative Physiology

ABSTRACT

Purpose: The epidemic of end-stage renal disease (ESRD) has steadily increased demand for transplantable kidneys, and the widening disparity between organ supply and demand is a major public health concern. Hypothermic machine perfusion (HMP) is widely used to preserve deceased donor kidneys for transplantation. Kidneys are harvested and flushed with crystalloid solution before HMP. This study tested the hypothesis that flushing kidneys with solution containing a colloid, hydroxyethyl starch (HES), minimizes edema and improves organ perfusion during subsequent HMP.

Methods: Kidneys harvested from anesthetized Yorkshire swine were flushed for 15 min with ice-cold Ringer's solution \pm 50 g/l HES, and then either biopsied or installed in a LifePort organ preservation system for 72 h hypothermic (2-4°C) machine perfusion (HMP) before biopsy. ATP contents in renal cortical biopsies were analyzed by UV-Vis spectrophotometry.

Results: Kidneys gained $49 \pm 5\%$ of initial mass during flush with control solution, but only another 3% to $52 \pm 5\%$ of initial mass over 72 h HMP. Kidneys flushed with HES-enriched solution gained only $18 \pm 3\%$ of initial mass ($P < 0.001$ vs control) during flush, but over 72 h HMP gained another 72% to $90 \pm 7\%$ above initial mass ($P < 0.001$ vs. control). Tissue water contents paralleled the respective weight gains (Figure). The HES-flushed kidneys experienced steeper declines in perfusion during HMP than the controls. Cortical ATP content (mmol/g dry mass) fell over 72 h HMP from 2.36 ± 1.40 to 0.44 ± 0.44 (mean \pm SD) in control kidneys, and from 1.36 ± 1.31 to 0.38 ± 0.16 in HES-flushed kidneys (both groups: $P < 0.05$, pre- vs. post-HMP).

Conclusion: Flushing kidneys with HES-enriched solution minimized edema before HMP, but exacerbated edema during subsequent machine perfusion, failed to preserve ATP, and was associated with a steeper decline in organ perfusion during HMP. The mechanisms responsible for edema exacerbation by HES-enhanced flush are under investigation.

EXTERNAL FUNDING SOURCE

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IACUC NUMBER

IACUC-2020-0011

A Rare Occurrence of Cardiogenic Shock after Cardioversion: A Case Report

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Cardiovascular

ABSTRACT

Background: Atrial fibrillation (AF) is a common cardiac arrhythmia that affects the health and lifespan of people and has been growing in prevalence with the aging population. AF leads to atrial remodeling, which increases the likelihood of developing treatment resistant AF. Risk factors for AF include obstructive sleep apnea, alcohol use, obesity, hypertension, and diabetes. Treatment consists of rhythm control, rate control, and thromboembolism prevention. If a patient fails to convert to sinus rhythm or remains symptomatic despite pharmacological treatment, the next step in management may include Direct Current Cardioversion (DCCV) or catheter ablation. DCCV restores sinus rhythm (SR) by using controlled shocks to the heart and is considered a safe and effective procedure for treating AF. Complications include arrhythmias, skin burns, and cardiac tissue damage. Following the restoration of SR, cardiac output (CO) generally improves. Cardiogenic shock is a rare occurrence after DCCV. This case report details one of these rare occurrences, where a patient with multiple comorbidities developed cardiogenic shock after DCCV for AF.

Case Information: A 65-year-old male with a history of heart failure with reduced ejection fraction, AF with prior ablation, atrial flutter, dilated cardiomyopathy, obstructive sleep apnea, chronic kidney disease, and implantable cardioverter defibrillator (ICD), presented to the emergency department (ED) with symptoms of dyspnea and shortness of breath. ECG showed atrial flutter with rapid ventricular response (RVR). Urgent DCCV was performed, restoring SR but precipitating cardiogenic shock, which required intubation and vasopressors. Since stroke volume remains constant in patients with dilated cardiomyopathy, the ICD was reprogrammed to raise the HR. Thereby improving the CO and resolving the cardiogenic shock. The patient remained stable for one month but had recurrent decompensated heart failure. ECG showed AF with RVR with a HR greater than 130 bpm. The patient was cardioverted again to sinus rhythm. However, the patient's condition soon deteriorated, wherein he developed shortness of breath, orthopnea, diaphoresis, and cold extremities. He was intubated due to his respiratory distress and started on milrinone, norepinephrine, furosemide, and an amiodarone drip. He nonetheless converted to AF with RVR, compromising his CO. This was evident clinically by his decrease in urine output, despite furosemide treatment. Urgent AV node ablation with a biventricular ICD upgrade was thus recommended. Postoperatively, as his condition improved, the patient was extubated and switched to oral diuretics. Amiodarone was discontinued, and his heart failure medications were slowly reinstated. Upon discharge, the patient was referred to another facility that specializes in heart failure and transplants.

Conclusion: Although DCCV is generally considered a safe and effective procedure, there are still risks associated with it. This case highlights the importance of considering underlying cardiac dysfunction in patients undergoing cardioversion for AF and the need for close monitoring and follow-up in these patients. Since not many cases showcasing these potential complications have been documented, this warrants further research to identify risk factors, complications, and ways to prevent harm to patients who may undergo DCCV.

Near Peer Ultrasound Education Evaluation

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Education

ABSTRACT

Ultrasound training is incorporated throughout the medical curriculum at Texas College of Osteopathic Medicine (TCOM) beginning in the Year 1 Physical Exam Course where students are introduced to the fundamental of Ultrasound as it pertains to each organ system being taught. In Year 2, the training is included in the Simulation Lab curriculum. In the past 4 years, ultrasound education at TCOM has become more formalized with the use of second year students as ultrasound teaching assistants. The purpose of our study is to examine the effectiveness of near peer teaching in the setting of ultrasound. Near peer teaching occurs when material is taught to students by their peers, and this has been proven to be an effective teaching technique in other settings. We hypothesized that medical students prefer near peer teaching to learn ultrasound, and that student teaching assistants will facilitate a better learning environment.

Medical students from the classes of 2022, 2023, 2024 and 2025 were surveyed about the effectiveness of near peer education. Results were initially published at RAD 2021, however in the past 2 years the Ultrasound teaching assistant program has expanded and become more formalized. 138 medical students completed the survey, and 78% of students responded that they learn effectively during ultrasound taught near peer sessions. 67% of medical students indicated that they prefer near peer teaching to another teaching style.

In addition, the teaching assistants from the TCOM classes of 2022, 2023, 2024 and 2025 were surveyed with 33 responses. 100% of the teaching assistants surveyed indicated that through the use of near peer education, being a TA enhanced their medical education.

Our results across multiple years of medical students demonstrate the utility of near peer teaching and that students prefer this method of learning. Point of Care Ultrasound is becoming a necessary part of medical education, as its importance in clinical medicine grows. Near peer teaching can be one way to implement ultrasound into medical school curriculums.

EXTERNAL FUNDING SOURCE

NIH

IRB NUMBER

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HASHIMOTO'S THYROIDITIS ASSOCIATED WITH RHABDOMYOLYSIS AFTER INFECTION WITH COVID19

PRESENTER

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AUTHOR(S)

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

General Medicine

ABSTRACT

This case study discusses the care of a 74-year-old female with three hospital admissions over the year 2022. There will be a detailed focus on the second admission. Her chief complaint for her second admission was generalized weakness and fatigue with an initial creatinine kinase of greater than 50,000 Units/L (reference range 25-192) and a thyroid stimulating hormone level of 178. She was initially treated with intravenous fluids, IV levothyroxine, and IV hydrocortisone. During the middle of her second hospitalization, intravenous immunoglobulin was added to her treatment regimen. The patient was discharged from her second hospitalization and readmitted one day later due to severe blood loss secondary to a muscle biopsy hematoma. The patient was discharged with baseline ambulation and mentation after receiving multiple blood transfusions in addition to the continuation of oral levothyroxine and oral steroids.

Conclusions: This case study represents another contribution to scientific literature towards the suggestion that Hashimoto's Thyroiditis is associated with severe rhabdomyolysis. In addition, this case study suggests a possible association between people developing autoimmune thyroiditis and rhabdomyolysis post-infection with COVID-19. In patients with rhabdomyolysis, physicians should consider ordering a TSH with close outpatient follow-up. Investigation into the use of intravenous immunoglobulin for severe Hashimoto's Thyroiditis may prove beneficial for patients.

Platelet Releasate Injection for a Novel Treatment of Ulnar Neuritis at the Elbow

PRESENTER

AUTHOR(S)

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Rehabilitative Sciences

ABSTRACT

Background: Ulnar neuritis is a common entrapment neuropathy in the upper extremity that results from chronic compression of the ulnar nerve. Typical conservative treatment includes activity modification or brace immobilization. Platelet-rich plasma (PRP), an autologous product of concentrated platelets, has yet to be thoroughly investigated as a treatment option for ulnar neuritis. Platelet releasate, the supernatant of thrombin activated PRP, has potential to accelerate healing in injured peripheral nerves by releasing growth factors that promote nerve repair.

Case Report: This case presentation discusses a novel treatment of ulnar neuritis with platelet releasate injection in a 42-year-old female patient presenting with right-sided neurogenic thoracic outlet syndrome and ulnar nerve entrapment. Initial imaging at the right elbow demonstrated ulnar nerve entrapment within the Arcade of Struthers. The patient's symptoms were first managed with home exercise and and dextrose 5% in water (D5W) hydrodissection at the elbow, which decreased but did not resolve her pain. Intraneural and perineural platelet releasate injection of the ulnar nerve at the elbow was subsequently performed. Six weeks post-procedure, the patient reported her pain was 80% better and continuing to improve. Provocative tests at the elbow were negative and imaging demonstrated a normal appearing ulnar nerve. Despite these results, the patient was not completely symptom-free; continued symptoms were attributed to her concomitant neurogenic thoracic outlet syndrome. While platelet releasate injection has not previously been explored as a treatment option for ulnar neuritis, this case demonstrates how platelet releasate injection may facilitate healing in an ulnar nerve injured by entrapment.

Conclusion: This case report investigated the use of ultrasound-guided nerve hydrodissection and platelet releasate injection for treating ulnar nerve entrapment. Although D5W hydrodissection proved useful in reducing the patient's pain and paresthesia, platelet releasate injection was instrumental in resolving the patient's localized entrapment. As current literature supports platelet releasate as a key driver of nerve regeneration, it is likely that the platelet releasate injection played a role in reducing the patient's pain by enhancing the healing response of the injured ulnar nerve. Further research is indicated to determine if the clinical application of platelet releasate injection may be solidified as an efficacious treatment modality for ulnar neuritis and other peripheral nerve entrapments. Given the outcome for this patient, this case illustrates the prospect for platelet releasate treatment to continue to be studied as a monotherapy or synergistically with D5W hydrodissection for ulnar nerve entrapment and similar compression neuropathies.

Pyruvate-enriched solution limits lactate and creatine accumulation in hypothermic machine-perfused kidney

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Integrative Physiology

ABSTRACT

With a 5% annual increase in incidence, end-stage renal disease (ESRD) is a mounting epidemic. Kidney transplantation is the only definitive treatment for ESRD, but the growing demand for transplantable kidneys greatly exceeds the supply, thus improved methods of organ preservation are urgently needed. Recently, renewed interest in hypothermic machine perfusion (HMP) has prompted refinements of perfusion solutions to improve graft performance and transplant outcomes. In previous studies, solutions containing the intermediary metabolite pyruvate prevented ATP depletion, detoxified reactive oxygen species, suppressed inflammation and optimized protection of ischemic myocardium and brain. This study aimed to examine the hypothesis that pyruvate-enriched preservation fluids provide robust preservation of histological structure and energy metabolism in porcine kidneys during 72 hours HMP. The study used 7 Yorkshire swine kidneys, which were harvested and immediately flushed with ice-cold Ringer's solution and then perfused with either control or 20 mM pyruvate-enriched Ringer's solution for 72 hours in a LifePort organ preservation system. Values for renal artery flow and resistance were recorded over time. After 72 hours HMP, the renal cortex was biopsied and analyzed for metabolite content via spectrophotometry, while the cortex and medulla were biopsied for histological evaluation. The results showed that pyruvate-enriched preservation fluids lowered creatine content by 89% ($P < 0.05$), and surprisingly lowered lactate content while increasing glucose-6-phosphate content, a source for maintaining antioxidant reducing power. Flow and resistance were comparable between the two groups, and histological analysis revealed interstitial and intracellular edema, varying stages of acute tubular necrosis and variable loss of overall glomerular architecture in both groups. In conclusion, pyruvate-enriched preservation fluids stabilized the cellular energy state, supplied glucose-6-phosphate for sustaining antioxidants, and shunted metabolites from the glycolytic pathway leading to lower lactate accumulation in the renal cortex. Further research is warranted to understand pyruvate's impact on oxidative stress and inflammation during HMP.

EXTERNAL FUNDING SOURCE

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IACUC NUMBER

IACUC-2020-0011

The Perplexing Plexus: An In-Depth Look at Post-Trauma Brachial Plexopathy

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Rehabilitative Sciences

ABSTRACT

Background: Lower trunk pathologies are a subset of brachial plexus injuries involving the C8 and T1 nerve roots. These lesions can affect all the downstream components that receive input from C8-T1, including the medial cord, median nerve, ulnar nerve, and radial nerve. Lower trunk injuries can diminish both motor and sensory components of the affected upper extremity. Common etiologies for lower trunk lesions typically involve hyperabduction trauma such as motor vehicle accidents, falls, shoulder dislocations and obstetrical traction injury. Along with a thorough history and physical, brachial plexus injuries are typically diagnosed through Nerve Conduction Study (NCS), Electromyography (EMG), and imaging.

Case Presentation: A 61-year-old male with a history of bilateral carpal tunnel release and bilateral ulnar nerve decompression presented to a physiatry clinic with left hand weakness following a fall on his left elbow three months prior. The patient also reported intermittent numbness in both hands involving all digits. NCS and EMG were completed and suggested mild left and severe right carpal tunnel syndrome, respectively.

Two months following the initial visit, the patient returned to the clinic presenting with improved numbness in both hands, but weakened left grip strength and persistent left elbow pain. A posterior interosseous nerve (PIN) lesion was suggested due to elbow involvement. Physical exam of the left upper extremity revealed 4/5 strength in wrist extension, extensor indicis proprius (EIP), interossei, and abductor pollicis brevis (APB). Left hand interossei atrophy was also noted on examination. Repeat NCS showed left mild carpal tunnel syndrome, consistent with his previous visit. To evaluate for a PIN lesion, the left EIP and extensor carpi radialis brevis (ECRB) was tested via EMG. The EIP showed decreased recruitment, but ECRB was normal. Further testing revealed decreased recruitment of the left first dorsal interossei (FDI) and left APB. To further specify the location of the lesion, the medial antebrachial cutaneous (MAC) nerve was tested, but NCS revealed normal findings.

With clinical judgment, the patient was diagnosed with a left lower trunk brachial plexopathy due to trauma. Despite an affected EIP, a PIN lesion was ruled out due to a normal ECRB. While the APB and FDI were affected, a medial cord lesion was ruled out due to an affected left EIP, which suggested a lower trunk lesion due to radial nerve involvement. An MRI of the elbow revealed lateral epicondylitis with 25-50% intrasubstance partial thickness tearing; while shoulder MRI results are currently pending.

Conclusion: This case illustrates an atypical presentation of a lower trunk brachial plexus injury following trauma. The utilization of diagnostic and clinical tools in our case proved instrumental in the differentiation of lower trunk lesions from medial cord and PIN lesions and may provide a valuable reference for physicians evaluating similar cases. Furthermore, this case demonstrates the importance of continued monitoring of upper extremity nerve injuries for progression of symptoms, especially following trauma.

The impact of the COVID-19 pandemic on the access to care for Type 2 Diabetic Patients

PRESENTER

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AUTHOR(S)

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COLLEGE/SCHOOL

HSC College of Pharmacy

ABSTRACT TOPIC

Diabetes

ABSTRACT

Background: Type 2 diabetic hemoglobin (HbA1c) A1c testing decreased substantially during the coronavirus (COVID-19) pandemic, resulting in gaps in care. Low socioeconomic populations may be affected in care received during the COVID-19 pandemic. The pandemic may have further amplified health disparities, such as inadequate HbA1c testing, and decreased resource availability, ultimately leading to potential health decline. The purpose of this study was to identify race/ethnicity predictors of gaps in care for HbA1c testing during the COVID-19 pandemic among patients with type 2 diabetes (T2DM).

Methods: This study included analysis of electronic health records from patients with T2DM at two healthcare systems (John Peter Smith Health Network and UNT Health). Times between HbA1c testing were compared pre COVID (March 1, 2019 – March 1, 2020) and during COVID (March 2, 2020 – March 1, 2021). Established patients (with two or more visits) at the two systems during the pre COVID period and at least one visit during the COVID period were included for analysis. Variables for analysis were selected using the Anderson Social Behavioral Model to assess the impact predisposing, enabling, and need factors had on gaps in HbA1c testing among different racial/ethnic groups during COVID-19. Data were analyzed using multilevel clustered survival models. Analyses were stratified by race/ethnicity (non-Hispanic White, non-Hispanic Black American, Hispanic, and other). Age, sex, BMI, visit modality (telemedicine or in-person), taking insulin (yes, no), at least one HbA1c above 8%, hypertension (yes, no), anxiety (yes, no), lipid metabolism disorder (yes, no), and private insurance (yes, no) were included in the models. Comparisons were made using multilevel clustered survival models to assess trends that occurred and the impact variables had in care gaps in type 2 diabetic patients during the COVID-19 pandemic.

Results: A total of 2,951 patients were included. Patients with HbA1c >8% pre-COVID had larger HbA1c testing gap times during COVID-19 for all race/ethnicities, compared with those with HbA1c ≤8%. Larger testing gaps among patients with diabetic medications (oral and injectables) during COVID-19 were identified in Non-Hispanic Black Americans (p=0.02) and Hispanics (p=0.01), compared to those without diabetic medications. Men experienced larger gap times in HbA1c assessments compared to females among non-Hispanic Black Americans. Having at least one telemedicine appointment was associated with a decreased gap time among Hispanics.

Conclusions: Research demonstrates a reduction in access to care for underrepresented populations due to COVID. Patients with diabetic medications (excluding insulin) experienced decreased HbA1c assessments, potentially resulting in worsened health. Inconsistent chronic disease management is associated with increased risk of all-cause mortality. Implementation of telemedicine and increased HbA1c testing is known to correlate with positive health overall.

EXTERNAL FUNDING SOURCE

Agency for Health Research and Quality

IRB NUMBER
2019-163

Assessing Postural Sway Among Older Adult Females with Hypertension

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

General Medicine

ABSTRACT

Purpose: Hypertension and use of antihypertensive medications have been generally suggested as risk factors for falls; however, supporting evidence remains unclear on the link between hypertension and balance. With minimal research assessing postural control using a force plate among older adults with hypertension, the purpose of this study is to evaluate the relationship between postural sway and blood pressure status and identify variables that contribute to falls.

Methods: This study is a retrospective, matched case-control analysis incorporating Quiet Stance Test data from the UNTHSC Human Movement Performance Lab for a case group of older adult females aged 55 to 94 with hypertension (n=100) and an age-matched and gender-matched normotensive control group (n=44) generated from previous studies conducted through the UNTHSC HMP Lab. The Quiet Stance Test involved participants standing barefoot with disposable foot covers, on pre-marked footprints on a force plate (Bertec, Columbus, OH and BioSway, Shirley, NY), both arms relaxed on the sides while looking at an eye-level target for three 10-second trials each in eyes open (EO) and eyes closed (EC) conditions. Twenty sway variables were analyzed using Paired Samples t-Test. Data were also stratified for age and height for One-Way ANOVA and Pearson Correlation tests. Tables were generated to compare mean differences between case and control groups in the EO and EC conditions. (UNTHSC IRB# 2013-102)

Results: Participants' ages ranged from 55 to 90 (M=70.7, SD=9.3) and height from 1.45m to 1.78m (M=1.62, SD=0.07) in the case group. In the control group, participants' ages ranged from 57 to 89 (M=68.8, SD=6.0) and height from 1.47m to 1.73m (M=1.62, SD=0.06). Roughly 80% of all participants identified as White. The Paired Samples t-Test comparing EC and EO conditions revealed significant mean differences ($p<.001$) for thirteen of twenty sway variables in the case group. Meanwhile, the control group showed no significant mean differences in any variable. The mean differences for four of twenty sway variables were significant ($p<.001$) for at least one of the height subgroups in the case group (EC condition), while the control group had no significant mean differences. The only variable that was found to have significant ($p<.001$) mean differences for at least one of the age subgroups is rotational frequency for the case group (EC condition). For the same group and condition, a significant positive correlation was found between rotational frequency and age ($r=0.404$, $p<.001$). The center of pressure's (COP) position is dynamic. Rotational frequency is a measure of COP instability and is the mean velocity of the COP traveling over a circular path defined by the mean displacement from the center position of the COP stabilogram.

Conclusion: These findings suggest there may be differences in balance between normotensive and hypertensive older adult females related to age and height. A limitation of this study is that the sampling of convenience included hypertensive subjects that also have back pain concerns. Further studies should include male participants, create more racially diverse research cohorts, and consider comorbidities as variables that may provide insight into other influences on sway.

IRB NUMBER

UNTHSC IRB# 2013-102

Implementation of changing clinical practices: Prenatal syphilis screening in Texas

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COLLEGE/SCHOOL

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ABSTRACT TOPIC

Microbiology / Infectious Disease

ABSTRACT

Purpose: Congenital syphilis can cause negative health outcomes including stillbirths, miscarriages, birth defects, and infant death. From 2016-2020, national congenital syphilis rates have increased from 16.2 to 57.3 cases per 100,000 live births. Texas congenital syphilis rates are significantly higher than the national rates and have increased 835% from 2016-2020. Prenatal syphilis screening by providers can avert maternal and neonatal mortality and morbidity, although there are conflicts between national professional organization's recommended guidelines and individual state screening mandates. State dissemination and clinical integration of updated screening mandates are imperative to reduce the rates of congenital syphilis in Texas. The purpose of this study is to understand the factors influencing implementation of prenatal syphilis screening guidelines into clinical practice.

Methods: Prenatal providers including physicians (MD/DO) and mid-level providers (CNM/NP/PA) in Texas were recruited to participate in an in-depth interview. Recruitment strategies included social media advertising, newsletters of professional organizations, and direct email recruitment. The interview guide was based on constructs from the Consolidated Framework for Implementation Research, an implementation science theory focused on identifying determinants, or factors, that influence translation into practice. Interviews were approximately 45 minutes in length, were conducted via Zoom or phone, were audio recorded and then transcribed by a professional. Data were thematically analyzed with emergent and theory-based codes.

Results: Respondents were certified nurse midwives and physicians (n=9) who discussed implementation of changing clinical practices in the context of the Texas Department of State Health Services (TDSHS) updated mandate for prenatal syphilis screening at delivery in 2019. Participants expressed difficulty with having clear communication and resources from TDSHS about changes, reliance on email updates from professional organizations for new screening recommendations, and both formal and informal colleague dialogues as sources of policy updates. Specific difficulties expressed were the confusing TDSHS website interface, ineffective email communications that are not practice-specific, and lack of data to understand the need for a change in practice for their populations. The interviewees discussed how population and professional ethics affect prenatal screening practices and the ease of changing orders once new policy changes were agreed upon by management stakeholders.

Conclusion: Varied responses from participants regarding the source of TDSHS updated mandates for prenatal syphilis screening indicate that there are no universally effective methods of communication between TDSHS and clinicians to understand, be notified of, and/or implement new mandates in a timely and uniform manner. The clinicians also noted deference to national professional organizations as institutions that they could rely on for clear communication about policy recommendations that highlighted their practice needs while considering TDSHS communications as required for practice rather than a source of clinically relevant state and community health data. Understanding of how clinician perceptions of prenatal syphilis risk for their patient populations would change with relevant local statistics within TDSHS communications would further elucidate roadblocks to integration of state mandates into clinical practice. The development of context specific

implementation strategies for providers in Texas can improve prenatal syphilis screening and ultimately reduce the adverse neonatal outcomes.

EXTERNAL FUNDING SOURCE

UNTHSC Early Stage Investigator grant

IRB NUMBER

2022-021

Demographic Factors Associated with Parents' Knowledge About Sexually Transmitted Infections

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ABSTRACT TOPIC

General Public Health

ABSTRACT

Purpose: Gender roles are usually discussed in the context of socialization, however, this can be extended to other facets of behavior, such as compliance with treatment of sexually transmitted infections (STI). Because of this, many times the burden of STI testing and relaying information to partners is left to women. Similarly, within traditional nuclear families, gender roles and norms create expectations for family members, but especially parents. For example, maternal roles often include tending to the children and home, while paternal roles usually include being a provider for the family. Though our current society continues to transform these gendered norms, some of these gender roles still linger. Because of this, it is expected to see these gender norms and roles reflected in knowledge about STIs. Other demographic factors such as race, age, and education level may have an impact on knowledge acquired about STIs. The purpose of this study was to explore the demographic factors, including gender, associated with parental knowledge of STIs.

Methods: We recruited parents of children aged 10-17 (n=230) via Centiment, an online survey panel. We assessed STI knowledge using a 27-item validated knowledge scale that included true and false statements. The scale included questions about Chlamydia, Gonorrhea, Herpes Simplex Virus (HSV-2), Human Immunodeficiency Virus (HIV), Human Papillomavirus (HPV), and Hepatitis B. An example of a question included was Genital herpes is caused by the same virus as HIV. Parents indicated their response (true/false/don't know) and answers were coded (incorrect/correct). Incorrect answers were coded as 0, correct answers were coded as 1, and "don't know" responses were automatically considered incorrect. There were 27 possible points based on the validated scale. Demographic questions included gender, age, race, parental STI history, and highest level of education. Descriptive statistics, univariate, and bivariate analyses were conducted in SPSS. A p-value of $p < .05$ was considered statistically significant.

Results: The average knowledge score was 12.5 (SD=6.2, range 0-27). Knowledge score was not correlated with parent age ($p=.62$) or child age ($p=.43$). There were no significant associations between knowledge and parent gender ($p=.06$), parent race ($p=.70$), parent education level ($p=.47$), child gender ($p=.08$), or child race ($p=.59$). However, 28% of parents reported a history of an STI, and knowledge score was significantly different among those with an STI history (14.5) compared to those without (11.6; $p=.001$).

Conclusions: We noted a significant difference in STI knowledge based on STI history. This is expected as those who have had experience with STIs and STI treatment would have increased knowledge about them. However, average knowledge scores were low overall, with no significant differences across several different demographic factors. This emphasizes a need for better sexual education across the life course. This also displays a need for targeted interventions to increase STI awareness and knowledge among parents, in general. Future studies should assess the specific gaps in STI knowledge among older adults and how sexual education information can be disseminated to this age group.

EXTERNAL FUNDING SOURCE

ASTDA Small Project Assistance

IRB NUMBER
1798874-2

Challenges in Recruitment of Young Adults Engaging in Sexual Behaviors and Alcohol Use

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ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Background: Young adults are at increased risk of negative outcomes, such as sexually transmitted infections and unintended pregnancies, due to alcohol use during sex, condomless sex, and inconsistent contraceptive use. We seek to adapt a brief intervention to address these health behaviors, which requires formative research with young adults engaging in alcohol use during sexual activity. Recruitment of young adults in research studies can be challenging. We examined the recruitment approaches used in this formative study to gain a deeper understanding of the challenges encountered in the recruitment of young adults for a sexual health and alcohol study to improve strategies and overcome obstacles.

Methods: The goal of recruitment for the formative study was to identify eligible participants through a screening survey and invite them to participate in a focus group. Inclusion criteria for the formative study were young adults aged 18-25, not in a monogamous relationship, had inconsistent contraception use or condomless sex, alcohol use during sex in the past month, and had Texas residency. The research team used several recruitment strategies: flyers, emailing community stakeholders to share materials, social media, and monetary incentives. We used the Plan Do Study Act (PDSA) cycle to examine our recruitment approaches in three cycles and reflect on the effectiveness of our recruitment methods. The effectiveness of each cycle was measured by the number of surveys that were completed, the number of eligible participants identified, and the number of resulting focus group participants. The research team reflected on challenges in each cycle.

Results: There were three recruitment cycles identified. Cycle 1 (January-February 2022) primarily focused on distributing flyers and contacting partner organizations to share materials with their clients; challenges included logistics, locations, and the ability to track this strategy. This cycle resulted in 253 surveys completed, 23 eligible potential participants, and 10 focus group participants. Cycle 2 (February-June 2022) incorporated social media advertising (e.g., Twitter, Craigslist, TikTok, and Reddit) to reach large audiences, but introduced issues such as social media platform policies, inauthentic survey results, and increased recruitment costs. This cycle resulted in 475 completed surveys, 10 eligible potential participants, and 1 focus group participant. Cycle 3, where inclusion criteria were broadened to increase the eligible population is preparing to launch to address these challenges.

Conclusions: Many challenges were identified in recruiting young adults engaging in condomless sex, ineffective contraceptive use, and alcohol use during sex to participate in this research study. Each recruitment strategy came with unique issues but a large discrepancy between audiences reached, and successful participants was constant in all strategies. Direct recruitment through partner organizations was effective but required considerable effort to ensure that the study was adequately advertised to potential participants. Social media marketing was effective in reaching large audiences but was complicated by platform advertising policies, false and repeated survey responses, and did not yield a cost-effective number of successful participants. These results suggest that broadening the inclusion criteria may increase the number of eligible participants.

IRB NUMBER
2021-102

Implications of Interactive Online Medical Education for TCOM Musculoskeletal Education

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ABSTRACT TOPIC

Education

ABSTRACT

Purpose: In the modern medical curriculum, students are required to learn increasing amounts of information, and the ability to adapt and expand the threshold of fundamental concepts is becoming increasingly important. Most recently, the COVID-19 pandemic has forced the medical education system to adapt to a new challenge - delivering a comprehensive medical education to students remotely without compromising the quality of education. As a result, online interactive learning modules were introduced into the second exam portion of the TCOM Musculoskeletal Systems 2 (MSS2) course. This study aims to retrospectively review the effects of this online, interactive, module-based format.

Methods: A retrospective review was performed to compare student performance before and after the implementation of these pandemic related changes. De-identified student data (n=685) from the 2019 pre-pandemic cohort and the 2020 and 2021 post-pandemic cohorts were utilized for the study. The dataset included student cumulative medical school GPA prior to the beginning of the course, class quartile rank, MSS2 exam scores and final course grades. Standard post-course surveys were utilized for the qualitative portion of the analysis, and an additional course satisfaction survey administered via google polls was added for the purpose of collecting anonymous student feedback and suggestions for improvement. Quantitative analysis was conducted on parametric and non-parametric variables. For parametric variables, the independent sample T-test was utilized to assess significant differences in a number of different variables, including both broad and specific statistical questions regarding the data.

Results: The implementation of the online musculoskeletal modules correlated to a significant difference between the course grades of the 2019 and 2020 cohorts with mean scores of 88.4 and 87.2 respectively ($p=.025$). A significant improvement was found in the second exam for the 2019 and 2020 cohorts ($p=.006$), whereas no significant difference was revealed between the first exam grades of the two cohorts ($p = 0.49$). The data analysis from the two years following the pandemic demonstrated a successful implementation of online modules with the significant improvement of exam grades in the second exam where the modules were incorporated, including in the 2021 cohort. These significant findings indicate a benefit of introducing such modules into the second exam. Post-course surveys revealed that 57% of students want to see interactive modules in future courses, with an additional 28% being neutral.

Conclusions: The addition of interactive modules to the MSS2 curriculum was beneficial as students were able perform significantly better on the relevant exam material despite entering the course with significantly lower GPAs. Furthermore, the majority of students responded positively to the possibility of seeing interactive modules used in future courses.

IRB NUMBER

2020-126

Calculating Average Transit Times to Estimate Health Impacts in South Dallas

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ABSTRACT TOPIC

Health Disparities

ABSTRACT

Purpose: Access to reliable transportation remains a significant social determinant of health, with far-reaching implications for employment, physical activity, food security, nutrition, and access to care. In Dallas, the National Equity Atlas estimates 1 in 10 households do not own a personal vehicle. These estimates worsen for households of color—nearly 1 in 5 Black households in Dallas lack a vehicle. The Baylor Scott & White Health & Wellness Center (BSWHWC) provides primary care and preventive health services for low-income, predominantly Black and Hispanic populations in South Dallas's Frazier neighborhood. Over 1 in 4 residents in this neighborhood do not have access to a vehicle. Studies on barriers to healthcare access have cited lack of vehicle access and extended travel times as significant reasons for missed appointments and poorer health outcomes.

The Integrated Population Health Trial (I-POP) is designed to evaluate if Community Health Worker (CHW) navigation helps individuals improve their health compared to individuals receiving usual care at BSWHWC. CHW navigation involves monthly meetings with a CHW over 10 months, to connect participants to resources and utilize motivational interviewing to promote participant choices toward health improvement. Participants without a car are hypothesized to have longer public transit travel time and more absences for CHW appointments. This analysis identifies the extent and impact of transportation barriers for research participation in I-POP.

Methods: Adult participants living within 10 miles of the BSWHWC were recruited for I-POP through flyers at BSWHWC and community centers. Participants completed informed consent and baseline measures, then were randomly assigned to either the intervention (receiving CHW monthly navigation) or usual care. Participants were included in this study if they were assigned to the intervention and relied on public transportation. Twenty-five of 100 participants met inclusion criteria. Street addresses were batch-fed through a public transit directions application programming interface (API) to generate average amount of time spent traveling to the BSWHWC for monthly CHW sessions at any possible appointment times (Monday-Saturday, 8:00am-4:30pm). Session attendance followed a somewhat uniform distribution and average travel time was moderately right-skewed. However, deviations from normal could not be fixed through transformation due to small sample size. To examine the relationship between CHW appointment attendance and average travel duration, a linear regression model was run controlling for age, gender, race, and income level.

Results: Preliminary results indicate the average travel duration time for participants is not significantly related to participants' attendance at CHW appointments ($r=0.000534$, $p\text{-value}=0.2390$). Age and race showed minimal impact on session attendance, while being female showed a stronger positive association with session attendance ($r=-2.90294$, $p\text{-value}=0.0591$).

Conclusions: Participating in research interventions requires organizations to understand community barriers to attendance. While transportation is documented as a significant barrier in many studies, this small sample did not show a significant relationship between attendance and travel time using public transit. Further research is needed to examine this barrier with a larger sample, and evaluate other modifiable variables, like

perceived benefits and overall satisfaction with study participation, that may increase participation at the BSWHWC.

IRB NUMBER

021-026

Effect of Sigma-1 Receptor Activation on Renal Injury and Hypertension in Female Mice with Lupus

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ABSTRACT TOPIC

Integrative Physiology

ABSTRACT

Systemic lupus erythematosus (SLE) is a female-dominant autoimmune disease with prominent renal injury and hypertension, contributing to its morbidity and mortality. Novel therapies to reduce these detrimental outcomes could be beneficial to SLE patients. The sigma-1 receptor (S1R) is a cytoprotective ligand-regulated chaperone protein that decreases protein aggregation, cellular stress, and cell death, thus preventing tissue injury. S1R activation with pharmacological ligands enhances cytoprotection in autoimmune diseases like multiple sclerosis and Huntington's disease; however, the efficacy of S1R agonists in SLE is unknown. We hypothesize that S1R activation via the agonist LS-1-127 will reduce renal injury and halt the progression of hypertension in SLE mice.

Female SLE (*NZBWF1*) and control (*NZW*) mice were weighed and urine collected via metabolic cages weekly starting at 30 weeks of age. Albuminuria was measured via dipsticks. At 33 weeks of age, SLE and control mice were treated with LS-1-127 (10 mg/kg IP) or equal volume of vehicle (10% DMSO; IP) three times a week for two weeks. At 35 weeks, mean arterial pressure (MAP) was measured in conscious mice using indwelling carotid catheters for two consecutive days and then mice were euthanized. Wire myography was used to assess potassium chloride (KCl)-induced contraction and acetylcholine (ACh)-induced relaxation in excised aorta. Markers of renal injury – urinary neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), and creatinine – as well as plasma double-stranded (ds)DNA autoantibodies were measured by ELISA.

Albuminuria was present in 44.4% (4 of 9) of SLE mice and no controls. LS-1-127 did not improve albuminuria in SLE mice (50%; 3 of 6). NGAL:creatinine ratio (ng/mg) was higher in SLE mice compared to controls (327.3 ± 119.8 vs 63.2 ± 4.3 ng/mg; $n=9-12$; $P=0.0007$). LS-1-127 did not significantly alter NGAL:creatinine ratio in SLE mice (484.3 ± 209.0 ; $n=6$) or controls (71.7 ± 5.2 ; $n=10$). KIM1:creatinine ratio (ng/mg) did not differ between groups. dsDNA autoantibodies were higher in SLE mice compared to controls ($6.9e5 \pm 1.1e5$ vs. $1.4e5 \pm 3.1e4$ U/mL; $n=9-10$; $P<0.0001$). LS-1-127 did not significantly alter dsDNA autoantibodies in SLE mice ($7.1e5 \pm 1.2e5$; $n=6$) or controls ($1.5e5 \pm 4.0e4$; $n=10$). MAP was higher in SLE mice compared to controls (146 ± 4 vs. 123 ± 3 mmHg; $n=9-10$; $P<0.0001$). LS-1-127 did not significantly alter MAP in SLE mice (150 ± 8 ; $n=6$) or controls (124 ± 2 ; $n=10$). KCl-induced aortic contraction was similar in SLE and controls (21 ± 7 vs. 25 ± 4 mM, $n=3-4$). Sensitivity to KCl after LS-1-127 treatment was 11 ± 3 and 21 ± 2 mM in SLE and controls ($n=2-4$). ACh-induced aortic relaxation did not differ between groups.

In conclusion, two weeks of S1R activation with LS-1-127 did not significantly alter markers of renal injury, autoimmunity, blood pressure, or vascular reactivity in female SLE mice with advanced disease. Further inquiry into the effect of LS-1-127 on the expression of renal proinflammatory cytokines will be conducted. S1R activation at different stages of SLE disease progression also warrants future investigation.

EXTERNAL FUNDING SOURCE

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IACUC NUMBER
IACUC-2020-0030

Health Equity Implications of Transgender Policies in the United States: A Legal Epidemiology Approach

PRESENTER

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ABSTRACT TOPIC

Health Disparities

ABSTRACT

Introduction: Transgender (trans) populations experience worse health outcomes compared to cis-gender populations, including higher rates of poor mental health, experiences of medical bias, and communicable diseases. These health disparities are broadly influenced by the political context within individual states that can perpetuate social exclusion. In the last five years, there has been a sharp increase in exclusionary legislation related to trans individuals that can deepen health inequality and exacerbate poor health outcomes. Using a legal epidemiological approach, we conducted a policy scan of state-level legislation in the United States to determine geographic distribution, frequency, and whether the legislation was trans affirming and/or exclusionary.

Methods: We searched the Westlaw policy database to identify proposed legislation in U.S. states between 2017-2021 using search terms related to “transgender.” The initial search identified 1280 results, of which, 698 proposed bills were included in the final analysis. Five researchers reviewed the proposed legislation and categorized each bill into “affirming” or “exclusionary” categories. Using a priori themes identified in the grey literature and refined among the research team, bills were further categorized by the theme of the legislation into 11 categories: athletics, bathrooms, administrative changes, affirmation care, religious claims, recognition, rights in the healthcare field, training revisions, criminal justice reform, education and school, and government augmentation. These categories were used to calculate affirming density, exclusionary density, and inclusivity scores and corresponding maps for legislation related to trans populations in each state.

Results: Of the 698 policies reviewed, 567 (81.23%) were affirming of trans identities while 131 (18.77%) were exclusionary of trans identities. Affirming legislation included policies related to government augmentation (20.81%), education/school (18.34%), administrative bills (18.17%), criminal justice reform/legal protections (15.34%), rights in the healthcare field (11.46%), training revisions (10.05%), recognition (4.94%) affirmation care (0.71%), and athletics (0.18%). Exclusionary legislation included policies related to athletics (58.78%), affirmation care (24.43%), bathrooms (7.63%), education/school (3.82%), religious claims (2.29%), administrative changes (1.53%) and rights in the healthcare field (1.53%). Affirming legislation was most prominent in the West Coast, the Northeast, and parts of the Midwest. Conversely, exclusionary legislation was highly prevalent among Southeast, South Central, and Mountain West regions.

Discussion: This study laid the foundation for further analysis of the political context and its influence on trans health. Exclusionary and affirming density maps indicate vastly different political contexts for trans individuals depending on US state. Such political contexts can contribute to social exclusion of trans individuals that exacerbates poor health outcomes. Further, the magnitude of legislation proposed was starkly different between affirming and exclusionary policies. Exclusionary policies focused on criminalization of trans-related issues such as gender-affirming care. Comparatively, affirming policies were largely focused on forms of representation related to local boards or governing committees (government augmentation). Representation of LGBTQ+ communities in government is incredibly important but may not negate the harm caused by the

criminalization of trans-related care. Future research is needed to investigate legal etiologies of health disparities seen in trans populations compared to cisgendered populations.

Transgender Healthcare and The Impact of Increased Politicization of Medicine

PRESENTER

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ABSTRACT TOPIC

Health Disparities

ABSTRACT

Purpose: Transgender (trans) people have a unique set of health needs that are often misunderstood and/or ignored in health settings. Such misunderstandings contribute to mental and physical health disparities when compared to the cisgender population, such as increased rates of anxiety, depression, suicide, substance abuse, adverse cardiovascular events, and other chronic health conditions. Addressing these disparities requires greater access to gender-affirming care (GAC) with providers who are comfortable and knowledgeable about trans individuals' unique health needs. However, recently there has been an increase in anti-transgender legislation across the United States. This raises questions about provider regulation and ability to provide culturally appropriate care to trans patients, and potentially widening access and care disparities among trans individuals. Future providers, including medical students, who are being trained during moments of heightened anti-transgender politics, may not feel sufficiently prepared to care for trans patients. This exploratory study examined 1) current medical students' knowledge and attitudes towards treating trans patients 2) gaps in transgender-focused content in medical curricula, and 3) medical trainings and their degree of impact on transgender healthcare.

Methods: A literature review was conducted by searching scholarly databases including PubMed using the terms related to transgender health, policy, medical students, gender-affirming care, health providers, and gender dysphoria. Articles that were 1) published after 2014 2) in English, and 3) available as full text were included. The search yielded 52 articles that were then reviewed for content on medical students' knowledge and attitudes about trans patients, gaps in medical curricula, and perceived efficacy of trans-focused trainings and educational interventions.

Results: Existing literature suggests that trans health disparities are largely related to provider lack of knowledge and training. Despite potentially positive attitudes regarding this population, most medical students feel their curricula lacks transgender-centered content. This includes diagnosing gender dysphoria, hormone-therapy, puberty blockers, and sex reassignment surgeries. Although some students may feel knowledgeable about trans individuals' needs overall, many report they still feel ill-prepared to work with trans patients. They request more clinical exposure to gain confidence with proper history taking and interview skills. When assessing the training modalities preferred by medical students, interactive interventions including direct communication with trans patients yield the greatest increase in perceived confidence levels. The most recommended training modalities for practicing physicians are attending professional conferences, acquiring direct clinical mentorship, and implicit bias self-awareness workshops.

Conclusion: This synthesis of current research highlights the need for increased trans-focused support in medical education, which will contribute to improving overall health outcomes, ease barriers, and ameliorate disparities for transgendered persons. In the current political context, physicians who provide GAC are faced with a unique set of social and legal challenges. Government intrusion of clinical decision-making may force physicians to forgo their obligations to transgender patients, thereby directly eliciting harm to an already marginalized population. Accordingly, current and future providers may need to engage in trans-focused advocacy efforts.

OMT Efficacy for Chronic Pelvic Pain Secondary to a Delayed Diagnosis of Endometriosis

PRESENTER

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ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Background: Endometriosis is a gynecological disease characterized by ectopic growth of endometrial tissue. Common symptoms include dysmenorrhea, dyspareunia, chronic pelvic pain, and infertility. Additionally, current research is showing an increased incidence of systemic inflammatory illnesses in those with endometriosis. Due to the variability in the presentation of symptoms and location of endometrial lesions, patients are often told their symptoms are consistent with normal menstruation and their true diagnosis is significantly delayed. Recent research suggests most patients experience a 7–9-year delay in diagnosis. Furthermore, after years of these troubling symptoms, treatment is not always effective at achieving pain relief. It has been found that up to 59% of patients continue to have pain after treatment. OMT has been poorly researched in this area, but currently available research has shown success in achieving pain relief for these patients.

Case Presentation: A 39-year-old female presented to the UNTHSC OMM clinic for evaluation of pelvic pain secondary to endometriosis. Though she experienced symptoms of severe dysmenorrhea and pelvic pain since menarche and dyspareunia, infertility, and other systemic inflammatory illnesses since early in her reproductive years, she was not given the diagnosis of endometriosis until she was 27, after a disproportionately painful pelvic exam prompted an ultrasound. This ultrasound revealed two endometriomas, measuring 5.7x3.6cm and 4.5x3.4cm. Six months later, after a failed trial of progesterone and continued growth of the lesions, she underwent laparoscopic removal of the cysts which confirmed the composition of these endometriomas. She was then placed on oral contraceptive pills for management of her disease. Initially these were taken to allow for monthly menstruation, and she found enough relief to make her symptoms bearable for the next six years. However, at age 34, she was advanced to continuous use due to catamenial migraines. This regimen allowed her to return to roughly 50% of her normal daily activities, though she was still limited due to chronic pelvic pain and stress-induced flare-ups. Finally in 2020, at age 39, she found the UNTHSC OMM clinic and began bi-monthly treatments for her pelvic pain. She reported that after being treated here she experienced immediate relief of her pain. This relief initially would last for roughly 1 week and then her pain would slowly return. After several months of regular visits, she was able to gradually space out her visits to as far as six months apart without breakthrough pain.

Conclusion: Endometriosis is a complex disease that leads to significant pain and diminished quality of life. Not only do these patients struggle with various gynecologic symptoms and systemic inflammatory flares, but they are also left to suffer for years without a diagnosis due to their pain being attributed to normal menstruation. After finally getting their diagnosis, many patients still do not get pain relief due to the reliance on medicinal treatments. This case is a clear example of the need for more intensive education for medical professionals in both the diagnosis of endometriosis and the addition of OMT to the treatment regimen.

Assessing tumor biopsy decellularization using contact angle method

PRESENTER

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ABSTRACT TOPIC

Pharmaceutical Sciences

ABSTRACT

Purpose: More than 30% of new female cancer cases each year are breast cancer, according to the National Cancer Institute, whose risk increases progressively with advancing age. To date, off-target toxicity remains a main drawback of anticancer therapy. Several drug delivery systems are developed to bypass this problem, and among these the nanoparticle-based delivery platforms have proved extremely promising. A successful example of this approach is liposome formulation which today is used to encapsulate drugs such as doxorubicin (DOXIL) and paclitaxel. A critical role in the development of anticancer drugs is played by preclinical testing, but animal testing is very expensive, time-consuming, and limited due to their different physiology. Using patient tissue biopsies may help identify promising drugs to advance to clinical trials, saving time and money. Extracellular matrix (ECM) in this context is well known to present an impact on anticancer drug efficacy by acting as a barrier between drug molecules and targeting cancer cells, but little has been done so far to quantify and characterize the behavior of drugs and formulations on it. ECM hydrophobicity, in particular, can affect drug penetration through tissue and tissue membranes changing drug absorption. We hypothesize that contact angle can be used as part of the pre-clinical screening of promising anti-cancer drug candidates by assessing ECM hydrophobicity and ECM-drug interactions. Here, we optimized a tissue decellularization process to test ECM hydrophobicity and interaction with liposomes using contact angle measurement.

Methods: An in-house modified optical goniometer instrument was used to measure the contact angle on glass slides and de-identified, commercially available breast cancer tissue sections (US Biomax Inc). Samples were deparaffinized by consecutive washing cycles in xylene, ethanol, and water. The slides were dried in the incubator for 60 minutes at 60 °C to ensure adequate tissue adherence. Tissues were then decellularized by up to three freeze-thaw cycles in water 0.1% w/v SDS (Sodium dodecyl sulfate). Contact angle measurements obtained at every step of the deparaffinization and decellularization process were used to determine the optimum tissue processing method. The contact angle of liposomal suspensions was then collected on glass and tissue sections that were processed accordingly.

Results: The optimum decellularization process for cancer biopsy sections was two freeze-thaw cycles using pure water; SDS was found to cause some tissue detachment from the glass slide. After each freezing cycle, contact angle was trending upwards. This indicates that tissue decellularization results in progressively more hydrophobicity, likely due to the removal of water-soluble proteins and polysaccharides. This effect was more pronounced in tumor tissue compared to healthy tissue from the same patient. Contact angles obtained using liposomal suspensions were lower than water contact angles and followed similar patterns.

Conclusions:

- Contact angle measurements can be used to quantify and optimize tissue decellularization.
- Decellularized biopsies are slightly more hydrophobic, an effect more pronounced in tumor tissue compared to healthy.
- Liposomes reduce contact angle due to their inherent surfactant-like properties.
- Contact angle may be used to distinguish how anti-cancer liposomes interact with tumor and healthy tissue.

EXTERNAL FUNDING SOURCE

Texas Center for Health Disparities, National Institute on Minority Health and Health Disparities

Association of Area Deprivation Index and hypertension, diabetes, dyslipidemia, and obesity: a cross-sectional study of the HABS-HD cohort.

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Cardiovascular

ABSTRACT

Background: Heart disease is a leading cause of death globally and the prevalence of cardiovascular disease (CVD) is expected to increase significantly in the United States over the next decade. Previous research has shown that socioeconomic status has a significant impact on CVD prevalence and outcomes, with risk factors for CVD being more prevalent in individuals from low socioeconomic groups. We aimed to investigate the association between neighborhood deprivation and the prevalence of major CVD risk factors (hypertension, diabetes, dyslipidemia, and obesity) in a Mexican American population compared to Non-Hispanic Whites.

Methods: A cross-sectional analysis was conducted to include 1867 subjects. 971 self-identified as Mexican American (MA), and 896 as Non-Hispanic White (NHW). These participants underwent a clinical interview, neuropsychological exam battery, functional examination, MRI of the head, amyloid PET scan, and blood draw for clinical and biomarker analysis. They were also assigned an ADI score based on participants living in the best and worst neighborhoods according to Area Deprivation Index (ADI) model.

Results: Sixty percent of the sample was female. MA were significantly younger (mean age 63.37 vs 68.64) and less educated (mean education years 9.69 vs 15.61 than NHW. Additionally, MA had a significantly higher prevalence of HTN, DM, and obesity. Only 12.3% of Non-Hispanic Whites lived in the most deprived neighborhoods (percentile 4), while 57.5% of Mexican Americans lived in the percentile 4 ranking areas ($p \leq .05$). There was a significant difference between non-Hispanic White participants living in the least deprived neighborhoods compared to participants living in the most deprived neighborhoods for HTN (OR = 2.14, 95% CI [1.31, 3.48]), DM (OR = 3.42; 95% CI [1.67, 7.01]), and obesity (OR = 3.03, 95% CI [1.86 to 4.95]). There was no significant difference in the odds of having dyslipidemia between non-Hispanic Whites living in the ADI quartile 1 when compared to those living in the ADI quartile 4. These results remained significant after adjusting for age, sex, education, and cardiovascular risk factors.

Conclusion: In conclusion, this study found the area deprivation index (ADI) is associated with cardiovascular risk factors such as hypertension, diabetes, dyslipidemia, and obesity. These findings suggest that socioeconomic status may play a role in the prevalence of certain health conditions among different ethnic groups. Further research is needed to understand the underlying mechanisms and to develop interventions that address health disparities among different ethnic populations.

IRB NUMBER

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Using the Model Aquatic Health Code to Grade the Safety of Swimming Pools in Houston, Texas

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ABSTRACT TOPIC

General Public Health

ABSTRACT

Purpose: Drowning and submersion injuries in the pediatric population are responsible for many unintentional deaths. Moreover, there are other associated injuries in young children such as water-borne diseases, falling, and diving injuries. The Model Aquatic Health Code (MAHC) developed by the CDC issues guidelines aimed to decrease disease, injury, and drowning events at aquatic facilities. Since no federal regulatory authority currently exists, there is wide variation in the inspection of aquatic facilities and implementation of the MAHC guidelines across state and local authorities. The aim of this study was to devise a grading system for swimming pools across the city of Houston by applying the MAHC guidelines to pool inspection data. The results may then inform measures to strategically provide pool operators and the public with safety information regarding swimming pools.

Methods: A cross-sectional study of commercial swimming pools and spas in Houston was conducted in 2016 using routine inspection reports. Each public pool in Houston is required to undergo annual inspections. Private residential pools are not required to be inspected annually and such reports were excluded. The MAHC was used to develop a grading system that assigned points to commercial swimming pools and spas based on violations as detailed in inspection reports. Letter grades were assigned 95-100% (A); 85-94% (B); 75-84% (C); <75% (F-Fail) based on overall percentage of compliance with MAHC and projected onto a map of the city of Houston.

Results: A total of 3107 commercial aquatic venues were inspected in Houston during 2016 with 3100 of these being located within the city of Houston. Each venue was graded for safety and had the following grade distribution: (A): 40.2%; (B): 0.5%; (C): 0%; and (F): 59.3%. The most frequent violations were related to swimming pool enclosures (18%) followed by self-closing gates (13.8%). The majority of swimming pools inspected were concentrated in southwest Houston.

Conclusions: The MAHC guidelines may be used to appropriately assess and grade swimming pool safety in jurisdictions in which they have not yet been endorsed. Many jurisdictions vary in their regulation and implementation of policies regarding swimming pool safety. There may be a need for more jurisdictions to update their pool inspection criteria using MAHC guidelines. Further, injury prevention measures can be used to devise injury prevention measures based on the spatial distribution of safety violations.

Association of Race and Receiving Mental Health Counseling in Patients Diagnosed with Depression

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ABSTRACT TOPIC

Health Disparities

ABSTRACT

Context: High prevalence of depression in the United States population is a rising issue, which warrants the need for understanding how to best target behavioral therapy as a treatment option for populations who are least likely to have received or to seek out such intervention.

Purpose: To determine if there is a significant relationship between race and frequency of mental health counseling as a treatment option in patients with depression.

Methods: This cross-sectional study included 949 patients diagnosed with depression, retrieved from the 2018 NAMCS (National Ambulatory Medical Care Survey) database. These patients were stratified by race as given in the NAMCS variable as "White", "Black", and "Others". Of those 949 patients, 97 subjects sought out mental health counseling. We performed statistical analyses to determine if race was a predictor for seeking out mental health treatment.

Results: An ANOVA statistical analysis demonstrated a significant difference in those who sought out mental health counseling and race ($p = .009$) amongst those patients diagnosed with depression. Age ($p < .001$) was another significant factor affecting whether these patients sought mental health counseling. 12/42 "Other" subjects (9.1%, $p < .001$) with depression sought mental health treatment, followed by 9/69 Black subjects (13%, $p = .024$), followed by 76/838 White subjects (9.1%, $p < .001$).

Conclusions: The results contradicted our initial prediction, which anticipated that the white population would show higher rates of receiving mental health counseling than black and other race populations. We attribute these findings to the differences in severity and perception of depression symptoms among different races. Limitations to the study include sample size availability, inconsistencies in what each physician constitutes as mental health treatment, coding inaccuracies, and confounding variables including socioeconomic status and age.

A mendelian randomization analysis of obesity on the development of Alzheimer's disease

PRESENTER

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COLLEGE/SCHOOL

School of Public Health

ABSTRACT TOPIC

Aging / Alzheimer

ABSTRACT

Purpose: To assess the causal associations between obesity and Alzheimer's disease (AD) using Mendelian randomization analysis based on summary statistics from genome-wide association studies (GWAS). The most recent GWAS as of November 2021 for AD and obesity were used, including newly identified risk single nucleotide polymorphisms (SNPs) that were associated with AD and obesity. Specifically, the AD GWAS identified 42 new risk loci, which have not been utilized in other studies. Thus, this study provides novel evidence for the causal associations of AD and obesity.

Methods: Genetic associations for the exposure (i.e., obesity; BMI $\geq 30\text{kg/m}^2$) were evaluated from a GWAS conducted on European individuals over age 18 in the FinnGen project ($n = 218,792$). Genetic associations for AD were evaluated from the whole exome sequencing data among European individuals aged 37-73 years in the UK Biobank study ($n = 111,326$ AD cases and 677,633 controls). Based on the above summary statistics, a Two Sample Mendelian randomization (MR) analysis using the Inverse-Variance Weighted (IVW) method was conducted to evaluate the causal association between obesity and AD. Sensitivity analyses including median-based, mode-based, and MR-Egger MR methods were conducted to confirm findings from the main MR analysis.

Results: Obesity was found to be associated with a decreased odds in the development of AD (Odds ratio = 0.91, 95% CI = [0.86, 0.95], $p = 0.0001$) according to the IVW method, suggesting a protective effect of obesity. The results of all sensitivity analyses were consistent with the main findings and determined the absence of horizontal pleiotropy and heterogeneity. Specifically, significant causal relationship between AD and obesity was identified in the IVW method and Weighted Median MR methods.

Conclusion: The protective effect of obesity on the development of AD is supported by the MR analysis in this study. Further research should be conducted on the underlying pathological mechanism to inform potential health interventions such as weight modification in mid versus late life.

A Qualitative Histological Comparison of Collagen Deposition Between a Diseased and Healthy Cadaveric Heart

PRESENTER

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ABSTRACT TOPIC

Structural Anatomy

ABSTRACT

Purpose: Fibrosis is a pathological process characterized by the overproduction of extracellular matrix (ECM), especially collagen. Type I collagen is the most abundant structural protein found in ECM and serves as an indicator for fibrosis. Although increased collagen accumulation is considered a normal aspect of aging, excessive collagen accumulation is also a notable hallmark observed in chronic cardiovascular disease. Numerous studies have examined collagen deposition using animal models and pathologic human cardiac tissue. However, few studies have investigated the normal accumulation of collagen in healthy human hearts. This study aims to perform a qualitative comparison of collagen deposition between a diseased and healthy human heart.

Methods and Results: This study utilized two hearts from cadaveric donors, one designated “diseased” and the other “healthy”. Each heart originated from a female in their 6th decade of life and had a body mass index within the normal range (18.5-24.9 kg/m²). The donor with the “diseased” heart had a known history of heart disease. Furthermore, gross examination revealed the “diseased” heart was enlarged (mass: 458.5 g; normal range: 230-290 g), had severe coronary artery disease, contained two implanted coronary artery grafts, and demonstrated left ventricular wall hypertrophy (thickness: 2.0 cm; normal thickness: ≤ 1.5 cm). In contrast, the donor with the “healthy” heart had no known history of heart disease and showed no visible signs of disease. Tissue samples were collected from the right ventricle, interventricular septum, and left ventricle from each heart and underwent routine histological preparation with Masson’s trichrome staining. Microscopic observation was performed to determine the pattern of collagen deposition within each section, classified as interstitial-perimyocyte, replacement, or mixed. Additionally, the location of collagen in each section of the ventricular wall was noted as being primarily within the inner 50% (endocardial side), outer 50% (epicardial side), or diffuse. To assess the reliability and repeatability of this study, an analysis of intra- and interobserver error will be conducted by the authors. Preliminary findings suggest the amount and patterns of collagen differs between the two hearts.

Conclusion: In this study, histology was used to qualitatively analyze the differences in collagen deposition between a diseased and healthy human heart. These findings highlight the importance of conducting a comprehensive study that examines the normal accumulation of collagen in healthy human hearts. Gaining an in-depth understanding of how collagen accumulates normally is critical for recognizing disease related changes.

Pediatric Weight Gain Rates in Fort Worth, TX Due to the COVID-19 Pandemic

PRESENTER

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ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Background: Childhood obesity is already a problem in the United States, with one out of three children being overweight or obese and one out of six being obese. The consequences from the COVID-19 lockdown seemed to have progressed into something bigger. During the pandemic, added stress amongst the pediatric population dramatically increased causing this population to snack more and exercise less. This change in eating habits and behaviors can have long term implications on their health currently and in the future.

Methods: Data from the outpatient Pediatric and Health Clinic at UNTHSC in Fort Worth, TX from January 2018 to May 2022 was used to assess this effect. Average weight gain year to year was computed and compiled for several zip codes in the North Texas area. The average weight gain was calculated based on the children's age, sex, zip code and their ethnicity and race.

Results: Within each variable the average weight gain had increased year to year. The average weight gain amongst the pediatric population in this study increased to 16.13% compared to 13.92% pre-pandemic. The increased weight gains are cumulative with each year, as with each year they are adding more weight on top of the weight they had gained the previous year. When we calculate the percent weight gain in specific age groups and genders, we see a higher increase in weight gain, with male children gaining more weight on average compared to females. When looking at different zip codes, we see greater increases in weight gain related to lower household incomes. Boyd had an average of 34.87% increase in weight post pandemic compared to 13.91% pre-pandemic.

Conclusion: The increased weight gain leads to an increase in obesity rates among the pediatric population and the future adult population. This will burden our healthcare system now and more so in the future. Further research needs to be conducted on the health disparities between different ethnicities and races and average household incomes.

Microfluidic Chip for the evaluation of therapeutics and carrier drugs in breast cancer tissue

PRESENTER

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ABSTRACT TOPIC

Pharmaceutical Sciences

ABSTRACT

Introduction: Breast cancer is the most common cancer in women where 1 in 8 will develop over the course of her lifetime. However, some treatments react differently depending on race and ethnicity. Unfortunately, there are no preclinical models capable of studying pharmacoeethnicity differences of drugs. Hence, racial differences are found late during clinical trials or after market adoption. The absence of a model that studies pharmacoeethnicity differences results in negative outcomes for the affected race. The objective of this project is to design and evaluate a microfluidic in-vitro platform to test therapeutics and carrier drugs, such as Doxil liposomes, in breast tumor tissue and compare properties based on the tissue's race and other attributes. The microfluidic device is capable of delivering a dual channel fluid system with the intention of emulating blood and interstitial fluid in tissue. The chip is unique from other systems by directly using human tissue and designing a microfluidic chamber specific to a patient's tumor allowing it to be used for personalized medicine.

Methods: To build a microfluidic platform, a 15 μm tumor section is mounted to a positively charged slide. Then capillary channels are etched at 120 μm diameter with an estimated precision $\leq 10 \mu\text{m}$, channel spacing is set to 350 and 500 μm . Channels are etched in glass slides using a 5W UV Laser Marking Machine with 70 mm f-theta lens, at a pulse rate of $\leq 15 \text{ ns}$. Current chip model requires etching two main capillary glass slides. Each slide is then covered by an intermediate thin layer per etched channel side. Afterwards, the slides are assembled with UV resin Loctite 349 and cured under UV light for 20 minutes. Finally, a third slide is used as the interface between the chip and the chromatography tubing. After assembly, the blood and interstitial fluid channels are loaded with deionized water and are flow and pressure tested. As a proof of concept, an acridine orange solution was used with a preliminary chip. Dye penetration was then measured using an inverted microscope.

Results: A total of 8 microfluidic chips have been successfully built, and an additional 19 chips are under development. The initial microfluidic chip prototype demonstrated tumor tissue was stained by an acridine orange solution by a total of up to 75 μm past the capillary channels. The preliminary chips exhibited chamber issues where interstitial fluid merged with the blood channel. This has now been successfully corrected in the current chip model. A total of 6 microfluidic chips will be used with a carrier drug, such as Doxil liposomes.

Conclusions: After method revisions, where are now capable of developing fully working microfluidic chips. Our preliminary studies demonstrate the capabilities of using our chips to test drug penetration in tissue. Our current objective is to measure drug penetration in breast cancer tumors based on race. Future studies will include additional method development to enable live tissue use and to measure additional drug properties.

EXTERNAL FUNDING SOURCE

Texas Center for Health Disparities Grant # 2U54MD006882-06

Association of Cancer with Alzheimer's Disease and related Dementias among older adults with chronic pains: TriNetX analysis with Multi-institutional Electronic Health Records

PRESENTER

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HSC College of Pharmacy

ABSTRACT TOPIC

Aging / Alzheimer

ABSTRACT

Introduction: Recent retrospective cohort studies have reported that non-cancer chronic pain, specifically non-cancer pain conditions (NCPCs), are associated with an increased risk of Alzheimer's disease and related dementias (ADRD) in older adults. However, a recent case-control study found that cancer-induced pain had a protective association with ADRD, suggesting that cancer pain's association with ADRD is inconclusive. Therefore, we analyzed the association of cancer with ADRD among older adults with chronic pain.

Methods: We adopted a retrospective cohort analysis. The cohort consisted of older adults with chronic pain in 2016 and 2017. The data used in this study is from the TriNetX Research Network, which provided access to electronic medical records (diagnoses, procedures, medications, and laboratory values) for patients from 64 healthcare organizations (HCOs). A propensity score-matched analysis of cancer and non-cancer patients used age, sex, race/ethnicity, surgery, factors influencing health status and contact with health services; endocrine, nutritional, and metabolic diseases; diseases of the circulatory system; nervous system; digestive system; musculoskeletal system and connective tissue; and mental, behavioral and neurodevelopmental disorders. The outcome variable was ADRD incidence, which occurred at least one year after the first chronic pain diagnosis.

Results: Before matching, among older adults with cancer, there were 212,739 and 465,316 with and without cancer, respectively. The 3-year cumulative incidence of ADRD was 2.97% (N = 6320) in the cancer group and 1.96% (N = 9096) in the non-cancer group. After propensity matching, there were 195289 participants in both groups. The cumulative incidence of ADRD was 2.79% (N = 5457) in the cancer group and 2.62% (N = 5124) in the non-cancer group (Risk Ratio = 1.07, 95% CI: 1.02-1.10). Secondary analysis of ADRD incidence in adults who died did not reveal a significant association between cancer with ADRD.

Conclusion: Our research has found that cancer is not associated with the risk of ADRD among patients with chronic pain. Our study estimates of ADRD incidence are lower than the national rates, suggesting the limitations of electronic health records in capturing true ADRD incidence.

The study's findings must be interpreted in the context of the study's strengths and limitations. For example, data were from 64 HCOs, and the study did not adjust for case-mix or practice differences. In addition, the study is limited to those seeking care in these HCOs and may have missed care obtained outside of these organizations. Thus, our estimates of ADRD incidence are substantially lower than the national ADRD incidence. Nevertheless, the study's strengths are the use of multi-institutional electronic health records, large numbers of cases and controls, and the ability to conduct propensity score-matched analysis with a comprehensive list of risk factors.

Keywords: Dementia, Alzheimer's disease, and Related Disorders, Cancer, Chronic Pain, EHR

Expression of Immune Receptors in Response to Chemotherapy Treatment in B and T Acute Lymphoblastic Leukemia

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COLLEGE/SCHOOL

School of Biomedical Sciences

ABSTRACT TOPIC

Immunology

ABSTRACT

Acute Lymphoblastic Leukemia (ALL) represents the most common pediatric cancer. Most patients (85%) develop B-cell ALL, however, T-cell ALL tends to be more aggressive and show less promising prognosis. Significant improvements in chemotherapy regimens caused a leap in the 5-year survival rates to surpass 90%. However, relapse significantly lowers the chances of survival to less than 50% due to resistance developed by malignant cells to chemotherapy. Natural Killer (NK) cells represent the cytotoxic compartment of innate immunity. As opposed to T cells, NK cells can recognize and kill malignant cells without the need for antigen presentation. NK cells currently represent a promising immunotherapy alternative to traditional chemotherapy. They directly kill cancer cells through activation/inhibition signals or through cytokine release and mediating an adaptive response. As targets of interest for our research, we chose LLT1, CD155 and PCNA as NK-inhibitory receptors and CS1, 2B4 as activation receptors. Previously, we have shown a significant decrease of LLT1, 2B4 and CS1 on T lymphoblasts of ALL patients collected from 42 subjects after induction chemotherapy and compared with samples from 20 healthy subjects. Based on the preliminary data, in this study we are investigating the effect of chemotherapy on the expression of those activating and inhibitory receptors. Cell surface protein expression and mRNA expression of these NK receptors pre- and post-Doxorubicin and Vincristine treatment of B and T ALL cell lines have been analyzed. Resistance to chemotherapy is one of the major reasons for failure of treatment in cancer recurrence. However, the cytotoxic potential of NK cells can be harnessed to overcome the chemo-resistance seen in leukemic cells.

The impact of tyrosine hydroxylase loss on dopamine signaling during nigrostriatal neuron loss in a rat Parkinson's disease model

PRESENTER

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COLLEGE/SCHOOL

Dual Degree

ABSTRACT TOPIC

Neuroscience

ABSTRACT

Purpose: Parkinson's disease (PD) is a neurological disorder resulting from the degeneration of nigrostriatal dopamine (DA) neurons. DA plays a major role in the control of movement initiation via the nigrostriatal pathway. The relationship between DA tissue levels and synaptic levels is poorly understood, and the impact of tyrosine hydroxylase (TH) loss upon synaptic DA levels is not well defined either. As the rate limiting enzyme of DA synthesis, tyrosine hydroxylase (TH) protein was evaluated against these indices of DA function. Since PD involves progressive loss of the nigrostriatal neurons and TH protein, understanding how synaptic DA levels may change against this decrease will shed light on whether compensatory processes are engaged to maintain synaptic DA levels, and can outline possible limits of such processes and their influence upon the timing of onset of hypokinesia, a major PD symptom.

Methods: We used the established rat neurotoxin model 6-hydroxydopamine (6-OHDA) utilizing stereotactic surgery to lesion the nigrostriatal pathway and emulate the pathological course of human PD, which features DA and TH loss in the Str proceeding at a faster rate than in the SN. Following microdialysis, brain tissue punches from the SN and Str regions of both lesioned and control rats were harvested at 7 and 28 days, and then analyzed by high-performance liquid chromatography to quantify both synaptic and tissue DA. We followed with TH protein analyses to statistically quantify the relationships between TH protein, DA tissue, and synaptic DA.

Results: Our results show that TH protein levels had a highly significant correlation against DA tissue levels in the lesioned Str and SN; however, only synaptic DA release levels in the Str following depolarizing stimulation had a significant correlation with TH protein. Additionally, only 15% of the variance in lesioned Str synaptic DA levels can be explained by tissue DA and TH concentrations when using a multivariate linear regression model. These results show that compensatory processes are engaged during nigrostriatal lesion to maintain synaptic levels, but these mechanisms are inadequate to offset major TH protein loss in the Str.

Conclusions: The particular significance of this study lies in its focus on extracellular neurotransmitter analysis – something that has not been extensively explored. Our findings will provide novel insight into how synaptic DA levels are affected by expected decreases in tissue content, thus deepening the current understanding on transmission within the basal ganglia and generating areas for further research.

IACUC NUMBER

IACUC-2021-0018

In Silico Analysis to Determine the Association of Specificity Protein (Sp) Transcription Factors, Sp1 and Sp3 and Survivin Expression with the Prognosis of Cancers Affecting Women

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Cancer

ABSTRACT

Background: Breast cancer is the most common invasive cancer in women worldwide. Studies have shown that breast cancer shares risk factors and genetic mutations with ovarian and uterine cancers which are also analyzed to be increasing in incidence. Clinically, diagnosis of concurrent genetically shared cancers like breast, ovarian, and uterine would have an impact on the treatment options and its course. Dysregulation of transcription factors like Specificity protein (Sp) 1 and 3 which remodel chromatin is responsible for many cancers. While the expression of Sp1 is documented to be upregulated in breast and ovarian cancer, and Sp3 only in breast; uterine cancer lacks such evidence. Baculoviral IAP repeat-containing 5 (BIRC5), also known as survivin, is an inhibitor of the apoptotic pathway and is found to be upregulated in breast, ovarian, and uterine cancer. Sp1, Sp3 and survivin are all associated with high expression in numerous cancers and lead to poor prognosis.

Objective: The objective of this study is to analyze the expression of Sp1, Sp3 and survivin in breast invasive carcinoma, ovarian serous cystadenocarcinoma, and uterine corpus endometrial carcinoma to evaluate the prognosis (in all patients and by race/ethnicity) of cancer patients using the data deposited in a public database.

Methods: Relevant data and Kaplan-Meier curves were obtained from accessing the public database, The Cancer Genome Atlas (TCGA) (a landmark cancer genomics program developed by the National Cancer Institute and the National Human Genome Research Institute). This data was used to screen for the expression status (upregulated or downregulated), significance and relevance to prognosis for all patients and in relation to race/ethnicity for breast invasive carcinoma, ovarian serous cystadenocarcinoma, and uterine corpus endometrial carcinoma.

Results: Sp1, Sp3, and survivin expression significantly impacted patient survival in breast invasive carcinoma (n=1211), ovarian serous cystadenocarcinoma (n=302), and uterine corpus endometrial carcinoma (n=581). When looking at Sp1 and combining data for all patients, there was a relevance in prognosis in ovarian serous cystadenocarcinoma (p=0.045). Additionally, there was an association between the marker and poor prognosis for race/ethnicity when looking at breast invasive carcinoma and uterine corpus endometrial carcinoma. Sp3 and survivin presented similarly when looking at combined and racial/ ethnic prognosis. Both Sp3 and survivin indicated a poorer prognosis for overall population survival in uterine corpus endometrial carcinoma (p=0.018 and p=0.015 respectively). They also presented with a worse prognosis when looking at race/ethnicity for all three listed cancers.

Conclusion: The findings from this study suggest an association of Sp1, Sp3, and survivin expression in breast invasive carcinoma, ovarian serous cystadenocarcinoma, and uterine corpus endometrial carcinoma and their prognosis. The results also suggest that these markers may contribute to poor prognosis for patients in certain racial/ethnic groups.

Multi-hazard assessment in Kyrgyzstan's Osh Region using Maximum Entropy

PRESENTER

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School of Public Health

ABSTRACT TOPIC

Other

ABSTRACT

Purpose: Climate change impacts natural processes that lead to increased warming and extreme precipitation. As global temperatures continue to rise, an increase in the frequency of climate- and weather-related disasters is expected. Over the past decade, approximately 200 million people were affected by disaster events, with 81,000 deaths per year on average. Majority of the impacts occurred in the 40 most mountainous countries, including Kyrgyzstan in Central Asia. More than 80% of the land area in Kyrgyzstan is mountainous and highly hazardous. The Osh Region in Kyrgyzstan, in particular, is a site that suffers multiple types of natural hazards, such as floods, landslides, earthquake, and drought. These hazards pose a great risk to the mountain communities. Currently, the susceptibility distribution of the multiple hazards in the Osh Region, and the populations exposed to it remain to be assessed. The goal of this study was to harmonize three natural hazards – flood, landslides, and wildfire – of the Osh Region in a generalized multi-hazard susceptibility map (MHSM) that incorporates bioclimatic and geo-environmental factors for disaster risk management and response planning.

Methods: Inventory maps for single hazard susceptibility were prepared by processing thematic layers from remotely-sensed data, hazard catalogs, and bioclimatic data. A total of 37 covariates (19 bioclimatic variables and 18 geo-environmental factors) were selected as predictors using Maximum Entropy (MaxEnt) machine learning algorithm. Accuracy metric of the predictive model was evaluated using the “receiver operating characteristic” (ROC) curve and computing for the “area under the ROC curve” (AUC-ROC). Moreover, MaxEnt was able to estimate percent variable contributions and permutation importance for each of the predictors. The generated single-hazard susceptibility maps were harmonized into a multi-hazard susceptibility map in ArcGIS 10.8.

Results: The results show significant predictive performance and degree of fitting of MaxEnt for flood, landslides, and wildfire, obtaining high AUC-ROC (> 0.9). The land cover covariate contributed to wildfire and landslide. Elevation covariate occurred most to wildfire and flood susceptibility. Distance to faults contributed to landslides, while precipitation of the coldest quarter contributed to flood. A MHSM was then generated after overlaying and fitting the single-hazard maps. The MHSM showed that 37% of Osh Region's area is susceptible to the three hazards. Within this area, 33% is susceptible to landslides, 17% to flood, and 5% to wildfire. The population exposed to these hazards will be investigated in a future study.

Conclusion: The multi-hazard susceptibility map can be a useful planning tool for government administrators in the Osh Region to identify areas susceptible to hazards at a regional scale. This information can promote risk-informed policy and investment decisions to minimize disaster-induced losses and damages, such as fatalities and infrastructure damage, in the long term.

E-Health Text Messaging based Intervention on Healthy Lifestyle Changes and Obesity in the Socioeconomically Disadvantaged Population

PRESENTER

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ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

The obesity epidemic, known to be a multifactorial medical condition, in the United States has been declared a public health crisis. Parental obesity more than doubles the risk of adult obesity among both obese and nonobese children under 10 years of age. (Whitaker, Wright et al. 1997) Naturally, parents are often the strongest role models of their young children, who tend to imitate their eating behaviors as well as other lifestyle behaviors. (Lubna, Paloma et al. 2021) Therefore, it is of paramount importance to have upstream intervention programs to make positive changes in the obesity-promoting lifestyle behaviors of parents that often contribute to. The e-health text messaging platform integrated six major contributing factors of obesity, which included caloric content and quality of diet, physical activity, sleep, social connection, tobacco, and stress management. We hypothesized that if we could change the attitudes, knowledge, and beliefs of the caregivers, then this would cause a ripple effect leading to their children adopting the same healthy lifestyles, thereby decreasing the prevalence of the obesity epidemic.

Subject 4 is a Black or African American female who was part of the intervention arm which received text messages every week for 6 months which included health education on 6 different topics. The participant was surveyed biweekly about her knowledge, attitudes, and behaviors regarding health education topics via text messages. Throughout the study, subject 4 showed high motivation to make positive changes in her life. Her goals consisted of sleeping 8 hours a night, staying hydrated, exercising 30 minutes daily, meditating, praying, and decreasing her sugar intake. Subject 4 mentioned that “consistency” and “accountability” are what motivated her. The platform was able to give her a sense of accountability by ensuring that she was staying consistent by monitoring her progress toward her goals. She mentioned that having goals for her habits impacted her health and wellness by keeping her “consistent.” She indicated that the program greatly supported her on her road to wellness at the end of the study and “it had helped her to stay positive and to leave bad habits.” At the 9 and 12-month follow-ups, she indicated on a scale of 1 to 10 (10 being the most consistent), 10 and 8 respectively, that she was continuing her goals/habits that she had formed to support herself on her road to wellness.

This case illustrates that an e-health intervention program may benefit individuals by providing a platform where they can create personal goals, have a form of accountability that encourages them to make small changes by providing health literate education briefs, and provides a connection to local community resources to support participants to reach their goals. Additionally, this intervention program showed a beneficial impact on the subject’s wellness as indicated by the post-survey responses. This highlights that having an intervention program may be a step in the right direction to making small positive lifestyle changes and eradicating the obesity epidemic one family at a time.

EXTERNAL FUNDING SOURCE

Ardmore Institute of Health, NIH

IRB NUMBER

PA-19-053

Stepwise Diagnosis of a Chiari Malformation Post-Concussion and Return-to-Play Management in a High School Soccer Athlete

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Other

ABSTRACT

Background: Limited data exist concerning recommendations on return-to-play for patients with a Chiari I malformation (CIM). A Chiari malformation is a condition involving the brain and spinal cord that results from a structural defect of the occiput. This leads to brain tissue extending through the foramen magnum which can place pressure on the cerebellum and spinal cord leading to neurological manifestations. Much of the symptoms associated with Chiari malformations are present due to the build-up of pressure around surrounding structures. (1)

Case Information: This case study details the management of a 15-year-old female soccer player who was diagnosed with a CIM following a traumatic brain injury (TBI). The patient initially presented to a sports medicine clinic with concussion signs and symptoms that magnified over the course of the first week following the TBI. The patient's increase in symptom severity combined with behavioral changes prompted further investigation, which led to the detection of a CIM. Her case emphasizes the potential for neurological deficits caused by a head trauma to be complicated by CIM. It likewise illustrates the need to evaluate prolonged concussion symptoms for potential anatomical abnormalities.

In this case report, we follow the patient's initial diagnosis of concussion and discuss the progression of her symptoms that warranted additional evaluation. We address the neurological workup involved in recognizing how this patient's presentation suggested a secondary cause for her symptoms. Furthermore, we review relevant literature in reference to current rehabilitative management for CIM.

Conclusions: This case presents a model for how an underlying CIM can exacerbate the development of symptoms acquired through a concussion. It also demonstrates the methods a physician can use in the progression of treatment and tools used to pursue when an initial TBI is not alleviated from conservative therapy or medication. Through this discussion, we provide clinicians with a valuable reference when assessing risk in athletes with CIMs who seek to return to their sport.

Review of an Advanced Case of Psoriatic Arthritis and Barriers to Management of Chronic Disease in the West Texas Region

PRESENTER

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ABSTRACT TOPIC

Health Disparities

ABSTRACT

Background: Psoriatic arthritis is a debilitating, inflammatory musculoskeletal spondyloarthritis associated with the skin condition psoriasis that affects the hands, feet, spine, and other parts of the body. Nearly 80% of patients develop the associated arthritis after skin lesions of psoriasis develop. Management of psoriatic arthritis can be difficult, with severe variants recommended to receive specialized care from a rheumatologist for optimal treatment. The clinical case that will be discussed refers to a patient presenting with psoriatic exacerbation, which progressed from skin lesions to psoriatic arthritis with unmanaged pain. Despite the severity of this progression, he received minimal education on psoriatic arthritis management.

Case Presentation: A 34-year-old male presented to clinic with a primary complaint of pain for uncontrolled psoriatic arthritis that had been diagnosed one year prior, two years after an original diagnosis of psoriasis. He reports the diagnosis of psoriatic arthritis was made after diffuse rashes spread over his body and extensor surfaces with increasing joint pain. At the clinic, the patient complained of weakness in his extremities; severe pain at elbow, ankle, knee, and toe joints bilaterally; a diffuse erythematous rash particularly at the ankles; and difficulty with daily activity due to pain. Notable physical exam findings included a personal history of psoriasis, joint pain, nodules growing past the distal interphalangeal joint of his hands and feet along with dactylitis and nail dystrophy consistent with psoriatic arthritis. Based on Classification for Psoriatic Arthritis criteria (CASPAR), he would be due to a score above 5 classified as having psoriatic arthritis. He has a known history of epilepsy, spinal stenosis, generalized anxiety disorder, chronic PTSD, and type 1 bipolar disorder. Patient reported recurrent methamphetamine use along with frequent use of marijuana for pain control. His social history was significant for lack of employment and symptoms worsening while uninsured. He stated an inability to attend scheduled appointments due to lack of transportation, the distance from Terlingua to the clinic in Alpine, TX, and inability to obtain telemedicine visits with his current provider.

Conclusion: This case study on management of advanced psoriatic arthritis examines the health disparities faced by patients in rural west Texas regions, including lack of patient education, access to qualified rheumatologists, and adequate resources to manage disease exacerbation. A literature search on PubMed was conducted to clarify the current standard of care for treatment of advanced psoriatic arthritis, as well as current restrictions in management within the West Texas area. For social determinant factors, the social vulnerability index for west Texas regions was reviewed using public Center for Disease Control and Prevention data to note qualified health centers for this level of need and found appropriate services are lacking within the town of Terlingua and its neighboring areas. In addition to the healthcare team, an appropriate and safe environment for those suffering with psoriatic arthritis also includes stable infrastructure, social support, and public transportation. Without public health measures and capable providers, there are increased barriers to care of chronic disease for those living in rural areas like Terlingua.

Investigating Geographic Information System integration of health service, community resource, and medical education data for collaboration to improve rural pediatric asthma outcomes

PRESENTER

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ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Purpose: Rural children are at a disadvantage when it comes to health, health care accessibility, education, environmental exposures, and socioeconomic status (SES). These factors contribute to rural-urban disparities in pediatric chronic health conditions such as obesity and asthma. With respect to asthma, emergency department (ED) visits are adverse outcomes that indicate poor control and inadequate preventive care. Community asthma programs are effective at enhancing services to improve asthma outcomes, but evidence suggests there is a lack of such programs in rural areas. Geographic Information Systems (GIS) are recognized as potentially powerful tools to guide the development of community health interventions, but there has been limited application of this method to address pediatric asthma disparities, especially in rural areas. The purpose of this study is to investigate the application of GIS to integrate pediatric asthma ED visit rates, community health resources, and Rural Osteopathic Medicine Clinical Training Sites (ROME) to identify potential sites for collaborative initiatives to improve rural pediatric asthma outcomes.

Methods: This study utilized ESRI ArcGIS software for mapping and preliminary spatial analysis. Through the Texas Department of State Health Services and internal resources, we obtained 2020, age-adjusted child and adolescent asthma emergency department visit rates (per 10,000), Rural Osteopathic Medical Education (ROME) Clinical Training and Preceptor Sites, current Community Health Worker (CHW) Training Sites, and location of Texas Critical Access Hospitals (CAHs). Using GIS spatial analysis tools, statistically significant areas with high pediatric asthma ED rates were identified. ROME and CHW within these areas were then located for potential collaboration.

Results: Through mapping visualization, the counties of Johnson, Coryell, Bell, McLennan, Lubbock, and Hale were identified as potential sites for collaboration to improve pediatric asthma.

Conclusion: Application of GIS can be utilized to identify spatial health inequalities and form coalitions for improvement. This study has identified potential ROME Clinical Training Sites and Community Health Worker Training Sites that are in areas with elevated rates of inadequate pediatric asthma management and adverse outcomes. Visualization of elevated pediatric asthma ED rates (suggesting a prevalence of uncontrolled pediatric asthma) helps to prioritize collaboration to improve rural pediatric asthma outcomes.

The Intersection of Mental Health and Hypertension

PRESENTER

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ABSTRACT TOPIC

General Public Health

ABSTRACT

Purpose: Mental health conditions such as depression and anxiety are serious public health issues globally. Likewise, hypertension is a significant public health issue across the globe and is the leading risk factor for chronic cardiovascular diseases and stroke. Several studies have reported the association between mental health conditions and chronic diseases such as hypertension and diabetes. This study aims to determine the association between mental health conditions and hypertension among adults living in the United States using data from the 2021 National Health Interview Survey (NHIS).

Methods: Secondary data analysis of 2021 NHIS data was conducted to explore the association between mental health conditions and hypertension among U.S. adults. Mental health conditions were determined using self-reported data on depression, and anxiety (whether or not they have even been told by a doctor or health professional if they had any type of depression or anxiety disorder). Hypertension was also determined by the self-report data by the participants who were diagnosed by a doctor or other health professional of ever having hypertension. Weighted multiple logistic regression models were conducted to measure the relationship between mental health conditions and hypertension. Models were adjusted for key covariates.

Results: In the 2021 NHIS survey, approximately 55% (unweighted) of the participants were female. Among the different mental health conditions, depression was significantly associated with hypertension among U.S. adults, in which adults with depression are 1.443 times more likely to have hypertension than those without depression in 2021 (OR=1.443; 95% CL 1.311, 1.589). Whereas anxiety was found to not have a significant association with hypertension among U.S. adults in 2021 (OR=1.051; 95% CL 0.947, 1.167) while controlling for covariates. The covariates measured include – serious psychological distresses, sex, educational levels, race, and ethnicity. Sex was also significantly associated with hypertension among U.S. adults in which males are 1.172 times more likely to have hypertension than women (OR= 1.172; 95% CL 1.106, 1.242).

Conclusion: Depression was significantly associated with hypertension among US adults in 2021. Consistent with the results of previous studies, the result from this study indicates that men are more likely to have hypertension than women. The results from this study support the evidence of the intersection between chronic conditions and mental health, suggesting the need for primary healthcare providers to support mental health in patients seeking care for chronic disease.

Impact of pH modulation and NaDC micellular behavior on Amphotericin B solubility

PRESENTER

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ABSTRACT TOPIC

Pharmaceutical Sciences

ABSTRACT

Purpose: Amphotericin B (AmB) has very poor water solubility ($< 1 \text{ ug/mL}$), resulting poor oral absorption. Thus, AmB is only commercially produced in intravenous (IV) formulations. One AmB IV formulation, Fungizone® (FZ), uses sodium deoxycholate (NaDC), a surfactant, and sodium phosphate, a pH-modifying agent, to dissolve AmB. As per instructions, the powder is dissolved in water and then diluted lower than NaDC critical micelles concentration with 5% dextrose. To understand why a low concentration NaDC could dissolve AmB, we investigated the mechanism of AmB dissolution in FZ preparation.

Methods: *AmB solubility in aqueous buffer solutions:* Aqueous pH buffers at pH 1.2, 4.5, 6.8, 7.8, and 11 were prepared. AmB powder was mixed with pH buffers at room temperature (RT) or 37°C for 24 h and processed for AmB concentration measurement via HPLC.

Impact of pH on NaDC micelle formation: NaDC was mixed into pH buffer solutions at 4 mg/mL concentration and separately dissolved into pH 11 buffer at 0.08, 0.2, 0.4, 4, 10, and 20 mg/mL concentrations. The solutions were measured by Dynamic Light Scattering (DLS) to evaluate micelle formation.

NaDC micelle formation in the presence of AmB at pH 11: Micelle formation in 4 mg/mL NaDC-Buffer solution was measured by DLS. Next, NaDC was mixed in pH 11 buffer, DI water, and 5% dextrose solution at 0.08, 0.2, 0.4, 4, 10, and 20 mg/mL concentrations, and measured via DLS. Additionally, AmB was mixed into NaDC media solutions at 0.1 and 5 mg/ml and measured via DLS.

Enhancement of NaDC and pH 11 on AmB solubility: NaDC was dissolved in pH buffer at 4, 10, and 20 mg/mL. AmB powder then was added into the NaDC solution and mixed at RT. At 1, 12, and 24 h, samples were collected prepared for HPLC analysis.

Fungizone® Preparation and Characterization: Lab FZ and commercial FZ solutions were prepared. The lab FZ solution was prepared by mixing ingredients at RT until the solution was visibly clear. Commercial FZ powder was reconstituted with DI water. FZ solutions were diluted 1:50 with filtered 5% dextrose. Following dilution, the commercial FZ was characterized via pH measurements, DLS analysis, and HPLC measurements.

Results: AmB is not stable at extreme pH with heat; therefore, solubility studies were performed at RT. AmB (pKa 5.5 and 10) had the highest solubility at pH 11 (216 ug/mL). NaDC has different micellular behavior in different pH conditions, generating lower CMCs at pH 7.8 and 11. Further, pH 11 was able to increase aqueous AmB solubility in the presence of NaDC.

Conclusion: Both pH 11 and NaDC can increase AmB aqueous solubility; however, pH 11 combined with NaDC can synergistically enhance AmB solubility significantly. Additionally, pH 11 facilitated stable AmB-NaDC micelles formation below NaDC critical micelle concentration in water. Thus, the initial reconstitution of FZ in water generated a high pH facilitated AmB dissolution via AmB-NaDC micelles formation. Once the micelles formed, they were stable for further dilution with 5% dextrose below the CMC of NaDC.

EXTERNAL FUNDING SOURCE

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The Measurement of Postural Sway and Dynamic Gait Index as a Indication of Balance Before and After Vestibular Rehabilitation Therapy: A Case Study

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Physical Medicine / OMM

ABSTRACT

Background: When managing patients with Benign Paroxysmal Positional Vertigo (BPPV), many clinicians follow patients' rehabilitation outcomes by tracking the patients' subjective symptoms, such as a sense of disequilibrium, postural imbalance, and gait disturbances. Postural sway data measurements are used to evaluate static and dynamic balance capacity in various contexts, including symptoms of vertigo. In comparison, Dynamic Gait Index (DGI) is a functional measure of dynamic balance often used in vestibular rehabilitation therapy (VRT). This case study examines the possible correlation of the patient's postural sway data with their subjective onset, symptoms resolution, and DGI score.

Case Presentation: A 58-year-old female presented to the outpatient office with a new symptom of dizziness and subjective gait disturbances. The patient described the dizziness as similar to "room spinning." Symptoms worsened with head movement and resolved after a few seconds of no head movement. She also noticed the dizziness while lying down and turning in bed at night. Associated symptoms included a right-sided temporal headache and hearing difficulty. The patient's physical exam revealed normal findings except for the following. The patient's gait showed flexed forward posture and a broad base of support. Speed was slow, with uneven stride lengths. The neurological exam showed new onset nystagmus only 1-2 beats bilaterally. The pursuit was slow without apparent saccadic movements. The left hallux showed dorsiflexor movement, while the right displayed plantar flexor movement with Babinski. With the physical exam findings, BPPV was diagnosed, but before starting VRT, MRI was performed due to the new neurological findings. The MRI revealed a chronic lacunar infarct in the right caudate nucleus of unknown onset since her last visit. The patient was referred to her primary care physician for appropriate neurology referral and secondary prevention. Meanwhile, the patient was cleared to start VRT to address persistent vertigo. DGI was obtained two times during VRT, and an objective evaluation of sway was collected each time patient presented to the clinic before and after VRT. The sway data was collected by asking the patient to quietly stand on a Bertec force plate (Bertec, Columbus, Ohio) for 30 seconds with their eyes open (EO) and eyes closed (EC). A total of 21 sway measurements were calculated to evaluate objective changes in balance. The variables derived from the patient's Bertec force plate data were graphed per visit and analyzed via t-test for significance in comparison to DGI, age (age bracket [50-70]), height (1.67 m range, $\pm 10\%$), and weight (90.45 kg range, $\pm 15\%$) matched control data from the Human Performance Lab at UNTHSC. Significant changes in sway measurements were found in EC data over 7 weeks of therapy.

Conclusions: The DGI displayed minimal change throughout VRT. The DGI evaluation time (15 minutes) prevents it from being implemented during a clinic visit, whereas postural sway collection (2 minutes) can be integrated into the patient intake. This report indicates the possible utility of outpatient collected sway data as an objective measure of balance in evaluating and managing patients presenting with balance and gait difficulties.

Molecular Docking Studies for Designing and Identification of Novel Bitopic Ligands for Sigma-1 Receptor

PRESENTER

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ABSTRACT TOPIC

Pharmaceutical Sciences

ABSTRACT

Purpose: Our goal is to identify more specific ligands for the Sigma-1 Receptor (S1R) by designing and docking various bitopic ligands then ranking them based on their interactions. The S1R is an intracellular, multifunctional receptor that is a target in many pathologies. S1R is found throughout the body, within the membranes of the nucleus, ER, and mitochondria, and the CNS is the primary site of activity. Bitopic ligands are those that combine the high affinity by binding to orthosteric sites and high selectivity by binding to allosteric sites on the same receptor. They are used to gain insights on molecular functioning of the receptor.

Methods: A set of 3 linkers were tested with a known allosteric binding compound and the one with highest affinity was selected to continue in the design process. Nine bitopic ligands were designed using known allosteric compounds, the selected linker, and a high affinity orthosteric compound. Ligands were minimized with Avogadro then PDBQT files for minimized ligands and S1R open-state confirmation were prepared with AutoDock Tools. All newly designed ligands were docked on S1R using Vina to determine their binding affinities. Interactions were visualized using Pymol and quantified using Protein Ligand Interaction Profiler.

Results: After testing 3 linkers from the literature, we identified 1 that gave highest affinity with our allosteric compound and selected to use it in the design of new bitopic ligands. Our results shows that all ligands docked in a bend conformation in the S1R. Specifically, bitopic ligands having benzazepine derivatives showed greater affinity to S1R. The number of hydrophobic bonds, hydrogen bonds, pi bonds, and salt bridges were identified for each interaction between the ligand and S1R.

Conclusions: The 1-2 compounds with the highest affinity and favorable interactions are candidates to be used for future drug design models.

Case Report: Infective Endocarditis With Pulmonary Emboli, Effusion, and Pneumonia (Last Methamphetamine Abuse 15 Years Ago)

PRESENTER

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ABSTRACT TOPIC

General Medicine

ABSTRACT

Background: Infective endocarditis of the right-sided native valve involves the tricuspid or pulmonic valve; isolated right-sided IE accounts for approximately 10 percent of all IE cases. Methamphetamine use is known to cause cardiac complications including vasospasms and damage to the myocardial surface.

Case Presentation: Patient is a 51-year-old Caucasian male presented to the ED with cough, fever, shortness of breath and wheezing for the last 2 weeks. Past medical history significant of COPD, hypertension (not on home medications), history of skin cancer of unknown type 10 years ago status postresection, methamphetamine use 15 years ago, current tobacco use disorder, and marijuana use disorder. Patient reported that his symptoms started with fever and a cough that is productive with yellow-colored sputum. He also lost about 15 to 20 pounds in the last 2 to 3 weeks. Patient also noticed hemoptysis and had a couple episodes of bloody sputum. He also reported worsening shortness of breath associated with wheezing and has been using albuterol nebulizer up to 4 times a day without much relief in symptoms. He denies sick contacts. He has been experiencing left upper quadrant abdominal pain worse with breathing/deep inspiration. Patient denies family history of blood clots. Work-up in the ED showed elevated leukocytosis with hyponatremia and mild hyperkalemia. Initial troponin was 0.06 and elevated BNP at 460. Urine analysis was only positive for marijuana. Patient's chest x-ray showed left sided pleural effusion. CTA chest with PE protocol was done and showed numerous cavitary consolidate to masses suspicious for septic emboli and left lower lobe pulmonary embolus with left lower lobe pneumonia and moderate pleural effusion. Day 1 he had a left thoracentesis showing exudative effusion. Day 3-5 PPD skin test, quant gold and AFB sputum cultures x3 are negative. BCX show initially MSSA and then repeat BCX show corynebacterium and staph capitis likely skin contaminant. Patient was placed on oxacillin for MRSA coverage. Day 5 TEE shows 1 cm vegetation in tricuspid valve confirming infective endocarditis. CT surgery is following outpatient for improvement of vegetation in 4 weeks with OP cardiology f/u. Heparin drip switched to Argatroban for heparin resistance and possible HIT. Argatroban bridged to warfarin. PT is now therapeutic. ANA is elevated 1:640, but further work up is negative. Patient will need continued IV antibiotic with oxacillin for at least 6 weeks. Will follow up echo with Cardiology in 4 weeks then reevaluate with ID and CT surgery. Order heparin resistance antithrombin III evaluate OP after acute treatment.

Conclusion: This case illustrates a unique presentation of infective endocarditis with pulmonary effusion, embolus, and pneumonia. Not certain what caused this patient case if it was his current use of marijuana or is methamphetamine use 15 years ago that just started presenting now.

Suicidal Ideation Among High School Adolescents in the United States

PRESENTER

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ABSTRACT TOPIC

General Public Health

ABSTRACT

Purpose: Suicidal ideation represents thoughts or contemplations about death and suicide. Suicidal ideation has become a growing concern since suicide is the second leading cause of death among adolescents in the United States. The purpose of this analysis is to explore the epidemiology of suicidal ideation and the association between suicidal ideation and actual suicide attempts among high school adolescents in the U.S.

Methods: The data source was the 2019 Youth Risk Behavior Surveillance System (YRBS). The sample size was 13,677. The primary variable was suicidal ideation measured from “During the past 12 months, did you ever seriously consider attempting suicide?” and categorized as yes or no. A secondary variable was actual attempt at suicide measured from “During the past 12 months, how many times did you actually attempt suicide?” and categorized as yes or no. Demographics including sex, race/ethnicity, grade, and sexual orientation were also measured. The statistical analyses used were logistic regression, pairwise differences using t-tests, and chi-squares and p-values <0.05 were considered statistically significant. Data were obtained from the CDC YRBS Explorer tool.

Results: Suicidal ideation decreased from 19.3% to 13.8% from 1999 to 2009. However, it increased from 13.8% to 18.8% from 2009 to 2019. Furthermore, females (24.1%), American Indian or Alaskan Native students (34.7%), bisexual students (48.5%), and those who had sexual contact with both sexes (58.9%) were significantly more likely to seriously consider attempting suicide compared to White students, heterosexual students and those with no sexual contact, respectively ($p<0.05$). Moreover, There was a significant association between seriously considering attempting suicide and attempted suicide ($p<0.01$). Among persons who considered suicide, 40.7% actually attempted suicide, compared to 59.3% who considered suicide and but did not attempt it.

Conclusions: Due to the growing prevalence of suicidal ideation among high school adolescents, more research is needed to be done to create interventions that can help students who are experiencing suicidal ideation and prevent suicide attempts. Furthermore, these interventions should aim to target females, Asian Indian or Alaskan Native students, and LGBTQ+ students since suicide ideation was higher among these populations.

Computational Pharmacology for Identifying and Refining Novel Inhibitors of the Regulator of G protein Signaling type-12 (RGS12) Protein Target

PRESENTER

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COLLEGE/SCHOOL

School of Biomedical Sciences

ABSTRACT TOPIC

Pharmacology

ABSTRACT

Purpose: Substance use disorders arise from persistent changes in CNS synaptic transmission, as caused by initial exposure to illicit substances that heighten dopamine levels in the brain's reward circuitry (a key event in establishing long-term drug-seeking behavior) [1,2]. The Siderovski lab recently discovered that mice lacking Regulator of G protein Signaling-12 (RGS12) are attenuated in their normal hyperlocomotion elicited by acute cocaine, amphetamine, or methamphetamine [3,4]. RGS12-deficient mice have increased dopamine transporter (DAT) expression and increased dopamine uptake within the ventral striatum [3]. The target for RGS12's action as a G α -directed GTPase-accelerating protein (GAP) is the presynaptic kappa opioid receptor (KOR) [4], as KOR activation is known to attenuate striatal dopaminergic tone [5]. Our hypothesis is that RGS12 directly modulates the output of dynorphin / KOR signaling to dopamine reuptake. Developing RGS12 inhibitors would provide complementary pharmacological means to test this hypothesis pre-clinically, including in rodent models. However, to date, there are no small-molecule inhibitors of the G- α : RGS domain protein-protein interaction that are not thiol-reactive covalent modifiers of the RGS protein (a highly undesirable chemical property anathematic to further drug development) [6].

Methods: Using the AtomNet® model, a deep convolutional neural network for structure-based drug discovery, we screened millions of compounds against the NMR structure of the RGS12 RGS domain (Protein Data Bank id 2EBZ; state 2) to identify 96 candidate compounds, followed by experimental testing of these candidate compounds using the Transcreener® GDP RGScreen™ developed in partnership with BellBrook Labs [7,8]. Follow-up computational chemistry is being performed with Schrödinger's suite of molecular dynamics software.

Results: Two hits out of the 96 candidate compounds were discovered to exhibit reproducible, double-digit micromolar IC₅₀ values in the Transcreener® GDP RGScreen™ assay. We then tested 192 analogs of the two original hits and discovered 33 analogs with measurable IC₅₀ values. Of the 33 congeneric compounds, all but one of the active congeners were structurally related to one of the original two hits, with a wide spread of IC₅₀ values and many with improved potencies (IC₅₀RGS12 = 0.84 – 153.2 microM). These hits do not inhibit the intrinsic GTPase activity of G- α .

Conclusions: To increase diversity of the chemical scaffolds capable of inhibiting RGS12 function in vitro, we are now performing computational modeling of this initial set of 33 congeneric compounds, including CPU-based molecular docking and GPU-based shape screening of new chemical libraries (including those sourced from MilliporeSigma, MolPort, and Enamine) using Schrödinger algorithms on a local HPC cluster. In vitro binding and structural studies, cell-based studies, and pre-clinical animal studies are also being planned to further characterize these congeneric compounds and future divergent chemotypes.

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EXTERNAL FUNDING SOURCE
NIDA

Contrast-enhanced micro-CT approaches for visualizing musculoskeletal development in neonatal mice

PRESENTER

AUTHOR(S)

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COLLEGE/SCHOOL

School of Biomedical Sciences

ABSTRACT TOPIC

Structural Anatomy

ABSTRACT

Purpose: While there are many forms of radiological imaging that can be used to gather anatomical data from biological specimens, computed tomography (CT) imaging has been the gold standard for visualizing dense tissue, such as bone, with detailed resolution. However, this imaging modality is not well suited for soft tissues (muscle, brain, abdominal organs, cartilage, etc.) due to their decreased tissue density. The inability to distinguish between soft tissues in CT scans limits our ability to investigate the bone-muscle interactions known to stimulate and direct bone modeling during early postnatal development. The development of contrast-enhancing staining agents, capable of binding materials to increase their radiodensity, has allowed for more accurate and enhanced visualizations of less dense soft tissues, such as muscle and brain structures. Contrast agents such as iodine have differential affinities for the different soft tissues in the body allowing for easier visualization and segmentation of soft tissues in relation to the skeleton. Previous studies have used contrast-enhanced CT (CE-CT) scanning to analyze early development of mice from prenatal stages to postnatal day 7. However, additional CE-CT imaging during the first three postnatal weeks is needed to understand muscle-bone interactions during critical periods of behavioral development, such as suckling and weaning. The goal of this project is to develop a CE-CT protocol and corresponding anatomical atlas showing the development of skeletal and soft tissue structures in the crania of neonatal mice from birth to weaning.

Methods: Neonatal and preweaning mice (B6C3Fe a/a-Col1a2OIM/J) were euthanized on day of birth (P0), postnatal day 7 (P7), and postnatal day 14 (P14). Ethanol-fixed tissues were submerged in 1.25% iodine in 70% ethanol (I2E) for 2-14 days, with the skin intact in order to preserve cutaneous musculature. Both pre-stained and post-stained tissues were scanned using a MRS CT-80 micro-CT machine (20 μm^3 voxel resolution).

Results: Preliminary CE-CT scans following 10 days in an iodine stain present improved visualization of soft tissue (brain structures, cranial muscles, salivary glands) when compared to the baseline bone CT scans.

Conclusion: These scans will be used to develop 3D models of musculoskeletal ontogeny from birth-weaning, providing insights into this critical developmental period. The use of CT contrast agents such as iodine offers new opportunities to investigate the anatomical interactions of bone and muscle during early development, and can be applied to investigate models of both normal growth and pathological disorders affecting musculoskeletal growth.

IACUC NUMBER

IACUC-2021-0015

Adult-Onset Still's Disease Masquerading as Candida Sepsis

PRESENTER

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COLLEGE/SCHOOL

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ABSTRACT TOPIC

General Medicine

ABSTRACT

Background: Adult Onset Still's Disease (AOSD) is a rare systemic inflammatory disorder characterized by daily fever, polyarthritis, and transient salmon-pink rash typically at the peak of fever. It is hypothesized to be a reactive syndrome triggered by an infectious process. However, the etiology is still unknown. The Yamaguchi diagnostic criteria is commonly used to classify AOSD. Although there is not a specific laboratory or imaging study used to diagnose AOSD, a serum ferritin > 1000 ng/mL is typically seen.

Case presentation: Here we present a case about a 66 year old male with a past medical history of hypertension, hyperlipidemia, uncontrolled type II diabetes mellitus (DMT2), atrial fibrillation, hypothyroidism, chronic knee pain, and tobacco abuse who presented to the hospital with subjective fevers, myalgias, and generalized weakness for 2 weeks. The patient also had a pruritic, erythematous rash in the bilateral lower abdominal region which extended to the inguinal folds over the last 15 days. Physical exam revealed oral thrush covering his tongue. The patient also had chronic, bilateral knee swelling, erythema, and warmth without formal diagnosis of arthritis in the past. The patient was febrile, tachycardic, and hypotensive on admission. Complete blood count was remarkable for leukocytosis with a white blood cell count of 12.35 K/mm³. Based on his initial presentation, the patient was diagnosed with sepsis secondary to candida infection. The patient's history of DMT2, Jardiance use, and tobacco abuse further elevated suspicion of candidiasis. However, his fever was non-responsive to antifungals, antibiotics, or antivirals. Given his bilateral knee, elbow, and wrist swelling, we investigated possible rheumatologic processes. Further workup revealed an elevated erythrocyte sedimentation rate (ESR) of 106 mm/Hr, elevated C-reactive protein (CRP) of 353 mg/L, and elevated ferritin of 29125 ng/mL suggestive of severe inflammation. The patient's daughter later revealed he had an erythematous rash most notable at the height of his fever. The Yamaguchi criteria were used to diagnose AOSD. Patient presentation was positive for four major criteria and two minor criteria. His elevated ferritin > 1000 ng/mL solidified the diagnosis. His fever ultimately improved after corticosteroid treatment.

Discussion: Diagnosis of AOSD still remains a challenge because it is a diagnosis of exclusion. Although the Yamaguchi criteria are the most sensitive criteria for identifying AOSD, cases do not always present classically. Sepsis is an exclusion criteria for AOSD. The patient's initial presentation was highly suggestive of sepsis, which initially delayed identification of AOSD. Also the salmon-pink rash that is classically presented with AOSD masqueraded as candida infection in addition to his oral thrush. This case illustrates the diagnostic challenges of AOSD. Delay in diagnosis remains a problem with AOSD, because delay can lead to increased risk of complications including disseminated intravascular coagulopathy (DIC), thrombotic thrombocytopenic purpura (TTP), macrophage activation syndrome, pulmonary hypertension, and diffuse alveolar hemorrhage. Further investigation is critical for understanding the etiology of AOSD as well as diagnostic protocols to expedite management and prevent life-threatening complications.

Sleep Insufficiency, Circadian Rhythms, and Metabolomics: The Connection to Metabolic and Sleep Disorders

PRESENTER

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ABSTRACT TOPIC

Neuroscience

ABSTRACT

Purpose: The majority of US adults who report experiencing insufficient sleep are more likely to suffer from metabolic disorders such as hyperlipidemia, diabetes, and obesity than those with sufficient sleep. Less is understood about the underlying molecular mechanisms connecting these phenomena. A systematic, qualitative review of metabolomics studies exploring metabolic changes in response to sleep insufficiency, sleep deprivation, or circadian disruption was conducted in accordance with PRISMA guidelines.

Methods: An electronic literature review in the PubMed database was performed considering publications through May 2021 and screening and eligibility criteria were applied to articles retrieved. The following keywords were used: “metabolomics” and “sleep disorders” or “sleep deprivation” or “sleep disturbance” or “circadian rhythm.” After screening and addition of studies included from reference lists of retrieved studies, 16 records were identified for review.

Results: Consistent changes in metabolites were observed across studies between individuals experiencing sleep deprivation as compared to non-sleep deprivation controls. Significant increases in phosphatidylcholines, acylcarnitines, sphingolipids, and other lipids are consistent across studies. Increased levels of amino acids such as tryptophan and phenylalanine are also noted. However, studies are limited to small samples of young, healthy, mostly male participants conducted in short inpatient sessions, limiting generalizability.

Conclusion: Changes in lipid and amino acid metabolites accompanying sleep deprivation and/or circadian rhythms may indicate cellular membrane and protein breakdown underlying the connection between sleep disturbance, hyperlipidemia, and other metabolic disorders. Larger epidemiological studies examining changes in the human metabolome in response to chronic insufficient sleep would help elucidate this relationship.

LGBTQ+ Young Adults and Likelihood of Receiving Hypothetical Chlamydia and Gonorrhea Vaccines

PRESENTER

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ABSTRACT TOPIC

Health Disparities

ABSTRACT

Background: Sexual and gender minority (SGM) young adults (those identifying as lesbian, gay, bisexual, transexual, and/or non-binary; often known as LGBTQ+) face a number of health disparities and are among the most at risk of acquiring sexually transmitted infections (STIs) such as chlamydia and gonorrhea. Candidate vaccines against chlamydia and gonorrhea are under development, but an understanding of the likelihood of receiving future vaccines among SGM young adults is vital to promote uptake among these populations. Prior research of STI vaccine acceptability and likelihood, such as that of the human papillomavirus vaccine series, has shown healthcare provider recommendation to be a strong driver of uptake among the general population. The likelihood of the SGM young adult population receiving potential chlamydia and gonorrhea vaccines, however, has yet to be explored. The purpose of this pilot study was to examine the likelihood of SGM young adults receiving future chlamydia and gonorrhea vaccines.

Methods: Sexually active young adults between the ages of 18 to 24 were recruited to participate in an online survey. Here, we present a sub-analysis of the SGM young adults (n=14) who completed the survey. Items included likelihood of receiving a hypothetical: chlamydia vaccine, chlamydia vaccine if it was recommended by a physician, gonorrhea vaccine, and gonorrhea vaccine if it was recommended by a physician (response options: not very likely to extremely likely, five-point scale). Univariate analyses were conducted using SPSS.

Results: Participants included 12 individuals identifying as gender non-conforming and 2 identifying as transgender, with mean age of 20.9 years. Only 21% (n=3) of participants were extremely likely to be vaccinated for gonorrhea, and this increased to 36% (n=5) when the vaccine was recommended by a healthcare provider. Similarly, only 21% (n=3) of participants were extremely likely to be vaccinated for chlamydia, which also increased with a recommendation from a healthcare provider to 43% (n=6).

Conclusion: Results indicate low likelihood of receiving both chlamydia and gonorrhea vaccines among this small sample of SGM young adults. Likelihood of receiving both chlamydia and gonorrhea vaccines increased, however, with provider recommendation, indicating a reliance upon healthcare providers to aid in informed decision making regarding STI vaccines among this vulnerable population. Educating clinicians on the disparities as well as the tailored needs of SGM young adults surrounding chlamydia and gonorrhea infection rates and vaccination should facilitate provider recommendation and subsequently increase likelihood of chlamydia and gonorrhea vaccine uptake among SGM young adults. Additionally, to address overall low likelihood, further interventions, such as inclusive messaging targeted to SGM young adults may be necessary. Future studies would benefit from further exploration of this topic with larger samples, comparisons to cisgender and heterosexual young adults, and identification of additional potential barriers to STI vaccine acceptability among this population.

EXTERNAL FUNDING SOURCE

American Sexually Transmitted Diseases Association

IRB NUMBER

1798874-5

Pharmacokinetic and Physicochemical Evaluation of Novel Drug Candidates for Retinitis Pigmentosa

PRESENTER

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COLLEGE/SCHOOL

Dual Degree

ABSTRACT TOPIC

Pharmaceutical Sciences

ABSTRACT

Purpose: Retinitis pigmentosa is a set of inherited ocular diseases that affect nearly 3 million people worldwide. The condition is inherited and causes the progressive deterioration of the retina. Retinitis pigmentosa begins with the loss of rod photoreceptors which cause night blindness and a decrease in peripheral vision. After significant loss of rod cells, cone cells also begin to die, decreasing central vision until complete blindness. More than 150 genetic mutations in 80 different genes have thus far been identified to contribute to progression pathways of the condition. Despite ongoing stem cell and gene therapy investigations, thus far there are no curative options. Most existing treatments focus on slowing the progression of retinal deterioration by reducing oxidative stress on the retina. Unfortunately, these treatments only achieve limited success and cannot halt progression. Recently, the sigma 2 receptor (σ_{2r}) was identified to be endoplasmic reticulum membrane protein 97 (TMEM97). This protein (σ_{2r} /TMEM97) has been shown to have neuroprotective effects on retinal cells and is thus of interest as a potential drug target for retinitis pigmentosa. Here we synthesized and tested a series of six compounds which have previously been found to modulate σ_{2r} /TMEM97. To determine which of these compounds is a suitable drug candidate, each underwent in vivo and in vitro testing with the goal of selecting the best candidate for further clinical development.

Methods: We tested the compounds in a rat model to determine retinal uptake following intravitreal injection. Each drug was dissolved in dimethyl sulfoxide (DMSO) and injected into the eye. At set time points, animals were sacrificed, and retinas were isolated from harvested eyes. The retina was separated and homogenized using sonication. A small portion was removed and underwent protein precipitation to purify the sample. The samples were then analyzed via liquid chromatography mass spectrometry (LCMS) to find the drug concentration remaining at each timepoint. In addition to obtaining a pharmacokinetic profile, the compounds were physiochemically characterized for chemical stability, solubility, in vitro drug release from vitreous humor, thermal analysis, and surface tension.

Conclusion: Our goal is to select those drug candidates with the highest chance of clinical success. The pharmacokinetic profiles as well as physicochemical characteristics and stability of the compounds obtained in this study revealed important differences between the compounds that were used in selecting which to advance to in vivo efficacy testing. Ongoing studies include completion of physicochemical characterization and in vivo efficacy in a retinitis pigmentosa rat model that will be used to identify top candidates for further development.

EXTERNAL FUNDING SOURCE

Gund Harrington Foundation and Foundation for Fighting Blindness

IACUC NUMBER

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Can Trust in Pharmacists Improve When They Have Complete Health Records?

PRESENTER

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COLLEGE/SCHOOL

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ABSTRACT TOPIC

Health Disparities

ABSTRACT

Intro: Pharmacists rank third amongst U.S. professionals for honesty and ethics. As one of the most accessible healthcare fields, we hypothesized that Since Ccommunity pharmacists with additional access to patient medical records would improve the pharmacist's ability to conduct MTM and subsequently strengthen the patient-pharmacist relationship.

Methods: This is a survey study administered as part of a randomized controlled trial (NCT03437694)e with the primary purpose of the impact of medication therapy management (MTM) on the health of persons living with Human Immunodeficiency Virus (HIV). As part of the larger clinical trial, participants were randomized 1:1 into the intervention arm (MTM with pharmacist access to patient health records) or the control arm (MTM without pharmacist access to patient health records). Patient health records were defined as updated labs, imaging results, and notes from their primary care provider. The inclusion criteria were African American, adults, and comorbid conditions including HIV on antiretrovirals, and the presence of hypertension and/or diabetes. The purpose of this survey study is to determine if there is a difference in the degree of participant trust based on the trial arms. Additional inclusion criteria for this study was completion of at least 5 out of the 9 scheduled visits. Participant surveys were excluded if they had unanswered responses.

The study was approved by the University of North Texas Health Science Center's IRB (#1436643/2018-094) which included the administration of participant surveys. The survey was an unvalidated, contained 43-item questionnairesassessed on a 5-point Likert scale (1 = Strongly Agree to 5 = Strongly Disagree), and administered at every MTM visit. Four questions related to participant trust were extracted from the larger survey administered at the fifth study visit. Reverse coding was used given the structure of the Likert scale and applied so that higher values represented better outcomes. For each participant, an average of the responses to the four questions was calculated. All categorical data were analyzed with descriptive statistics. Since patients were not matched, an independent t-test was used to compare the survey scores between arms.

Results: A total of 58 participants were included with an average age of 55 years. The majority of the surveys were from participants assigned to the control arm (57%). The average trust score for the intervention arm was 4.82 ± 0.39 . The average trust score for the control arm was similar at 4.82 ± 0.41 ($p = 0.99$).

Conclusions: The results demonstrated an overall strong degree of trust in pharmacists conducting MTM. There was no statistically significant difference in participant's attitude or expression of trust towards the capability of the community pharmacist regardless of pharmacist access to additional medical records. The lack of statistical difference could be explained by the small sample size, unmatched participant characteristics, and the overall high agreement signifying an already trusting relationship between participant and pharmacist. This is in line with other data suggesting that the field of pharmacy is one of the most trusted fields in healthcare.

IRB NUMBER

1436643/2018-094

Effect of selective ganglion stimulation on hypertension in systemic lupus erythematosus

PRESENTER

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COLLEGE/SCHOOL

School of Public Health

ABSTRACT TOPIC

Integrative Physiology

ABSTRACT

Purpose: Systemic lupus erythematosus (SLE) is a female-dominant autoimmune disease that causes widespread inflammation in various organs. Inflammation precedes the prevalent hypertension in the disease. The cholinergic anti-inflammatory pathway (CAP) is an endogenous neuroimmune pathway that reduces inflammation upon stimulation. We hypothesize that stimulation of the CAP by selective activation of the superior cervical ganglion will halt disease progression and hypertension in SLE.

Methods: Female SLE (NZBWF1) and control (NZW) mice received unilateral microinjections of pAAV-hSyn-hM3D(Gq)-mCherry, a designer receptor exclusively activated by designer drug (DREADD), or pAAV-hSyn-mCherry (vehicle) at the superior cervical ganglion (SCG) at 32 weeks of age. SCG DREADD injections generate muscarinic receptors on SCG neurons that are activated by the designer drug, clozapine N-oxide (CNO), ultimately leading to neuronal stimulation and potentially activation of the CAP. At 33 weeks of age, mice with SCG DREADD received a daily s.c. injection of CNO (3mg/kg) for two weeks. At 35 weeks, mice received a catheter implant in the carotid artery to measure mean arterial pressure (MAP) for two consecutive days followed by euthanasia and tissue collection. Plasma was collected biweekly via retro-orbital bleeding. Plasma samples were used to quantify double-stranded (ds) DNA autoantibodies.

Results: dsDNA autoantibodies were higher in SLE than control mice ($8.6e5 \pm 1.8e5$ vs. $5.1e4 \pm 1.1e4$ U/mL; $p=0.0002$; $n=13$). SCG DREADD did not change dsDNA autoantibody levels in SLE mice ($1.1e6 \pm 2.6e5$ U/mL; $p=0.1410$; $n=6$) or control mice ($5.4e4 \pm 1.5e4$ U/mL; $p=0.6549$; $n=9$). MAP was significantly higher in SLE mice compared to control mice (150 ± 9 vs. 122 ± 3 mmHg; $p=0.0009$; $n=5-9$). SCG DREADD did not change MAP in SLE mice (137 ± 2 mmHg; $p=0.2572$; $n=6$) or controls (127 ± 3 mmHg; $p=0.7678$; $n=9$).

Conclusion: These data suggest that selective activation of the CAP at the level of the SCG using DREADD did not significantly alter disease severity or blood pressure in female SLE mice with advanced disease. Future studies will determine the effect of selective ganglion stimulation on inflammatory outcomes.

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EXTERNAL FUNDING SOURCE

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IACUC NUMBER

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Annexin A2 in tumor-derived extracellular vesicles: Molecular contributions in metastatic triple negative breast cancer

PRESENTER

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COLLEGE/SCHOOL

School of Biomedical Sciences

ABSTRACT TOPIC

Cancer

ABSTRACT

Purpose: Tumor-derived extracellular vesicles (TEV) are highly implicated in tissue-specific metastasis. Additionally, TEV interacts with the distant microenvironment to shape a pre-metastatic niche (PMN) for homing the tumor cells.

Annexin A2 (AnxA2) is a plasma and endosomal membrane-associated protein. Its high levels have been correlated with poor distant metastasis-free survival and poor overall survival in triple negative breast cancer (TNBC) patients. It is also abundantly present in TEV and recruits TEV-associated cargo such as proteins and microRNAs.

Our lab reported that in vivo education with AnxA2 depleted EV led to reduced TNBC metastasis to lungs and brain suggesting a key role in the formation of a PMN. While the presence of AnxA2 in EV has been reported, its contribution in the formation & development of PMN via EV is still unexplored. We aim to evaluate the implications of AnxA2 in EV & elucidate the mechanisms promoting TNBC metastasis.

Methods: We used shRNA- mediated gene silencing to stably downregulate AnxA2 in organotropic TNBC cell lines derived from the parent MDA MB 231 cells. Differential ultracentrifugation was used to isolate EV from cell culture supernatant & size analysis was done using NTA. Biological characterization was done in concordance with MISEV 2018 guidelines using immunoblotting. Additionally, the EVs will be subjected to quantitative proteomic and transcriptomic analysis to identify differentially expressed proteins and genes upon loss of AnxA2.

Results: Upon depletion of AnxA2 protein, we observed a significant effect of AnxA2 depletion on its physiological role in plasmin generation. We observed a size distribution of the isolated EV between 30-300 nm. Using immunoblotting we confirmed reduced levels of AnxA2 in EVs derived from AnxA2 depleted TNBC cells. We verified their purity using EV enriched markers - ESCRT, Heat shock proteins & tetraspanins such as CD81, CD9, CD63 & confirmed the absence of negative markers - GM130, calnexin & cytochrome c. Interestingly, we observed a reduced yield of EV with AnxA2 depletion indicating a potential effect on EV biogenesis & release.

Conclusion: The role of AnxA2 in TEV biogenesis, release and selective cargo loading will lead to potential identification and understanding of the novel secretory and EV protein that may act as a functional regulator in promoting advanced metastasis in TNBC.

EXTERNAL FUNDING SOURCE

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Control Case Study: E-Health Text Messaging Based Intervention on Developing Lifestyle Changes Related to the Improvement of Childhood Obesity

PRESENTER

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ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Background: The prevalence of chronic diseases in the United States including heart disease and cancer is majorly attributable to adverse lifestyle factors such as smoking, physical inactivity, poor diet, stress, negative emotion, etc. (CDC, 2012). Recent studies have shown that mothers with unhealthy lifestyles serve as an impetus for childhood obesity (Dhana et al, 2018). Community health promotion efforts and lifestyle interventions are successful in introducing healthy behaviors and promoting its adherence (Dickinson et al., 2006; Kent et al., 2015; Pekmezi, Marquez, & Marcus-Blank, 2010; Tucker et al., 2014; Tucker et al., 2016). Our study evaluates the utilization of an E-health text message system as an effective intervention for caregivers of obese pediatric patients to improve lifestyle behaviors that influence childhood obesity.

Case Presentation: A 30 year old African American female presented to the Pediatric Mobile Clinic with her 3 year old child who had a BMI in the 82nd percentile. The caregiver and child met the inclusion and exclusion criteria including adequate biometric markers before they were randomized to one of 2 intervention arms: control health group or e-health group. This subject was randomized into the control intervention arm. Participants of the control arm received weekly text messages for 6 months inquiring subjects on any SMART goal and duration of their choosing as well as assessing their motivation and confidence related to that goal (scored on a scale of 10). They also received follow-up messages asking introspective questions regarding habit formation and messages with self-scripted inspirational statements. The intervention arm differed in that the SMART goal chosen by subjects had to focus on one of six lifestyle medicine factors emphasized for that week's duration. The SMART goals input by this subject centered on improving the outlook, organization, and control of her finances and career. The subject's motivation scores were similar to her confidence scores for each specific goal even though they varied overall. More importantly, both scores trended upwards within self chosen goal periods lasting ≥ 3 weeks. Additionally, a common theme emphasized in the subject's responses to introspective questions regarding her goals focused on maintaining "positivity". The patient indicated a 7/10 on her 6-month exit survey, highlighting that the program "somewhat" supported the patient on a road to wellness by helping her "break things down into achievable goals each week".

Conclusions: This case illustrates the role an E-health intervention program had in helping the patient construct and keep track of achievable goals. The program was still beneficial to the control-intervention arm subject as indicated by her exit survey. Observed increases in confidence and motivation scores within prolonged goal periods highlights the impact this program had in establishing the self-accountability necessary for conceiving new goals and maintaining consistency. In effect, this case emphasizes how the intervention aids in promoting a subject's intrinsic motivation in relation to the development of their goals and eventual habits. Overall, this case suggests that having any intervention in place, even to the degree involved within case controls, is significant compared to no intervention.

EXTERNAL FUNDING SOURCE

Ardmore Institute of Health, NIH

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Health Champions for Health Equity, a Rapid Review

PRESENTER

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Texas College of Osteopathic Medicine

ABSTRACT TOPIC

General Public Health

ABSTRACT

Purpose: This study aimed to synthesize existing knowledge from peer-reviewed literature on the usage of “health champions” in K-12 settings to improve health outcomes. Traditionally, community health initiatives aimed at K-12 students have been led by outside adults or appointed school leaders. While successful, one of the limitations frequently encountered was a disconnect between the leader and the target audience. To determine whether this issue could be addressed using peer-led interventions, a rapid literature review was conducted.

Methods: A Cochran Rapid Review was conducted due to time and resource constraints. A consultation with a research librarian generated a search strategy suitable for the scope of this project. Using databases ERIC, PubMed, and SCOPUS, an initial list of 602 articles was systematically reduced to 18 publications. The inclusion criteria included studies done in the United States in the past 10 years (2012-2022) to maintain relevance. After applying these criteria, an initial screening of the title/abstract and full-text analysis was performed to develop the final reference list. A data extraction tool was then used to yield the following results.

Results: The majority of health champions were students from their respective schools. Nutrition based interventions were the most common at the elementary school level. High school students had the widest array of interventions such as mental health improvement and tobacco usage reduction. Overall, peer health champions lead to better health intervention objective learning, more participation in the programs, and more student satisfaction.

Conclusion: Findings suggest that peer led interventions targeted at K-12 students are effective in improving participation in program activities. Students had more exposure to the learning material when the program utilized peer mentorship components which resulted in better objectives achievement. Additionally, having university or professional school students as mentors increased community involvement. Creating a working relationship between both K-12 educators and students from universities and higher education facilities is vital in building support for schools with limited resources.

Medication Management of Children with ADHD: Communication Strategies to Improve Safety

PRESENTER

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COLLEGE/SCHOOL

HSC College of Pharmacy

ABSTRACT TOPIC

Patient Safety

ABSTRACT

Background: Attention Deficit and Hyperactivity Disorder (ADHD) is a common neurologic disorder that affects children and adolescents and can persist into adulthood. According to the National Center for Health Statistics, there is an estimated prevalence of 4.4% to 5.2% in the general U.S population, but 7.8% of the school-age population (more than 6 million children in the U.S.). Getting children to follow a treatment regimen can be challenging and medication adherence is an essential determinant of clinical success. Pharmacist-comanaged ADHD programs may provide an improvement in medication management strategies in children. The objective of this study was to systematically review medication management models that provide safe and effective care to children and adolescents with ADHD.

Methods: A comprehensive and systematic literature search using PubMed from 2013-2023 was performed and included search terms: "Attention Deficit Disorder with Hyperactivity/diagnosis", "Practice Guideline", "Attention Deficit Disorder with Hyperactivity/drug therapy", "Stimulant", "Non-Stimulant", "Protocols", "Models", "Safety", "Pharmacist", and "Treatment". Article abstracts were reviewed and considered for inclusion if they used an appropriate ADHD rating scale to measure efficacy of therapy and evaluated relevant therapy. After reviewing the selected articles each article was graded based on the CEBM levels of evidence. Two authors independently reviewed the titles and abstracts for inclusion of relevant studies. Full text was reviewed to determine final inclusion. If confusion existed regarding article inclusion/exclusion, it was resolved by discussion between two authors. Results were reported according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). A table was developed to record findings from each included article and contained year of publication, author, title, research design, interventions, findings, source, and grade.

Results: A total of 22 articles were included in this review. A variety of guidelines exist regarding ADHD diagnosis. Most follow DSM-V although no clear consensus has been developed. Based on a patient's age, stimulants are a typical first line therapy in treating children and adolescents with ADHD. Stimulants pose a variety of safety concerns including reduced appetite, insomnia, and cardiovascular events. Based on stigma regarding stimulant use, parents have sought nonpharmacologic options to therapy. Characteristics of pharmacist co-managed ADHD programs include a standardized protocol for assessment, referral, and follow-up, psychosocial intervention, titration and monitoring of medications/adverse effects, and a communication plan. Successful programs include medication management provided via in-person as well as telehealth visits and a majority of patients with a current Health Plan membership.

Conclusion: Pharmacist co-managed ADHD programs have been shown to be effective in the improvement of safety outcomes for children and adolescents with ADHD. ADHD remains a prevalent and growing topic among parents, teachers, caregivers, and healthcare providers. Further research, including highlighting outcomes associated with combined pharmacological and psychosocial treatments, is warranted to improve safety. Depending on the patient's current health status, medical history, and use of other medications, parents need to work with their physician and pharmacist to determine the best treatment.

Unassigned Albuterol Legislation

PRESENTER

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ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Introduction: Asthma is a reversible chronic obstructive lung disease that affects over 6 million children ages 0-17 in the United States. An asthma attack is sudden and can be triggered by allergens such as mold, dust, cold weather, or tobacco. An asthma attack leads to airway narrowing through smooth muscle constriction, excess mucous production, and inflammation. Symptoms include chest tightness, wheezing, and anxiety. Acute asthma symptoms are commonly managed through short-acting beta agonists (SABA) like albuterol and best practice guidelines recommend these medications always be available to those with the condition. However, data suggests that only 20% of students with a diagnosis of asthma have access to albuterol in schools. To increase access to SABA among students experiencing respiratory distress, schools may “stock” albuterol and adopt standing delegation orders issued by a consulting physician. This is referred to as “unassigned albuterol.” According to the Asthma and Allergy Foundation of America (AAFA), there are 14 states with legislation in place regarding the use and administration of unassigned albuterol in K-12 schools. In 2021, national professional organizations endorsed guidelines that identified 4 essential components and 4 recommended components for state legislation regarding unassigned albuterol. The purpose of this study is to investigate alignment of existing state legislation with the 2021 national guidelines.

Methods: The stock albuterol legislation was obtained from each state’s online repository of legislation and systematically reviewed by two independent researchers to assess whether or not it was aligned with each of the essential and suggested components of the national guidelines. Where there was lack of consensus on alignment, the component was reviewed by the full research team. A matrix was created presenting these findings.

Results: From our comparative analysis of the fourteen states that currently have legislation for unassigned albuterol administration, we observed a widespread lack of alignment with national guidelines. All states had at least one essential or recommended component that was not aligned with guidelines. States ranged from a low of one misaligned component, to a high of six misaligned components. Among essential components of the guidelines, the recommendation for training was particularly problematic as it was only fully addressed by three states, was partially addressed by 8 states, and unaddressed by three states.

Conclusion: This study highlights the lack of alignment between existing state legislation and national guidelines. It also highlights the importance of national guidelines to inform policy that supports implementation of best practice. For those 36 states that have not yet established legislation for unassigned albuterol, these results may help identify potential models for policy that aligns with national guidelines and supports best practice to meet the needs of children with asthma at school. Additionally, results suggest that training requirements for school health staff may benefit from greater attention from state and national stakeholders responsible for school asthma services, and by those involved in policy.

A Case Report of Multiple Myeloma in a Middle-Aged Male Patient

PRESENTER

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COLLEGE/SCHOOL

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ABSTRACT TOPIC

General Medicine

ABSTRACT

Background: Multiple Myeloma is a neoplastic plasma cell disorder that results in proliferation, and thus overactivity, of plasma cells to produce immunoglobulin light chains, causing end-organ damage due to proteinemia. Clinical symptoms commonly manifest as renal insufficiency, with hypercalcemia and high blood creatinine, bone marrow dysfunction, such as anemia and osteolytic bone lesions or severe osteopenia, and infection due to suppression of humoral and cell-mediated immunity. While a majority of patients affected are older than 60, younger patients can also be affected; however, clinical factors such as reversibility of renal function, response to chemotherapy, molecular markers, and the need for hemodialysis show greater clinical correlation to differences in outcomes.

Case Information: This patient is a 42 y.o. male with no past medical history who presented to the ED after his PCP informed him that he had “abnormal labs.” Patient reported back and chest pain for 3 months, which he attributed to a motor vehicle accident, as well as increased fatigue and weight loss ~25 lbs in past 2.5 months. Labs were remarkable for anemia, of Cr 26 (previous baseline of 0.7 1 year ago), BUN 136, Ca 17.8, and K 6.7. CT CAP revealed multiple lytic lesions throughout and was admitted to ICU for continuous renal replacement therapy (CRRT) and evaluation of acute kidney failure in the setting of lytic bone lesions.

At this time, nephrology, hematology/oncology and palliative services were consulted for management of patients’ renal function, concerning lab findings with lytic lesions, and pain, respectively. Serum protein electrophoresis (SPEP) was ordered and indicated a kappa light chain myeloma, later confirmed by bone biopsy. He completed 5 days of plasmapheresis and was started on chemotherapy treatment for multiple myeloma, consisting of the CyBorD therapy regimen (cyclophosphamide, bortezomib, dexamethasone). Patient was transferred out of the ICU and began conventional hemodialysis (HD). At time of discharge, patient would follow with Oncology and undergo HD on an outpatient basis. Patient was also treated with Denosumab given his hypercalcemia with plan to continue as outpatient after dental clearance as well as EPO in the outpatient setting given his anemia.

Conclusions: Multiple Myeloma is a disease primarily affecting older patients, with rates peaking in the seventh decade, and as is common with multiple types of cancer, was commonly thought to have been more severe when presenting in younger patients, as a higher proportion may have cytogenetic abnormalities and physical manifestations of disease on imaging. There does not seem to be any defining presenting clinical features that may differentiate between younger and older patients presenting with signs of Myeloma. Regardless of age, certain presenting clinical factors have been associated with poor outcomes, some of the main ones being creatinine on presentation, platelet count, and serum albumin. In regards to the patient mentioned in this case, creatinine on presentation and maintenance of renal function on hemodialysis are risk factors relating to his disease prognosis, although individual patient factors and treatment options should not be overlooked.

Increased Fibronectin Serotonylation in Stretched Optic Nerve Head Astrocytes

PRESENTER

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ABSTRACT TOPIC

Eye / Vision

ABSTRACT

Purpose: Elevated intraocular pressure contributes to glaucomatous optic nerve degeneration by inducing biomechanical stress at the optic nerve head (ONH), especially in the lamina cribrosa (LC). ONH astrocytes (ONHA) in the LC respond to biomechanical signals through extracellular matrix (ECM) remodeling activities, promoting tissue fibrosis and damage to retinal ganglion cell axons. The enzyme transglutaminase 2 (TG2) plays a role in ECM remodeling, in part, due to its ability to post-translationally modify and cross-link ECM proteins. A unique post-translational modification mediated by TG2 is “serotonylation” - the transamidation of the monoamine serotonin (5-hydroxytryptamine, 5HT) to glutamine residues on proteins. It is speculated that serotonylation contributes to fibrotic tissue remodeling, but this process has not been studied in ocular tissues or in primary glial cells. In this study, we examined changes in the serotonylation of fibronectin (FN; a major ECM glycoprotein) by ONHA after exposure to cyclic stretch.

Methods: Primary human ONHA strains (n=3) were exposed to 0-12% cyclic stretch for 24h using a FlexCell FX-6000 system. Cell lysates and conditioned medium samples were collected from stretched and control cells. Serotonylation was assessed by probing for serotonin in samples of FN immunoprecipitated out of conditioned media. Protein levels for potential extra- and intra-cellular mediators of serotonylation were examined using western blotting of concentrated conditioned medium samples and cell lysates, respectively.

Results: Serotonylated fibronectin was detected in ONHA. Exposure to stretch increased the amount of fibronectin that was serotonylated by 2.49-fold ($p=0.0080$). After stretching, extracellular FN levels were not changed. Extracellular TG2 levels were increased by 3.76-fold ($p=0.0004$). In cell lysates, post-stretch levels of both FN and TG2 were decreased by 5.56-fold ($p=0.0181$) and 2.51-fold ($p=0.0441$), respectively. Additionally, serotonin 2A and 2C (5HT2A, 5HT2C) receptor levels were unchanged, and serotonin transporter (SERT) levels decreased by 2.94-fold ($p=0.0297$).

Conclusions: Increased FN serotonylation by TG2 is observed in ONHA after exposure to 24h of 0-12% cyclic stretch. Serotonylation may promote increased FN-crosslinking and fibrotic ECM remodeling, an important feature of glaucomatous pathology. The secreted TG2 – which was elevated in response to stretch – is likely to be the primary mediator of this increased serotonylation. The observed decrease in SERT may lead to increased extracellular 5HT levels, which increases the substrate availability for TG2-mediated serotonylation. Though unchanged, activity at the 5HT2A/C G-coupled protein receptors could increase the availability of intracellular calcium required for TG2 activity. Future experiments will be focused on furthering our understanding of how these proteins may interact to promote serotonylation.

An Atypical case of Hemophagocytic Lymphohistiocytosis possibly secondary to Systemic Lupus Erythematosus Flare in a Female Patient

PRESENTER

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ABSTRACT TOPIC

Immunology

ABSTRACT

Hemophagocytic Lymphohistiocytosis (HLH) is a rare autoimmune disease in which histiocytes and lymphocytes attack the body's own resulting in severe fever, organ damage, and pancytopenia. Initial signs and symptoms of HLH can mimic common infections, malignancy, hepatitis, or encephalitis making it difficult to distinguish.

Case Presentation: A 33-year-old female presented to the hospital for daily recurrent fevers ongoing for 2 weeks. Four weeks prior, patient underwent a dilatation and curettage procedure for a molar pregnancy. Patient endorses 5 kg unintentional weight loss, heavy night sweats, nausea, vomiting, and chills. She immigrated to the U.S. from Nepal three years prior.

Upon admission, her labs were significant for pancytopenia. Her physical exam was significant for bilateral axillary lymphadenopathy. She was subsequently started on broad-spectrum antibiotics due to concern for possible endometritis. All infectious workup was unremarkable. After 5 days of antibiotic treatment, she continued having cyclical fevers without resolution of symptoms.

CT imaging revealed bilateral lymphadenopathy that was concerning for possible malignancy. Her lymph node biopsy was significant for necrotizing granulomatous lymphadenitis (NGL). NGL is very nonspecific and includes a wide array of differentials from malignancy, infectious etiology, or autoimmune disease. Bone marrow biopsy was significant for pancytopenia and depleted iron stores. While waiting for her biopsy results, autoimmune work up was initiated as patient reported diffuse joint stiffness, dry mouth, and a malar rash. Autoimmune work up was significant for elevated ANA titer and elevated IL2- receptor. However, C3, C4, RF, anti-ds DNA, anti-Smith, and CCP within normal limits. Initially, rheumatology believed this was not a lupus flare as C3 and C4 levels were normal. About 8 days after admission, the patient started experiencing right upper quadrant pain and labs revealed significant transaminitis and proteinuria. However, autoimmune hepatitis panel was negative. On day 15 of admission, the patient's malar rash resolved and she was afebrile for 2 days. Due to her clinical improvement, Adult onset Still's disease and Kikuchi's lymphadenitis were high on the differential, which usually spontaneously resolve. However, on day 17 of admission, patient started to experience high grade fevers and became very hypotensive. Her labs showed worsening transaminitis, elevated triglycerides at 517, and elevated ferritin level above 40,000. Due to her worsening clinical condition, she was started on high dose steroids and hydroxychloroquine for HLH and possible acute lupus flare. After initiation of treatment, patient started to show signs of clinical improvement and labs were trending in the right direction.

The patient met 4/17 diagnostic criteria for lupus and 5/8 diagnostic criteria for HLH. However, it was hard to determine in HLH was primary, secondary to an acute lupus flare, or secondary to stress from a miscarriage. Although the patient met diagnostic criteria for lupus; normal complement levels make a lupus flare less likely. In HLH, bone marrow biopsy usually shows the presence of macrophages, but hers only showed pancytopenia and iron depletion. This case emphasizes that clinicians cannot always rely on typical diagnostic findings and sometimes must treat based on a risk-benefit analysis.

NON-COMPETITION POSTER

Opioid Crisis Breakdown in Tarrant County

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ABSTRACT TOPIC

General Public Health

ABSTRACT

Purpose: It is undisputed that opioids, while they have inherent medicinal value, can be abused recreationally leading to devastating effects. According to the CDC, Texas had the 6th most related deaths from opioids in 2019[1]. There were 3136 opioid related deaths in 2019 in the state of Texas [1]. It has been noted by physicians that Tarrant County in particular has seen a high incidence. The purpose of this research was to quantify the data surrounding opioid use in Tarrant County. Data from the National Institute on Drug Abuse shows that overdose deaths from opioids have risen steadily across the country in the last decade with a sharper increase in the last few years [2].

Methods: Using a database from the Texas Department of State Health Services we identified all calls, visits, and deaths related to opioid use [3]. The following metrics were used: Total opioid related deaths in Tarrant County and opioid deaths filtered by age, sex, race, education status, and marital status in Tarrant County. Total emergency department (ED) visits and ED visits per 100,000 population and per 100,000 ED visits in Tarrant County. The type of opioid related to each ED visit in Tarrant County was quantified as well. Finally, poison center opioid-related calls were totalled in Tarrant County.

Results: Out of 254 counties in the state of Texas, Tarrant County recorded the 5th highest number of opioid related deaths in 2019, with 75 total deaths and a rate of 8 per 100,000 population. These opioid related deaths were most focal in the age range of 18-44 (72%). Of the total deaths, 65% of them were white and 68% were male. Of note, 70% of the users who died were not married, while 30% were married. Of these deaths, the most significant portion were by non-heroin opioids (34%), followed by heroin users (15%). In addition, in 2019 there were 244 poison center calls related to opioids. Finally, in 2019 there were a total of 774 ED visits related to opioids, with a rate of 87.5 visits per 100,000 ED visits.

Conclusions: As indicated in the results, both the state of Texas and Tarrant County have been negatively impacted by the epidemic rise in opioids. Texas has sought to alleviate some of the disparities, and funding was received by the U.S. government. Beginning in May 2017, under the Texas targeted Opioid Response Program, Texas has received over \$280 million in federal funding to address the opioid crisis [4]. However, the data presented in the case report (objective opioid related outcomes in 2019) demonstrates that more needs to be done. In response to the high prevalence of deaths, emergency room visits, and opioid related calls, it is critical that Texas mounts a proportional response. This response may be both systemic and individualistic as people are educated on the effects of opioids and what they can do to prevent negative outcomes.

Assessing HSC Health Pediatric Clinic Adherence and Barriers to HealthySteps Screenings

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ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Purpose: HealthySteps is a program created to provide developmental support to patients aged up to three years old and their families. Children are monitored to make sure they are reaching developmental milestones. Implementation and adherence to the HealthySteps competencies are monitored yearly per clinic. Each clinic can self-assess through a Fidelity Implementation Checklist, where each indicator is graded as either: did not begin, does not meet fidelity, approaching fidelity, meets basic fidelity, or meets optimal fidelity. When the optimal goals of HealthySteps are followed, the program had nationwide significant benefits for the patients, parents, and pediatric care team.

Methods: The UNT Health Science Center Pediatric Clinic was analyzed for its implementation and fidelity to HealthySteps developmental and autism screening competencies. Data was collected from Jan. 2017 – July 2022 beginning when HealthySteps was implemented at the clinic and analyzed yearly. The number of patients receiving at least one developmental screening a year and one autism screening by 28 months were calculated from the total number of patients 0 – 3 years of age.

Results: Developmental screenings have improved from “Approached Fidelity” to “Meets Basic Fidelity,” while autism screenings have gone from “Approaching Fidelity” to “Does Not Meet Fidelity.”

Conclusions: Barriers to patient screenings could include the following: patients coming late to appointments leading to a rushed visit, tablet technology failure, data entry issues from patient check-in to EHR, EMR content access, new staff not being aware of the HealthySteps program and its benefits, and staff forgetting to administer the screenings. To begin reaching for the “Meets Optimal Fidelity” target, the most attainable goal is to establish better communication between the clinic and HealthySteps specialists with more consistent scheduled meetings.

Multiple Myeloma in a Cadaver: A Case Report

PRESENTER

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ABSTRACT TOPIC

Cancer

ABSTRACT

Introduction: Multiple Myeloma (MM) is a malignant neoplasm characterized by the abnormal proliferation of monoclonal immunoglobulin producing plasma cells within the bone marrow. The risk of developing MM is 0.76%; however, risk factors include age, BMI, gender, and race. Common complications include destructive bony lesions and renal insufficiency. Extraosseous myelomatous masses are a rare finding, identified in less than 5% of patients with MM, and its presence is associated with more aggressive, advanced stage disease and poor prognosis. These masses can impact many organ systems but most commonly involve the spleen, lymph nodes, liver, and kidneys. Pancreatic involvement, however, is extremely rare. Infiltration of the pancreas by myeloma cells has an incidence of 2.3% based on autopsy studies.

Case Information: A medical dissection of a 58 year old woman was performed in the UNTHSC Center for Anatomical Sciences. The donor was 5'4", 114 pounds, with a BMI of 22.3. The donor presented with a history of chronic tobacco use at 2 packs/day, unspecified broken bones, MM, and chemotherapy. The examination of the cadaveric specimen yielded insight into the systemic ramifications of MM, uncovering various pathological deviations. The donor's lung tissue exhibited signs consistent with prolonged usage of tobacco, as evidenced by the presence of discoloration and mottling. The kidneys displayed extensive scarring and a significant presence of adipose tissue. Most significantly, a large pancreatic tumor measuring 17 x 5.8 x 4 cm and weighing 167.65 g was found encasing the splenic artery. The sectioned tissue sample looked uniformly tan-white, firm, and mottled. Further dissection revealed an additional neoplastic growth on the posterolateral wall of the pelvic cavity. This tumor was situated anterior to a bony lesion on the sacrum and was found to be impinging upon the surrounding neurovasculature.

Conclusion: This case exemplifies the complexities and nuances of Multiple Myeloma, highlighting the systemic nature of the disease and the need for a comprehensive understanding of its potential complications. Identification of scarring in the cadaver's kidney indicated that the patient's MM had caused the congregation of monoclonal immunoglobulins in the renal tissue, triggering profibrotic mechanisms and impaired renal function. The sacral bony lesion is a characteristic MM manifestation of heightened bone reabsorption and elevated osteoclast activity. Furthermore, this may have also led to the donor's history of unspecified fractures in the arm and leg. The discovery of a large pancreatic neoplasm in this case is an extremely rare complication of MM, with an incidence of only 2.3%. Metastatic pancreatic involvement is not normally diagnosed as an aspect of the clinical progressive course of MM and is associated with poorer prognoses. Therefore, this case serves as a call to action for the medical community to continue to explore and understand the underlying mechanisms of extraosseous myelomatous masses and their presentation to improve the diagnosis and treatment of patients with MM. It is a testament to the ongoing need for research, education, and awareness in the fight against this debilitating disease.

Major Musculoskeletal Injuries and the Menstrual Cycle: A Case Study

PRESENTER

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ABSTRACT TOPIC

General Medicine

ABSTRACT

Background: There is a clear difference between males and females in the incidence of certain sports injuries. For example, females are about 9 times more likely to experience anterior cruciate ligament (ACL) tears, while males are about 7 times more likely to experience calcaneal (Achilles) tears. These discrepancies warrant further evaluation into the core differences between males and females, one of which is the menstrual cycle. During the first 15 days of the of the menstrual cycle, estrogen levels rise. There is discussion in medical literature about estrogen's effects on the musculoskeletal system, which may begin to correlate these injury rates and menstruation.

One study measured estrogen levels and presynaptic inhibition in males and females during day 1 and day 15 of the menstrual cycle, and found that both measurements were significantly different on day 15. This suggests that as estrogen concentration increases in the first half of the menstrual cycle, gamma-aminobutyric acid (GABA) in the spinal cord is attenuated, decreasing pre-synaptic inhibition, resulting in altered skeletal motor control.

Another study evaluated estrogen's effect on failure load, which is the force necessary to break or tear a certain object. It analyzed two groups of ovariectomized rabbits, administering estrogen supplementation to one and not the other. It found a reduction in failure load in the hormonal substitution group, implying that tendons and ligaments under estrogen's influence could rupture at a lower applied force.

Another study analyzed the extracellular matrix (ECM) enzyme lysyl oxidase (LOX), which oxidizes lysin in collagen and elastin, mediating the cross-linking between these ECM fibrils. It showed that estrogen inhibits LOX activity in engineered ligaments, implying that the increased estrogen *in vivo* may decrease the stiffness of tendons/ligaments in women, leading to increased risk of injury.

This case illustrates two major musculoskeletal injuries in a young female patient that both occurred within the first fifteen days of her menstrual cycle.

Case information: 17-year-old female sustained a right ACL tear during a track meet on day 5 of her menstrual cycle. The same female at age 27 sustained a left Achilles tear during a recreational volleyball game on day 6 of her menstrual cycle. In both occurrences, the patient had no previous injury to the area, no medical conditions, and was not taking any medication.

Conclusions: The fact that both of this patient's major musculoskeletal tears occurred during the first week of her menstrual cycle suggests that changing hormones may have influenced these injuries. The studies that support this conclusion have evaluated estrogen's effects on the musculoskeletal system and concluded that estrogen has been shown to 1) decrease presynaptic inhibition, 2) reduce failure load, and 3) decrease the stiffness of tendons/ligaments. This research together may begin to explain the correlation between this patient's injuries and her menstrual cycle. More research is needed on this topic, so that we can definitively identify all risk factors for these kinds of injuries and begin to take steps toward prevention for the appropriate athletes.

Quality Improvement Project: Advanced Care Planning in Rural Family Practice Clinics

PRESENTER

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ABSTRACT TOPIC

General Public Health

ABSTRACT

Introduction: Advanced Directives ensure patient's autonomy at the end of life. This project's purpose was to assess the outcomes of integrating discussions in patients over 65 with an educational resource discussing Advance Care Planning (ACP) and analyzing the change over one year in a family practice clinic with intervention vs. a family practice clinic without intervention.

Methods: Data was collected at two family practice clinics. In Fall 2021, patients at clinic 1 were provided patient education on ACPs and provided resource material. Clinic 2 did not have this intervention take place. All patients 65 years or older were eligible for this study. A chart review was performed on each patient during the study period to determine if an ACP had been created within the last 5 years.

Results: During the study period, a total of 167 patients were eligible. 64 at B&W Healthcare and 103 at Family Health Clinic. At the clinic with intervention, 89% of the eligible patients had an updated ACP within the past 5 years in Fall 2022, compared to the 9.7% at the clinic lacking intervention.

Conclusion: This project demonstrated how the lack of documented ACP and the need for ACP education among those 65 years and older in rural family practices can be addressed in primary care visits. Future interventions should involve EMR flags to identify those who lack an updated ACP. The goal of discussing ACPs is to have an ongoing conversation to exchange, deliberate, and clarify values and responsibilities.

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EXTERNAL FUNDING SOURCE

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Mosquito-borne disease detection in urban-rural interfaces in Fayette County, Texas

PRESENTER

AUTHOR(S)

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ABSTRACT TOPIC

Microbiology / Infectious Disease

ABSTRACT

Purpose

Arthropod-borne viruses, called arboviruses, are transmitted through mosquito and tick bites and have been known to cause serious illness and outbreaks. With at least 55 species of mosquitoes in Texas and cases of West Nile (WNV), Chikungunya (CHIKV), Zika (ZIKV), and Dengue (DENV) viruses reported in South Texas in the last 5 years, identification and monitoring of arbovirus presence in mosquitoes in Texas is necessary for prevention of future outbreaks. The goal of our study was to understand which mosquito species are found at urban-rural interfaces in South-Central Texas and identify which pathogens those mosquitoes may be carrying.

Methods

We collected mosquitoes from six properties in Fayette County, TX using BG Sentinel 2 traps at two time points: Spring and Fall. After visually identifying the genus of each mosquito, mosquitoes were individually homogenized and co-extracted from DNA/RNA. Then, we used real-time PCR to test for the presence of ZIKV, WNV, DENV, and CHIKV.

Results

A total of 358 mosquitoes were collected over both trips. Our study focused only on the female mosquitoes (N=229, 64.0%) from this collection, as males do not transmit disease. We collected 143 female mosquitoes in Spring 2021 and 86 in Fall 2021. Five total genera of mosquitoes were identified from these two collections. In trip 1, these included: *Aedes* (N=65, 45.5%), *Anopheles* (N=9, 6.3%), *Culex* (N=9, 6.3%), *Culiseta* (N=1, 0.7%), and *Psorophora* (N=38, 26.6%), with 14.6% (N=21) unable to be visually identified. From trip 2, identified genera included: *Aedes* (N=9, 10.5%), *Anopheles* (N=7, 8.1%), *Culex* (N=28, 32.6%), and *Psorophora* (27, 31.4%), with 17.4% (N=15) unable to be visually identified. After analyzing our samples via multiplex real-time PCR for presence of ZIKV, WNV, DENV, or CHIKV, we found all mosquitoes to be negative for these pathogens.

Conclusion

Our study focused on a subset of mosquitoes from South-Central Texas where arboviruses are common. We collected mosquito species that are known to carry and transmit arboviral diseases, however, we did not find any evidence of infection of four major arboviruses in Texas. However, we were unable to test for additional viral pathogens in this study. Interestingly, more *Culex* and *Psorophora* were observed in Fall, where *Aedes* mosquitoes predominated in the Spring. In addition to mosquito preferences, this may be due to differences in weather and feeding activities of the different species. Continued identification of mosquitoes and pathogen surveillance remain important to disease control to allow for early detection and prevention of serious mosquito-borne infections.

Influence of Gender on the Association between Race and Disability: California Health Interview Survey

PRESENTER

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School of Public Health

ABSTRACT TOPIC

Health Disparities

ABSTRACT

Purpose: Disability is common in older adults: 40% of those 65 years or older live with a disability in the US. Women typically have higher rates of disability than men in later life. Moreover, minority groups have also been shown to have a higher prevalence of disability than their White counterpart. However, there is very little research regarding the role of gender in the association of race with disability. We aimed to examine whether the association between race and disability differed by men and women.

Method: We conducted a cross-sectional analysis using data from the 2015-2016 California Health Interview Survey (CHIS) in adults aged 65 years or older (n=15,044). Due to the complex survey design in CHIS, we accounted for complex sampling weights in all analyses using SAS v9.4. Physical, mental, and emotional disabilities were recorded by participants, and disability was dichotomized as present or absent. Race was classified as Hispanic, Asian, Black, White, and Other. We generated sex- and race-specific descriptive statistics and used multivariable logistic regression to estimate sex-stratified associations between race and disability, adjusting for age, education, marital status, cigarette smoking, arthritis, hypertension, diabetes, mental distress, and walking for work or pleasure.

Results: The mean age was 71.5 years for men (range 65-85 years) and 72.2 years for women (range 65-85 years). Participants were predominantly female (59.4%). The majority of participants were White (71.0%) followed by Hispanic (11.4%), Asian (10.7%), Black (4.3%), and other race/ethnicity (2.5%). The prevalence of reported disability was higher among females than males (52% vs. 47%, $P=0.0002$). The prevalence of disability was highest for Hispanics (60%), followed by Other race/ethnicity (50%), White (48%), Black (48%), and Asian (43%) individuals. Among women, in fully adjusted models, Hispanic individuals were more likely to have reported a disability when compared with white women (OR=1.67, 95% CI= 1.07–2.60). Among males, Hispanic individuals were as likely to have reported a disability as White males (OR=1.03, 95% CI=0.68-1.56). The association between race/ethnicity and disability was not statistically significant for other race/ethnicities.

Conclusion: We observed that Hispanic women were more likely to report disability when compared with White women. Further research should be conducted to understand possible factors that contribute to the association between race and disability differently in women than men.

EXTERNAL FUNDING SOURCE

N/A

Carotid arterial stiffness and cerebral blood flow variability in individuals with mild cognitive impairment

PRESENTER

AUTHOR(S)

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COLLEGE/SCHOOL

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ABSTRACT TOPIC

Aging / Alzheimer

ABSTRACT

Purpose: It is unclear whether cerebral blood flow variability is a sign of impaired vascular function or an adaptation to chronic cerebral hypoperfusion in individuals with cognitive dysfunction. Elevated arterial stiffness increases transmission of pulsatile pressure to the brain, but the relationship between arterial stiffness, the magnitude of cerebral blood flow variability, and cognitive dysfunction is unknown. In this pilot study, we hypothesized that carotid artery stiffness would be higher in individuals with mild cognitive impairment (MCI) compared with individuals with normal cognition (NC), resulting in higher cerebral blood flow variability.

Methods: In individuals with MCI (N=5) or NC (N=7), R-wave to common carotid artery (CCA) pulse wave velocity (PWV) was assessed as an index of arterial stiffness (via tonometry). CCA velocity (CCAv) and middle cerebral artery velocity (MCAv) were measured via transcranial Doppler ultrasound, with concurrent measurements of mean arterial pressure (MAP) via finger photoplethysmography. The amplitude of MAP, CCAv, and MCAv oscillations in the low frequency range (LF; 0.07-0.15 Hz) were assessed via fast Fourier transformation, and normalized to total power (0.04-0.4 Hz) for each participant to account for high inter-individual variability. Relationships between R-wave-carotid PWV and LF variability in CCAv and MCAv were assessed via correlational analyses.

Results: There were no between-group differences for R-wave-carotid PWV (MCI: 0.91 ± 0.16 m/s vs. NC: 0.87 ± 0.07 m/s; $P=0.70$), mean CCAv (MCI: 31.8 ± 8.8 cm/s vs. NC: 29.7 ± 2.0 cm/s; $P=0.54$), mean MCAv (MCI: 50.9 ± 6.5 cm/s vs. NC: 47.9 ± 12.7 cm/s; $P=0.63$), or MAP (MCI: 102.1 ± 10.2 mmHg vs. 104.7 ± 13.8 mmHg; $P=0.73$). While there was also no difference between groups for nLF power of CCAv (MCI: 0.28 ± 0.03 au vs. NC: 0.33 ± 0.10 au; $P=0.41$), nLF power for MCAv was lower in the MCI group (MCI: 0.26 ± 0.07 au vs. 0.43 ± 0.12 ; $P=0.02$). Overall, there was a strong positive correlation between R-wave-carotid PWV and CCAv nLF power ($R=0.81$, $P=0.005$), but a weaker relationship for MCAv nLF power ($R=0.56$, $P=0.09$). While sub-group correlational analyses are limited based on the small sample sizes, relationships between R-wave-carotid PWV and CCAv nLF power were high for both MCI ($R=0.98$, $P=0.02$) and NC ($R=0.79$, $P=0.06$) groups, but were lower for MCAv nLF power (MCI: $R=-0.12$, $P=0.88$; NC: $R=0.69$, $P=0.13$).

Conclusion: Contrary to our hypothesis, there were no differences in R-wave-carotid PWV between groups, and blood flow variability was either similar between groups (for CCAv), or lower in the MCI group (for MCAv). Overall, there was a strong positive relationship between R-wave-carotid PWV and blood flow variability in the CCA, which was also observed in sub-analysis of the MCI and NC groups. Future investigations with a larger sample size are needed to definitively determine the role of arterial stiffness on cerebral blood flow variability with cognitive dysfunction.

EXTERNAL FUNDING SOURCE

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Recognizing the Central Nervous System as a Site of Pediatric Sarcoma Relapse: A 3-Patient Series

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Cancer

ABSTRACT

Background: Sarcomas are diverse malignancies derived from primitive mesenchymal cells that are difficult to diagnose and treat. Advances in local control techniques, chemotherapy regimens, and imaging modalities have led to improvements in both morbidity and mortality in pediatric patients. However, one-third of patients develop disease relapse. Previously, intracranial metastasis was thought to be rare. The incidence of sarcoma brain metastasis is thought to have increased and is associated with grim outcomes.

Case Information: Case 1 – A male Asian infant was born with a mass involving lower left extremity requiring through the knee amputation shortly after birth. Pathology confirmed infantile fibrosarcoma (IF). He was started an IF-based regimen after pulmonary biopsy confirmed metastatic disease. Two months after chemotherapy completion, 5.6 x 7.2 x 6.3 cm intracranial tumor was found with pathology confirming metastatic IF. Despite salvage chemotherapy and entrectinib, he continued to have increased neurological symptoms and died.

Case 2 - Ten-year-old Caucasian female presented with 8-month history of progressively enlarging right foot mass measuring 6.2 x 4.5 x 4.2 cm, consistent with Ewing Sarcoma upon biopsy. PET scan showed bilateral pulmonary metastatic disease with lymph node involvement. Chemotherapy and radiation therapy (XRT) were started. After completion of cycle 6, she had increased neurological symptoms and imaging showed 5 x 6 cm temporal mass with hemorrhage. Brain XRT, palliative chemotherapy, and Ruxolitinib were started; however, the patient subsequently died.

Case 3 – Six-year-old Hispanic female with large mass arising from right proximal humeral metaphysis with evidence of bilateral pulmonary metastasis. Biopsy confirmed metastatic osteosarcoma and chemotherapy was started. Although the patient was treated further with methotrexate, salvage chemotherapy, palliative XRT, and Pazopanib, she began to develop neurological symptoms over several weeks before passing.

Conclusions: We note this is the only report of IF brain metastasis, a rare report of sarcoma lymph node metastasis, and each patient was treated with an immunotherapy agent. Caregivers in cases 2 and 3 reported new-onset neurological manifestations prior to identification of new brain metastasis, indicating a lag in detection of new intracranial relapse in asymptomatic sarcoma patients. We suggest implementing a brief review of systems screening tool focused on concerning neurological manifestations to screen for brain metastasis.

Geriatric Practice Leadership Institute (GPLI): An Age-Friendly Program

PRESENTER

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COLLEGE/SCHOOL

Faculty/Staff

ABSTRACT TOPIC

Education

ABSTRACT

Purpose

According to the Institute of Medicine, immediate steps must be taken to educate and train both the current and future health care workforce to work collaboratively in addressing the diverse needs of the growing older adult population. Most healthcare professionals had very little education or clinical training in the care of older adults nor the most effective ways to work as a clinical team.

Methods

The Geriatric Practice Leadership Institute (GPLI) is a collaboration between two universities providing interprofessional teams of early and mid-career professionals with the skills and knowledge needed to leverage leadership skills to effectively work within interdisciplinary teams to provide age-friendly care to older adults. The GPLI incorporates the Institute for Healthcare Improvement (IHI) Age-Friendly Health Systems 4Ms' Framework into the training.

The GPLI is an on-line, team-based program which engages 5-7 teams each session. Module topics include Age-Friendly Health Systems, organizational culture, leading self, leading interprofessional teams, and quality improvement. Additionally, teams select and complete a quality improvement project based on the Age-Friendly Health Systems 4Ms and submit final report and presentation. The teams are also assigned a coach for support. Continuing education credits and a micro-credential are available to participants. Participants complete a survey following the completion of the program.

The GPLI has been funded by the Health Resources and Services Administration (HRSA) Geriatrics Workforce Enhancement Program grant (numberU1QHP2873), which currently covers all costs for participants.

Results

The GPLI has trained over 175 healthcare professionals during the past 7 years with teams representing ambulatory to emergency responder organizations. Participants were all asked to complete a survey to gauge the program's success. When asked about how valuable the information was in the program in a post-completion survey, 100% of participants answered 'very' or 'extremely' valuable. Additionally, all participants answered either 'very' or 'extremely' valuable when asked how useful their executive sponsor was in supporting their team's involvement and project.

Conclusion

After many years of offering the program, many lessons have been learned, and consistent themes have emerged from the teams who have been the most successful. These include team representation from all levels of the organization, a focus on culture change, and flexibility to change and adjust, especially during the COVID-19 pandemic.

EXTERNAL FUNDING SOURCE

HRSA

IRB NUMBER
2018-081

Systematic Review of Focus Group Discussions & Mixed Method Surveys Regarding Colorectal Cancer Screening

PRESENTER

AUTHOR(S)

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ABSTRACT TOPIC

Cancer

ABSTRACT

Background:

Colorectal cancer (CRC) screening has a significant potential to decrease mortality from CRC. Many published studies have used either focus groups or structured interviews to identify barriers and facilitators of CRC. However, a systematic review of methods and findings from focus groups is lacking.

Objective:

The objective of this study was to conduct a systematic literature review that describes the characteristics of focus group participants and synthesize major themes of CRC screening barriers and facilitators. A secondary objective was to identify the impact of barriers related to social determinants of health (SDoH) factors.

Methods:

A systematic review of qualitative studies was conducted on CRC screening focus groups following ENTREQ guidelines and the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA). Our inclusion criteria were as follows: (1) empirical scientific studies with a qualitative focus group or mixed methods study design; (2) that have been published in a peer-reviewed journal; (3) from January 1, 2012, and August 12, 2022; (4) in English; (5) exploring the attitudes, beliefs and behaviors related to adults and colon cancer screening; (6) face-to-face and online format. Keyword searches were conducted in the electronic databases PubMed and SCOPUS. After review, 31 studies contributing to our research questions were found eligible for inclusion.

Results:

Findings revealed that the number of participants per focus group (where reported) ranged from 2 to 23 participants with a median of 6 participants. There was a range of 20 to 232 total focus group participants per study while the mixed method studies ranged from 25 to 492. Most of the studies utilized education, income level, and access to healthcare as social determinants of health factors. The most commonly reported SDoH variable noted as a barrier to CRC screening was the lack of recommendation or education of a screening by their healthcare provider (15 of 31, 48%) with embarrassment or disgust regarding the procedure as a secondary barrier (11 of 31, 35%).

Conclusions:

Main themes for barriers and facilitators that emerged from the review were insurance status and awareness of the benefits of screening. Commonly reported concerns for barriers were embarrassment or disgust regarding the procedure and lack of trust in their provider relationship. Previous awareness of this disease through family history was a common facilitator. Opportunities to increase CRC screening arise in ensuring education and access to alternatives that provoke less embarrassment, such as FIT or FOBT tests.

Sponsorship:

None

Cervical Myelopathy secondary to Hirayama Disease in 16-year-old male

PRESENTER

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Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Physical Medicine / OMM

ABSTRACT

16-year-old male with past medical history of asthma presented to the ED with a chief complaint of months of persistent numbness, tingling and twitching sensations in his left calf and toes. The patient also noted weakness, paresthesia and loss of muscle mass of his left hand and wrist, and inability to straighten his fourth and fifth digit. Physical exam showed weakened hand grip and wrist flexion/extension with left forearm and intrinsic hand muscle atrophy. Patient had a positive Hoffman sign and brisk reflexes with no other neurologic deficits. CK elevated at 296. MRI of the brain showed volume loss with signal abnormality and enhancement in the lower cervical spinal cord (C4-C7). Findings were consistent with a non-acute, non-expansile myelopathy.

Hirayama Syndrome (HS) is a rare condition caused by anterior movement of the posterior dural sac of the cervical spine during neck flexion, resulting in cord compression. Although a self-limiting condition, HS can cause chronic motor disabilities, including weakness of the extremities and loss of fine motor movements: resulting in diffuse muscle atrophy and contractures. Early interventions are key to preventing complications. Cervical collars have shown to be very effective. Nerve conduction studies can show the extent of nerve loss and possibility for reinnervation.

If not treated early, cervical fusion is the only remaining intervention for HS, resulting in severe loss of cervical mobility, leading to functional, social and occupational disability. Education on prognosis and prevention of motor deficits will facilitate informed decision making, expedite diagnosis, and encourage patient compliance. Physical therapy has shown to not only reduce long term complications, but also help patients with residual motor deficits reach functional independence.

General Anesthesia for Biopsy of Pediatric Mediastinal Mass with Tracheobronchial Compression

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Other

ABSTRACT

Background: Mediastinal masses present anesthesiologists with significant challenges during the peri-operative period. These challenges include but are not limited to managing tracheobronchial compression, atelectasis, adequate ventilation, venous compression, and adequate systemic circulation. Bronchial compression can cause air trapping, meaning air can enter a section of the lung with enough pressure, but the compression prevents air from escaping the lung. This presents a problem for positive pressure ventilation (PPV). If using PPV, the positive pressure can surpass the compression when entering, but air cannot escape, causing an increased volume of entrapped air. This leads to two significant issues: 1) Decreased healthy lung volume leading to inadequate ventilation, and 2) Mediastinal deviation causing kinking of the IVC, leading to decreased preload and insufficient circulation. We recommend sustained spontaneous ventilation and lateral positioning to prevent these issues. Case Presentation: A 7-month-old __male,__ without significant past medical history, presents with a left-sided mediastinal mass. The mass caused left bronchial compression with subsequent air trapping in the lower lobe. An echo was performed to make sure the patient could tolerate general anesthesia to biopsy the mass. The echocardiogram resulted in no abnormal findings. The anesthesia team decided to use spontaneous breathing in order to prevent further air trapping. While the patient was under anesthesia the oxygen saturation began to decrease, and one of the anesthesia team members decided to give PPV. An x-ray was taken in the OR showing increased air trapping. The arterial line showed a physiologic tamponade causing a decreased systolic pressure of 50mmHg on each inspiration the patient took. Conclusion: Even when an echocardiogram results in no abnormal findings, it is still unsafe to use PPV ventilation because physiologic tamponade can be produced with increased air trapping. This is no longer postulated but is shown with the x-ray and arterial line findings.

Correlation Between Timed Up and Go Test and Neuroimaging in Mexican American and Non-Hispanic Americans with Alzheimer's Disease

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Aging / Alzheimer

ABSTRACT

Purpose:

Alzheimer's Disease (AD) is a progressive neurodegenerative disease that causes cognitive and functional impairments. Abnormal amyloid plaque accumulation is known to be specific for AD, demonstrated by previous amyloid Positron Emission Tomography (PET) studies showing abnormal amyloid plaques levels in subjects in the early stages of the disease, not exhibiting clinical manifestations. 1,2 Hispanic Americans are underrepresented in AD research. This study explores the possible relationship between the amyloid plaque level visible on amyloid PET scans and non-specific Physical Performance Tests such as Timed Up and Go (TUG) among Mexican Americans and non-Hispanic white American subjects. Furthermore, this study explores the possible correlation between rising amyloid plaque levels and declining function measured by simple physical performance tests such as TUG in outpatient clinics for AD patients.

Methods:

Data were analyzed on n= 2076 Participants (n= 1037 Non-Hispanic White, n=1039 Hispanic, Mexican American) from the Health and Aging Brain Study- Health Disparities All participants underwent as part of the HABS-HD protocol cognitive testing, functional/medical examination, blood draw, and neuroimaging. Amyloid PET scans (with Neuraceq/florbetaben F18) were conducted with defined regions of interest (ROIs) included the frontal, anterior/posterior cingulate, lateral parietal, and lateral temporal cortex. All participants completed the Timed UP and Go (TUG) test along with other gait measures as part of the functional examine. The TUG is a measure of functional mobility, higher scores mean worse performance on the measure. Chi-square (Sex) and t-tests (Age, Education, TUG performance) were used to examine differences in demographic characteristics across ethnic groups. Linear regression models were conducted to examine the relationship between Amyloid PET imaging and a functional measure (TUG) and the significance was set at $p < 0.05$

Results:

In our study, we found a statistically significant correlation between TUG time and increased amyloid uptake only in the lateral parietal region in Mexican American subjects ($p=0.049$). The other ROIs in Mexican American subjects showed no statistically significant correlation between TUG time and increased amyloid uptake. All ROIs in Non-Hispanic Whites showed no statistically significant correlation between TUG time and increased amyloid uptake.

Conclusion:

This study aimed to examine the relationship between physical performance measures (such as the TUG) and amyloid uptake. TUG is a non-specific physical performance measure often used in outpatient offices with older adult patients and is shown to correlate with cognitive decline.³ Using PET scans, we theorized that TUG results might correlate with the amyloid plaque level; however, our results were inconsistent with our initial hypothesis. On the other hand, this study did reveal a correlation between TUG time and increased amyloid uptake (only in the lateral parietal region) with subjects of Mexican descent, therefore; highlighting the

importance of exploring ethnic differences in AD research. Finally, this study is limited by a small sample size, and future work with additional samples should help examine the TUG and amyloid uptake relationship and ethnic differences.

IRB NUMBER
2016-128

Lymphatic Malformation Discovered Post-Tonsillectomy in a 5-Year-Old Female

PRESENTER

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ABSTRACT TOPIC

Structural Anatomy

ABSTRACT

Background: Lymphatic malformations (LM) are benign tumors of the lymphatic vessels that are a result of congenital abnormalities in the lymphatic system. They are found most in children younger than the age of 2 and are frequently localized in the head and neck regions. Despite being benign, LM still have potential for invasion, so they should still be monitored after discovery.

Case Information: A 5-year-old female presented to her otolaryngologist with recurrent serous otitis of both ears and enlarged tonsils and adenoids. The physician then performed a bilateral myringotomy with tube placement, and a tonsillectomy/adenoidectomy. A few days after the tonsillectomy, she presented with significant swelling, fever, lymphadenitis, and a large, layered fluid collection localized over the right side of her face and neck. The swelling was drained by interventional radiology; and then, an MRI was performed, which showed large cystic structures around the right parotid gland, temporomandibular joint, and pharyngeal area that was consistent with a LM.

Conclusion: Lymphatic malformations are primarily diagnosed in children. In this case, both the location and the method of discovery of this structure were uncommon. This LM was found in the parapharyngeal space, right next to the tonsil. Typically, LMs are not found this high in the head and neck region. Furthermore, this LM was likely only found due to the preceding tonsillectomy/adenoidectomy, which may have introduced an infectious nidus to the structure causing it to become inflamed and causing systemic symptoms in the patient. This case illustrates that the parapharyngeal space should be considered for LM and an infectious nidus post-surgery may lead to systemic symptoms. The treatment involved incision and drainage, with subsequent follow up with hematology/oncology for further clinical management.

Post-operative acute dyskinetic reaction with possible association to Ondansetron administration

PRESENTER

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ABSTRACT TOPIC

Pharmacology

ABSTRACT

Background: Acute dyskinetic reactions after the administration of general anesthesia are uncommon, with the differential diagnosis including adverse drug reaction, local anesthetic reaction, in addition to a possible underlying psychiatric illness. Prior cases studies have been published demonstrating cross-reactivity and extrapyramidal symptom-onset with the temporal association of Ondansetron administration.

Case Description: 38-year-old female, with PMHx of T1DM, depression, anxiety, OSA, GERD, and chronic generalized muscle weakness, was scheduled to undergo an elective Laproscopic Cholecystectomy. Home medications reviewed prior to the procedure included Cymbalta, Wellbutrin, Protonix, PO Zofran, and Insulin. Anesthesia given for induction was Versed (2 mg), Fentanyl (100 mcg), IV Lidocaine (70 mg), Propofol (200 mg), defasciculating dose of Rocuronium (5 mg), Succinylcholine (120 mg) prior to intubation. Additional Rocuronium (35 mg) was later administered. Intra-operatively, IV Decadron (10 mg), IV Zofran (4 mg), Toradol (30 mg), Ephedrine (10 mg), Dilaudid (1 mg), Labetalol (10 mg), and Sugammadex (200mg) were provided for proper maintenance of vital signs, pain control, and paralytic reversal. Glucose level was monitored and maintained throughout the case with patient's continuous glucose monitor. Procedure lasted approximately 40 minutes, with no associated complications. Patient displayed spontaneously breathing prior to extubation and was transferred to the Post-Anesthesia Care Unit (PACU). While in the PACU, vitals were stable with patient speaking and asking questions to nurse within 15 minutes. Patient was transferred back to Same-Day Surgery (SDS), where she requested additional nausea medication and was given IV Zofran (4 mg). Minutes later, the patient began showing signs of acute dyskinesia of the head, neck, and upper extremities, in addition to acute dystonia of the eyes, consistent with extrapyramidal symptoms. Within 5 minutes of symptom onset, Diphenhydramine (50 mg) and Versed (3 mg), were given to alleviate the extrapyramidal side-effects. Limited symptom improvement was noted, and patient was subsequently given Ativan (2 mg). Patient showed improvement after the administration of Ativan and was transferred to the ICU for close observation. Treatment, with IV Benadryl and Ativan, was continued for the proceeding 48 hours in the ICU. Patient's condition continually improved, with occasional relapse of mild symptoms. Although definitive etiology of patient's symptoms is unknown, Neurology was consulted and agreed that symptoms could have been caused by a medication reaction to Ondansetron, in addition to possible exacerbation of an underlying psychiatric illness. It was confirmed that proper treatment was provided with complete resolution of symptoms expected, with no long-term sequelae.

Conclusion: This case illustrates and provides additional insight on the proper treatment regimen for the rare occurrence of acute dyskinetic reaction post-anesthesia, associated with administration of Ondansetron.

Attractiveness of Anthropometrically Average Facial Anatomy: Is the Whole a Sum of Its Parts?

PRESENTER

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ABSTRACT TOPIC

Other

ABSTRACT

Goals/Purpose: Literature suggests that faces that possess average anatomy for the population are considered more attractive. When patients seek facial cosmetic surgery, they often have a certain feature or features that they desire improvement on. With the subjective and evolving nature of beauty, it can be difficult for plastic surgeons to differentiate between relative change and definite improvement. Thus, identifying ideal dimensions of facial features would provide evidence-based guidance for aesthetic surgery. This study aims to investigate the independent relationship between measurements of anthropometrically average facial features and perceived beauty, as well as their relative importance to each other and the overall perception.

Methods/Technique:

Ratings: To assess perceived attractiveness, crowdsourcing, a well-founded online method of studying aesthetic and reconstructive outcomes, was utilized. The photographs were uploaded to Google Forms with multiple-choice responses ranging from 1-7, with 1 and 7 being the least and most attractive, respectively. The images were presented in a random order to each respondent. Monochrome photos were used to negate the biases of hair, skin, and eye color.

Measurements: Our female and male cohorts each consisted of standardized frontal-view photos of 41 individuals, with 1 composite derived from the other 40. Composite images were generated using Webmorph.org, which is a web-based software that specializes in averaging and transforming faces. Each face had the same number of standardized points placed manually to delineate the position of facial landmarks. The corresponding points allowed for averaging each facial landmark across all the faces to develop the composite. All photos were calibrated by interpupillary distance. Next, linear facial features (including measurements of the upper face, middle face, lower face, and facial height and width) were measured by pixels with WebMorph.org. Lastly, angular facial features were measured in degrees using Mirror software.

Statistical Analysis: A t-test was used to verify that the composite with average facial features was the most attractive in each cohort. After verifying that the average faces were most attractive, a Spearman correlation test calculated correlation coefficients between facial measurements and perceived attractiveness. A larger correlation coefficient indicates a stronger association between average facial measurements and perceived attractiveness. $p < 0.05$ was considered significant.

Results:

For the male and female cohorts, the respondents ($n=870$ and 876 , respectively) found the composites (derived from average facial anatomy) significantly more attractive than the rest of the cohort (both $p < 0.0001$).

For the male cohort, only anthropometrically average upper lip height had a statistically significant correlation with attractiveness (Table 1) ($R=0.376$; $p=0.017$).

For the female cohort, only anthropometrically average bigonial width had a statistically significant correlation with attractiveness ($R=0.352$; $p=0.026$).

Conclusion: Our study identifies average male lip height and average female bigonial features significantly correlated with perceived beauty. Though overall average faces were found to be significantly more attractive, the majority of facial features when independently analyzed for their correlation with beauty were not found to be significantly associated. Our findings suggest that the attractiveness of the average face is not largely due to the summative attractiveness of its individual facial components.

Identification of proteins affected by increased intraocular pressure in the glaucomatous female mouse retina by label-free proteomics

PRESENTER

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COLLEGE/SCHOOL

Postdoctoral Fellow

ABSTRACT TOPIC

Proteomics

ABSTRACT

Purpose:

Mass spectrometry-based retina proteomics using animal models of human diseases has enabled novel insights into ocular neuropathology's such as in glaucoma, as it holds promise for disease biomarker discovery. However, publicly accessible data on retina proteins affected by ocular hypertension (OHT) in animal models utilized males, or sex was not disclosed. Recently, female animals were chosen to advance therapeutic antibody development against glaucomatous neurodegeneration with retina proteomics support. Therefore, our retinal proteomics-based investigation intended to fill a knowledge gap by focusing on OHT-induced changes of protein expressions in the glaucomatous female retinae compared to normotensive controls.

Methods:

Proteins were extracted from the retinae of normotensive female mice (control, n=5) and OHT mice (n=5) in which increase of intraocular pressure was induced by the magnetic microbead method. After reduction, alkylation and digestion by trypsin, bottom-up shotgun proteomics analyses of the samples were done using data-dependent nanoflow liquid chromatography–electrospray ionization tandem mass spectrometry (LC–ESI-MS/MS) on a hybrid Orbitrap instrument (Thermo Fisher Scientific). MS/MS spectra were searched against the UniProt mouse protein sequence database using the SEQUEST search engine in Proteome Discoverer (version 2.4; Thermo Fisher Scientific). Validation of proteins identifications using stringent criteria and label-free quantifications (LFQ) employing spectral counting to detect regulated proteins between groups using t-tests were performed using Scaffold (version 5.1.2; Proteome Software). Targeted proteomics on selected biomarkers was designed and analyzed using SkylineTM (MacCoss Lab software). Mapping to protein interaction networks and biological processes was done through Ingenuity Pathway Analysis[®] (IPA[®], Qiagen).

Results:

Our discovery driven data-dependent nanoflow LC–ESI-MS/MS analyses covered nearly 1200 retinal proteins with <1% false discovery rate. Among these proteins, 168 were significantly affected by OHT based on LFQ. Bioinformatics analyses by IPA[®] revealed important diseases and functions triggered by OHT pertaining to neurological and ophthalmic pathologies. The topmost protein interaction network represented neurological disease, organismal injury and abnormalities. The molecule activity predictor of IPA[®] revealed important canonical pathways, including inhibition of synaptogenesis signaling and mitochondrial dysfunction leading to degeneration of central nervous system tissue. Another prominent protein interaction network represented nervous system development and function, as well as organ development. In addition, this network also displayed downregulation of neuroprotective crystallins owing to OHT. Neuronal crystallins have been identified not only as biomarkers to monitor the progression of OHT-induced retinal neuropathy and evaluate neuroprotective interventions, but also as potential druggable targets or possible protein therapeutics to prevent glaucomatous neurodegeneration. Parallel reaction monitoring-based targeted proteomics validation of significant OHT-regulated retina proteins are currently underway to establish them as potential preclinical

biomarkers and/or therapeutic targets. In addition, our studies will be expanded to investigate sex as a biological variable affecting ocular neurodegeneration associated with glaucoma.

Conclusion:

We anticipate that biological information one can derive from our dataset at the protein expression level will provide inspiration for future hypothesis-driven experimental studies focusing on knowledge gaps involving the biology of glaucomatous neurodegeneration.

EXTERNAL FUNDING SOURCE

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The Success Rate of Cryoablation vs. Radiofrequency Ablation for the Treatment of Atrial Fibrillation

PRESENTER

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Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Cardiovascular

ABSTRACT

Atrial fibrillation (AF) is a heart rhythm disorder of the atrium caused by impulses that attack the Atrioventricular (AV) node and block signals to the ventricles. There are two types of catheter ablations that attempt to cure AF: radiofrequency (RF) ablation and cryoablation. RF ablations use an irrigated open-tip catheter to burn lesions in a point-by-point fashion around the pulmonary veins to stop the irregular electrical signals. Cryoablations use a balloon catheter that inflates in the pulmonary vein to freeze the tissue, which stops the irregular electrical signals. While both methods are adequate, the more effective procedure is a topic of debate. This study was performed at Baylor Scott and White Hillcrest hospital in the Cardiology Department. The data was obtained from 45 patients who suffered from AF from January 2017- June 2018. The purpose of this study was to evaluate the success rates of RF ablations and cryoablations within the Baylor Scott and White Hillcrest hospitals by measuring the readmission rates of patients who repeated an ablation. The initial success rates of RF ablation and cryoablation were calculated to be 88% and 95%, respectively. Even though this study aligns with other studies performed by Frankel Cardiovascular Center and CarolinaEast Medical Center, it was noted that the sample pool is small and limited to Baylor Scott and White Hillcrest.

Accessory Muscle from the Trapezius Muscle into the Thoracolumbar Fascia

PRESENTER

AUTHOR(S)

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Structural Anatomy

ABSTRACT

Background: As part of the superficial back musculature, the trapezius and latissimus dorsi muscles play an integral role in upper body mobility. The trapezius functions in neck extension and movement of the scapula, allowing motions such as elevation, depression, upward rotation, and retraction. The latissimus dorsi functions to internally rotate, adduct, and extend the arm. Anatomical variations of these muscles have been previously reported in literature and are associated with aplasia, hypoplasia, agenesis, and variations in vasculature and innervation.

Case Information: We present our discovery of a unique trapezius muscle variant that was discovered upon standard cadaveric dissection. The variant is approximately 6.0 cm in length. The accessory muscle is observed to originate from the inferolateral fibers of the trapezius and inserts into the superomedial fibers of the latissimus dorsi muscle. The inferior aspect of the muscle-tendon runs continuously with the latissimus dorsi muscle tendon, ultimately inserting into the thoracolumbar fascia. The superior aspect of the muscle belly narrows to fuse with the deep surface of the trapezius muscle. The middle portion of the accessory muscle was surrounded by its own fascial sheath, separating it from both the superficial cutaneous tissue and the deep musculature.

Conclusion: Anatomical variants arise commonly in individuals, and their clinical significance - especially in the routinely used upper body muscles - can either impair quality of life or be asymptomatic. More specifically, accessory muscle variants, like the one we found, are important to note due to their use in surgical procedures, relevance during diagnostic imaging, and their potential for clinical manifestations (such as pain syndromes and scoliosis). We suggest that accessory muscle variants could offer alternative options to surgeons when considering tendon transfer procedures. Next, we propose that the presence of a unilateral accessory muscle could play a role in scoliosis. The trapezius and paraspinal muscles, and their connections with the spinal vertebrae, contribute to the balance of forces that, when imbalanced, may present as idiopathic scoliosis. Previous studies have shown that abnormalities in the paraspinal muscles, like the trapezius, have a strong correlation with idiopathic scoliosis. Lastly, we suggest the presence of unilateral accessory muscles may give rise to pain symptoms.

HPV and Other Vaccination Rates in Texas: Association with Racial and Ethnic Distribution

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Health Disparities

ABSTRACT

Background: Human Papilloma Virus (HPV) is a sexually transmitted disease responsible for ~70% of cervical cancer worldwide and can result in genital warts, anal, penile, and oropharyngeal cancers. Since the adoption of HPV vaccines, high-risk HPV incidences have decreased by 50%¹. Vaccination is recommended from ages 11-26 and requires 3 doses to be up to date. While vaccination rates have increased, racial and ethnic minorities are less likely to complete the series, with rates of initiation and completion particularly low amongst African American adolescents².

Objective: This project examined the association between rates of HPV and other regularly recommended vaccines at the national, state-wide, and county level with consideration given to racial and ethnic distribution.

Methods: Data was collected from the Centers of Disease Control and Prevention (CDC) and the National Immunization survey. Vaccination rates were compared between HPV, Tdap, and MenACWY vaccines at the national, state-wide, and county level³. Racial and ethnic makeup was also compared in these regions⁴.

Results: When compared to the Tdap and MenACWY vaccines, vaccination rates for HPV (UTD and ≥ 1 dose) were significantly lower across national, state-wide, and county levels. The national vaccination rate for HPV UTD and ≥ 1 dose were 48.6% and 65.5% while the rates for Tdap and MenACWY vaccinations were 88.7% and 85.1%. Additionally, Texas had an overall lower vaccination rate of 39.7%, 57.8% and 83.2% for HPV UTD, HPV ≥ 1 dose, and Tdap, respectively. Texas county vaccination rates were lowest in Dallas County with HPV UTD at 35.7%, HPV ≥ 1 dose at 54.5%, and Tdap at 77%. Dallas county has the highest percentage of African American and Hispanic residents when compared to other major Texas counties, Texas, and national average. The non-white population in Dallas county makes up 48.5% while it is 32.3% and 28.2% at the state and nation level.

Conclusion: While HPV vaccine rates have increased since its induction in 2006, it is still among the lowest vaccines received across all populations. This study suggests that there is a correlation between vaccination rates and racial/ethnic distributions. African Americans and Hispanics at the national and county level were shown to have the lowest vaccine rates, especially African American girls. Further analysis is required to determine the source of such health disparities and further links to socioeconomic factors.

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Evaluating a Nail-Plate Combination Implant in Treatment of Distal Femoral Fractures: A Case Series

PRESENTER

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COLLEGE/SCHOOL

Texas College of Osteopathic Medicine

ABSTRACT TOPIC

General Medicine

ABSTRACT

Distal femur fractures are severe injuries that have varying management among orthopedic surgeons. These fractures are thought to be caused by high-energy trauma in younger patients and low-energy injuries in older patients. These fractures account for approximately 6 to 7% of all fractures and the gender distribution is estimated to be 33.4% male and 66.6% female. Additionally, there is increase in distal femoral fracture incidence after the age of 60 in both genders. Therefore, these fractures require optimal treatment to prevent disability and improve patient quality of life.

Current treatment for distal femur fractures can vary broadly but in this study, we focus on intramedullary nailing and plating. Intramedullary nailing has been championed as less invasive as it offers minimal disruption of soft tissues and endosteal arterial supply. Nailing of extremely distal periarticular fractures is becoming more common because of better load sharing and minimal soft tissue stripping compared to plating. In comparison, submuscular locking plates have become standard in these fractures and offer several advantages. These include more flexibility in periprosthetic fractures, preservation of blood supply to the periosteum, decreased time under anesthesia, and lower blood loss. The purpose of this case series is to qualitatively examine the outcomes of patients who received a nail-plate combination for their distal femoral fracture.

A chart review of 10 patients who received a nail and side plate combination at JPS Hospital was conducted. These patients underwent surgery from August 2021 to May 2022. They consisted of 4 males and 6 females with a mean age of 63 years (range of 36 to 89 years). For each patient, an outcome of union or nonunion was recorded along with time since surgery. The nailing system used was the Synthes Retrograde Femoral Nailing System.

When examining results, only 6 patients had follow up visits. 4 of the 6 patients achieved union at times of 3, 4, 6, and 8 months since date of surgery. Meanwhile, the remaining 2 patients had nonunion. One of these nonunion patients required hardware removal and has not achieved union at 5 months. The other nonunion patient has yet to achieve union at 7 months.

When compared to current literature, two studies have shown promising results with the nail-plate combination. The first had 8 patients with 100% union rate while the second had 15 patients with 93% union rate. The union rate in this study is relatively lower at 66%. However, this can be attributed to variables such as severity of initial injury, patient compliance, comorbidities affecting healing, and implant manufacturer. The rationale behind the combination technique is creating a stable and balanced fixation that allows for immediate weight bearing and mobilization post-surgery. While it shows promising results, more research in larger cohorts need to be done before the nail-plate combination can be evaluated against traditional methods.

Relationship of Down Syndrome with Keratoconus and Gonadotropins

PRESENTER

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ABSTRACT TOPIC

Eye / Vision

ABSTRACT

Purpose: Down syndrome (DS), also known as trisomy 21, is a common genetic disorder of chromosomal nondisjunction. DS has been strongly associated with Keratoconus (KC); however, the exact pathobiology remains unexplored. KC is one of the most significant corneal disorders which is characterized by thinning, cone-shaped protrusion, and steepening of the cornea leading to a significant reduction of visual acuity and even blindness. The aim of this study was to investigate the relationship of DS with KC in the context of gonadotrophic hormones.

Methods: This study adhered to the declaration of Helsinki. Fifty-eight healthy controls (29 male, 29 female), one hundred and forty-nine KC (112 male, 37 female), and eighty DS (44 male, 36 female) patients were recruited for this study. Plasma samples were collected from all participants. We investigated the expression of Gonadotrophin-releasing hormone (GnRH) and Follicle stimulating hormone (FSH) using enzyme-linked immunosorbent assay (ELISA).

Results: Significant downregulation of GnRH expression was observed in KCs when compared with healthy ($p = 0.0006$) and DSs ($p = 0.00249$). GnRH was significantly downregulated in KC and DS males, compared to their healthy counterparts, while no significance was observed in females across all diseases. Significant upregulation of FSH levels was observed in DSs compared to both healthy and KCs ($p < 0.0001$). FSH expression was also significantly elevated in both DS males and females when compared to healthy and KCs.

Conclusions: Our results revealed downregulation of GnRH, but upregulation of FSH in DS participants as compared to KCs. These findings provide new insights into the potential association between DS and KC, and substantiate the role of gonadotropins. Further studies are warranted to further understand the underlying mechanisms and potential implications for the treatment and management of these conditions.

EXTERNAL FUNDING SOURCE

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U-87 MG glioblastoma multiforme cell line expresses cell surface PCNA, a prospective target for Natural Killer Cell-mediated immunotherapy.

PRESENTER

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COLLEGE/SCHOOL

Dual Degree

ABSTRACT TOPIC

Cancer

ABSTRACT

Purpose: Glioblastoma multiforme (GBM) is the most common form of primary brain cancer in adults and carries a dreadful five-year survival rate of less than 7%. Current commonplace treatment options include surgery, chemotherapy, and radiation. Recently, there has been a move to pursue immunotherapy avenues to improve patient outcomes. These therapies often depend upon the identification of molecular antigens that are particular to cancer cells. Some antigens, such as EGFR, are overexpressed on a significant percentage of GBM tumors and are useful as targets for immunotherapies. However, to address GBM tumors that do not overexpress well-known antigens, our lab set out to identify novel antigens on GBM as future candidates for Natural Killer (NK) cell-mediated immunotherapy. Previously, our lab has demonstrated that cell surface-bound Proliferating Cell Nuclear Antigen (PCNA) can serve as a target of NK cell-mediated killing of several cancers. Cell surface PCNA is not expressed on healthy, non-malignant cells – making it an attractive immunotherapy target. We have also previously shown cell surface PCNA to be expressed on other GBM cell lines (LN-229 and LN-18). We set out here to investigate the potential expression of cell surface PCNA on U-87 MG cells. **Methods:** Based on the prior studies, we examined the expression of PCNA on the U-87 MG GBM cell line via flow cytometry using PE-labeled antibodies specific for PCNA. For comparison, we did the same experiment in the same setting with LN-18 cells, one of the previously mentioned cell lines that expressed PCNA. **Our hypothesis:** U-87 MG cells would show increased detection of fluorescence signal of anti-PCNA antibodies when compared to the fluorescence detection of negative control groups (no staining group and PE-isotype control group). **Results:** PCNA was identified to be expressed on U-87 MG cells via the detection of increased fluorescence signal versus negative controls, though to a lesser degree than that of LN-18 cells. **Conclusions:** Based on our results, we concluded that cell surface PCNA is expressed on the U-87 MG cell line and is a candidate for studying NK cell-mediated immunotherapy in *in vitro* contexts using U-87 MG cells. Currently, we are evaluating blocking inhibitory signals to NK cells mediated through the PCNA-NKp44 interaction to target GBM for NK cytotoxicity in U-87 MG cells.

EXTERNAL FUNDING SOURCE

CPRIT Grant# RP210046

Ketogenic Diet Increases Mitophagy in a Mouse Model of Glaucoma

PRESENTER

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Faculty/Staff

ABSTRACT TOPIC

Eye / Vision

ABSTRACT

Purpose: We have previously shown that limiting dietary intake to high fat, low protein, and negligible carbohydrate results in mitochondrial biogenesis, and in the case of glaucoma, a reduction in neurodegeneration of retinal ganglion cells (RGCs). In this experimental follow-up study, we wanted to examine the effect of the ketogenic diet on mitophagy, or mitochondrial recycling, within the glaucomatous retina.

Methods: MitoQC mice were placed on a ketogenic diet or standard rodent chow for 5 weeks and ocular hypertension (OHT) was induced via microbead injection. The MitoQC reporter mice have a pH-sensitive mCherry-GFP tag on the outer mitochondrial membrane that results in retention of red fluorescence when mitochondria bound for recycling are engulfed by lysosomes. The FIJI (ImageJ) macro MitoQC counter was used to quantify red puncta (mitolysosomes) in sectioned retina as a measure of mitophagy within the RGCs and Müller glia.

Results: Mitophagy in RGCs, as measured by red puncta, was significantly decreased by ocular hypertension in the control retina (Control + OHT) in comparison to naïve control retina (Ctrl; $p < 0.0001$). The ketogenic diet (KD) resulted in a significant increase in mitolysosomes in RGCs when compared to Ctrl ($p < 0.0001$), Control + OHT ($p < 0.0001$) and KD + OHT ($p = 0.0089$). The ketogenic mice with OHT showed a significantly higher RGC-associated mitolysosome number than Control + OHT mice ($p < 0.0001$). In contrast, mitolysosomes quantified in the Müller glia of Control + OHT mice were significantly higher than the naïve control mice ($p = 0.0127$). Mice in the KD ($p = 0.0001$) and KD + OHT ($p = 0.0005$) groups had significantly greater mitolysosomes than the control Müller glia, however there was no difference in mitophagy between the Control + OHT, KD, and KD + OHT Müller glia groups.

Conclusion: Our data demonstrates that mitophagy is managed differently within RGCs and Müller glia of mouse retinas. The KD promoted mitophagy within the RGCs to a degree that overcame the decline of mitophagy after OHT in the control group. Within the Müller glia, the KD was redundant because OHT alone increased mitophagy to similar levels as the KD. These findings suggest a divergence of mitochondrial homeostasis in RGCs and Müller glia that may reflect the different metabolic needs of these cell types.

EXTERNAL FUNDING SOURCE

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IACUC NUMBER

2022-0026

Effects of Amyloid β on Recollective Memory: Sex and Hormone Differences

PRESENTER

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Texas College of Osteopathic Medicine

ABSTRACT TOPIC

Aging / Alzheimer

ABSTRACT

PURPOSE:

Alzheimer's disease (AD) is linked with increased memory loss and inability to learn new topics. One of the defining neuropathological features of AD is amyloid beta ($A\beta$) plaques in brain regions, such as the hippocampus. The hippocampus brain region is important for memory and learning. AD risk is elevated in individuals older than 65 years old, especially menopausal women. Menopause is an aging associated endocrine event in which the ovaries stop producing estradiol but continue producing testosterone. Testosterone can be aromatized to estradiol, but aromatase is not functional in women with AD. Therefore, post-menopausal women with AD have more androgens than estrogens than pre-menopausal women and aged men. Androgens can be neuroprotective or neurotoxic depending on the cellular environment. It is unknown what the impact of androgens and sex are on amyloid beta's effects on the brain, (e.g., hippocampus) and behavior (e.g., memory). We hypothesize that females with the hormonal condition of androgens in the absence of estrogens will exhibit increased recollective memory in response to hippocampal injection of $A\beta$.

METHODS:

To investigate the role of androgens and sex on $A\beta$ associated memory impairments, adult male and female Sprague-Dawley rats were gonadectomized to remove circulating sex hormones. A subset of these rats was given either cholesterol or dihydrotestosterone (DHT), which cannot be converted into estrogen. To model AD, rats were injected with 5ug/ul of $A\beta$ oligomer fibrils 1-40 or vehicle shams in the CA1 region of the hippocampus. One week after $A\beta$ hippocampal injections, the rats were assayed for short term and long-term recollective memory via a 1-hour and 24-hour Novel Object behavioral test. The Novel Objective behavioral tests examines recollective memory by quantifying the time spent with a novel object versus the time spent with a known object. Data was quantified with a three-way ANOVA with sex, hormone, and $A\beta$ as independent variables. Tukey's was used as a post-hoc test.

RESULTS:

Sex differences were observed between hormone-deficient rats exposed to $A\beta$. Specifically, males exhibited worse short term recollective memory (1 hour novel object) compared to females. DHT had no effect on recollective memory, regardless of $A\beta$ exposure. No effects were observed in the long-term recollective memory (24-hour novelty test).

CONCLUSIONS:

Our results indicate that $A\beta$'s effects on short term recollective memory is influenced by sex chromosomes, as we observed sex differences in the hormone deficient (cholesterol) treated animals. However, DHT did not impact these recollective memory. These results indicate that recollective memory in AD is impacted by the sex chromosomes and not androgens.

EXTERNAL FUNDING SOURCE

NIH; Promoting Diversity in Research Training

IACUC NUMBER

2021-0025

Polyglandular Autoimmunity: Two Cases of Type 1 diabetes (T1D) accompanied by Addison's disease (AD)

PRESENTER

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ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Background:

Type 1 diabetes (T1D), present in ~1:500 children, is often accompanied by other autoimmune conditions, notably chronic lymphocytic thyroiditis. Involvement of other endocrine organs, however, is rare. Autoimmune impairment of more than one endocrine system is referred to as an autoimmune polyglandular syndrome (APS), categorized as type 1 (APS-1) or type 2 (APS-2). In addition to T1D, APS-1 is characterized by 1 or more of the following: candidiasis, hypoparathyroidism, and/or AD; while APS-2 involves AD and/or chronic thyroiditis². The lifetime risk of developing a 2nd endocrine autoimmune condition in individuals with T1D is ~1:5, and usually occurs during adulthood. While children may be affected, such reports are unusual and generally limited to case studies. APS-2 is rare in childhood, with a prevalence of ~ 1:100,000⁴. We present two children with APS-2.

Case Information:

Case 1: A 6-year-old Caucasian male, who was diagnosed with T1D at 3 years-of-age, presented with persistent vomiting which required hospitalization. Although his diabetes was reasonably well controlled prior to his hospitalization, the child was noted to be overly sensitive to insulin during this admission, during which he experienced several episodes of hypoglycemia. Laboratory testing revealed metabolic acidosis, hyponatremia, and hypocortisolemia. Appropriate testing confirmed primary adrenal insufficiency; the latter, along with his T1D, being consistent with APS-2.

Case 2: A 15-year-old Caucasian male experienced an unexplained 20 lb. weight loss. After developing fever, routine laboratory tests were reported to be characteristic of diabetic ketoacidosis (DKA) - hyponatremia, metabolic acidosis and hyperglycemia. With treatment, his DKA resolved, and he began conventional insulin therapy. However, follow-up laboratory tests demonstrated persistent hyponatremia. Additional studies confirmed the presence of AD, consistent with APS-2.

Conclusion:

These previously healthy children developed T1D accompanied by AD, characteristic of APS-2. The presence of both conditions significantly increases the risk of potential life-threatening complications in affected children⁵. Individuals with both T1D and AD have a 2.5-fold increased risk of adrenal crises, compared to those with isolated AD⁶. Timely diagnosis of polyglandular autoimmunity is critical to help inform clinical decision-making, and to avoid adverse outcomes. The diagnosis of APS is often hampered by common symptoms such as: fatigue and weakness, unexplained weight loss, increased thirst, frequent urination, irritability, nausea and abdominal pain, and changes in appetite². Management is complicated by the effects of glucocorticoid levels on insulin sensitivity. For example, these patients have a risk of increased insulin sensitivity and hypoglycemia in the early morning hours prior to the next glucocorticoid dose¹. Patient education is key for understanding the interactions between the two conditions as well as the effects of diet, physical activity, and emotional stress². While the onset of APS is variable, most patients tend to develop autoimmunity sequentially over a period of many years². APS-2 has been linked primarily to genes coding for

major histocompatibility complex, particularly DR3-DQ2 and DR4-DQ8 variants⁶. Physicians should be vigilant in assessing children with autoimmune-related conditions, such as T1D, and although rare, aware of the potential for additional autoimmune-mediated organ failure in some.

Parenting styles and driving under the influence of cannabis among US adolescents

PRESENTER

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School of Public Health

ABSTRACT TOPIC

General Public Health

ABSTRACT

Objective: Access to cannabis and synthetic THC alternatives is increasingly widespread. Moreover, there is no federal minimum age for purchase, and inconsistencies between state laws. Some parenting behaviors are associated with substance use among their adolescent children. However, it is unclear whether certain types of parenting behaviors are associated with driving under the influence of cannabis (DUIC). The current study examines this association.

Methods: We utilized cross-section data from the 2016-2019 National Survey on Drug Use and Health. The analytic sample (N=17,878) was comprised of adolescents aged 14 to 17 who had driven a car in the past 12 months. Parental warmth, monitoring, and conflict were recoded and measured ordinally. Weighted frequencies and multivariable analyses were conducted using SAS 9.4.

Results: Multivariable regression results indicated significant associations between DUIC and all types of parenting behaviors measured: warmth ($p<0.01$), monitoring ($p<0.001$), and conflict ($p<0.001$). Each one unit decrease in parental warmth, monitoring, and conflict, was associated with an increase in the odds of DUIC by 16% (OR=1.16, 95% CI 1.035–1.30), 18.3% (OR=1.18, 95% CI 1.07–1.31), and 50% (OR = 1.50, 95% CI 1.24 – 1.82), respectively. Past cigarette (OR=4.72, 95% CI 3.89–5.73, $p<0.0001$), and alcohol use (OR=12.47, 95% CI 9.28–16.76, $p<0.0001$) are strongly associated with DUIC. Compared to White adolescents, Non-Hispanic Native-Americans had 2.10 times the odds (95% CI 1.19–3.67, $p=0.03$) and non-Hispanic Asians had 0.61 times the odds (95% CI 0.30–1.25, $p=0.04$) of adolescent DUIC. Adolescents aged 16 to 17 had greater odds of DUIC (OR=2.96, 95% CI 2.12–4.12, $p<0.0001$) compared to younger adolescents aged 14 to 15.

Discussion: Our findings indicate adolescents with parents that engage in high warmth, high monitoring, and low conflict behaviors have decreased odds of DUIC. Past adolescent cigarette and alcohol use are also strong indicators of DUIC.

Expression of Specificity protein 1 in tumor tissues and its impact on the prognosis of cancer patients with an emphasis on race/ethnicity

PRESENTER

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ABSTRACT TOPIC

Cancer

ABSTRACT

Background: Specificity protein (Sp) transcription factors (eg., Sp1, Sp3 and Sp4) play a vital role in growth and development. Sp1 is known to regulate genes that are critical for angiogenesis, tumor growth and metastasis. The overexpression of Sp1 is associated with poor prognosis in some cancers for all populations, however, it may vary depending on the demographic background.

Objective: The objective of this project is to analyze the expression of Sp1 in various tumor tissues and evaluate the association with the prognosis of cancer patients using the publicly available online data sets. The other goal is to understand the impact on prognosis with race/ethnicity.

Methods: Data was obtained from the publicly available resources, The Cancer Genome Atlas (TCGA) (a landmark cancer genomics program developed by the National Cancer Institute and the National Human Genome Research Institute). Information was collected for 34 cancers and screened for the expression status (upregulated or downregulated), significance and relevance to prognosis of all patients and in relation to race/ethnicity.

Results: The information on the level of Sp1 expression was not available for 11 of the cancers in the database. The results are presented for the cancers that TCGA provided Sp1 expression information for. In 60% of the 23 cancers screened, Sp1 expression significantly impacted patient survival resulting in a poorer prognosis. The significance range was between $1.2E-02$ to $4.43E-10$. In a third of cancers evaluated, Sp1 expression affected the prognosis of patients depending on race/ethnicity. Interestingly, the association of Sp1 with poorer prognosis was found in certain racial/ethnic patients, despite there being no significant effect on the prognosis when combining the data for all patients. Glioblastoma, lung squamous cell carcinoma and prostate cancer are among the cancers that showed relevance to prognosis based on race/ethnicity even though there was no response on the overall survival of all patients combined.

Conclusion: These preliminary observations suggest an association between Sp1 expression in tumor tissues with the prognosis of some cancers. The results also suggest that Sp1 can differentially affect the population and may contribute to a poorer prognosis for patients belonging to a certain race/ethnicity in some cancers.

An Unusual Presentation of Subcutaneous Inguinal Hematoma Mimicking Ovarian Torsion: A Case Report and Review of Literature

PRESENTER

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ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Background: Ovarian torsion is a condition in which an ovary rotates around one of the supporting ligaments that provides stabilization and perfusion in the pelvis, and can present as a medical emergency due to the rotation hindering blood flow. This is most often the infundibulopelvic (IP) ligament which connects the ovary to the lateral pelvic wall, but can also occur with other ligaments as well. Inguinal hematomas tend to present as a post-operative finding due to procedures such as inguinal hernia repairs. However, there are little to no reported occurrences of ovarian torsion presenting with inguinal hematoma.

Case Presentation: A 36 year-old female presented to the emergency department with a chief complaint of left lower pelvic pain presenting with a large inguinal hematoma which had occurred two days earlier after intercourse. The patient stated she has a history of inguinal hematomas occurring after intercourse, however she stated that the bruising from this incidence was larger, more painful, and longer lasting than previous occurrences. Patient history includes a hysterectomy with bilateral salpingectomy and a left ovarian cyst that still remained. All laboratory values were unremarkable and vital signs were within normal limits. Using transvaginal ultrasound arterial blood flow to the left ovary was difficult to visualize, however venous blood flow was accounted for. The patient was suspected to have a left ovarian torsion and underwent a diagnostic laparoscopy. The decision was also made with the patient to perform a left oophorectomy due to her left ovarian cyst which can increase the occurrence of ovarian torsion, and was most likely contributing to her recurrence of this type of injury. At the time of surgery, the laparoscopy revealed that the left ovary was not extensively torsed and was adequately perfused. However, during the procedure an aberrant vessel was identified branching off of the IP ligament and terminating along the pelvic wall at the same location in which the inguinal hematoma was presenting externally. This aberrant vessel was ligated via electrocautery, and the patient tolerated the rest of the surgery without complications. The patient recovered and was discharged home with two week and two month follow-up appointments scheduled. These follow-up appointments revealed that her inguinal hematoma and pelvic pain resolved completely and that there was no negative impact to ligating the vessel.

Conclusion: This case investigates a cause of pelvic pain due to aberrant vessels which can present similarly to a case of ovarian torsion. This case serves to provide a possible etiology of pelvic pain presenting with inguinal hematoma, in which there are not many situations similar to this case in the current literature.

Iatrogenic Ureter Injury and Repair: Comparing Suture Versus Suture and Glue in Ureter End-to-End Anastomosis

PRESENTER

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ABSTRACT TOPIC

General Medicine

ABSTRACT

Funding: Dallas Southwest Osteopathic Physicians

The ureter is a delicate structure due to its size and anatomical location. It is found deep within the retroperitoneal space and the lower third of the ureter lies adjacent to numerous pelvic structures such as the uterine artery, cervix, vagina, colon, and iliac vessels, and due to its proximity, the ureter is subject to unintentional accidental injury during diagnostic or medical procedures, termed iatrogenic. This paper and associated aim to explore the odds of iatrogenic ureteral injuries (IUI) when comparing different surgical methods, discuss the best preventative options and review the current repair measures, as well as any associated complications. The aim of this study focused on ureter transection that require surgical repair using a ureteroureteral anastomosis, a procedure that ligates the free ends of the transected ureter together.

Ureters were obtained from anesthetized Yorkshire pigs via standard laparotomy [protocol: IACUC-20-0011]. Ureters were transected laterally midway along the length of the harvested ureter. In Group A ureters, 2 standard stay sutures were placed 180° degrees opposite one another to anchor the ureter and ligated using a simple continuous running suture technique. In Group B, ureters were anchored in a similar fashion with stay sutures and ligated using glue to perform the anastomosis. 500 mL saline was then flushed through the ureter to assess the structural integrity of the ureteroureteral anastomosis.

Group A ureters showed less stricture formation and fluid leakage at the site of anastomoses, indicating that the standard suture technique used in ureter repair is a safe and reasonable gold standard. In contrast, Group B ureters showed stricture formation and some fluid leakage at suture/glue line, indicating the method of ureter anastomoses was inferior. When IV saline was pushed in Group B ureters, the fluid often exited the ureter at both the suture site and the end portion of the ureter, more so than the Group A ureters. Future study needs to be conducted in suture/glue method as it is promising. However, it is not at the level where it can replace current ureter repair end to end anastomoses gold standard.

*These authors are solely listed in alphabetical order

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EXTERNAL FUNDING SOURCE

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A case of inclusion body myositis masquerading as statin-induced myopathy

PRESENTER

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ABSTRACT TOPIC

General Medicine

ABSTRACT

Background: Inclusion body myositis (IBM) is a common acquired myopathy in individuals older than 50 years of age. This idiopathic inflammatory myopathy carries an insidious progression with frequent delays in diagnosis and a high incidence of misdiagnosis resulting in significant morbidity and disability for affected individuals. Clinical features include asymmetric weakness predominantly affecting the quadriceps and/or finger flexors, and a slow, progressive course leading to loss of ambulation and dysphagia. Creatinine kinase (CK) levels are usually less than 10 times normal and erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) fall within normal limits. Myositis-specific autoantibodies are typically absent in patients with IBM; however, highly specific positive cytoplasmic 5'-nucleotidase 1A (cN1A) autoantibodies can help distinguish IBM from other forms of myositis, such as polymyositis. There is an association of IBM with autoimmune diseases, such as Sjögren's syndrome, sarcoidosis, and some lymphoproliferative disorders. Unlike many other autoimmune diseases, the condition typically affects males more frequently with a male-to-female ratio of approximately 3:1. Mean age of symptom onset ranges from 61 to 68, with over 20% of patients developing symptoms in their forties.

Case presentation: A 71-year-old male patient with a long-standing history of hypertension and dyslipidemia was evaluated for complaints of progressively worsening proximal muscle weakness, fatigue, and dyspnea for more than 2 years in duration. He had been prescribed 40 mg of atorvastatin and was presumed to have statin-induced myopathy after taking the drug for 1 year. Physical examination revealed an otherwise healthy male with proximal muscle weakness with stable vital signs. CK was within normal limits and CRP was 6.6. He was noted to have a negative ANA screen extensive myositis and HMGCR antibody, but was found positive for cytoplasmic 5'-nucleotidase 1A (cN1A) autoantibodies, thus confirming suspicion of IBM. MRI of the thigh demonstrated generalized muscular atrophy with no active inflammation. Given the prolonged nature of the disease in the patient, no active inflammation was noted. He is responding well to tapering doses of steroids and other immunomodulatory options being discussed with him.

Conclusion: This case illustrates the importance of appropriate recognition of IBM, and the challenges associated with diagnosis and management. This acquired myopathy may be mistaken for other conditions such as statin-induced myopathy and should be considered in the evaluation of progressive muscle weakness in individuals over 50 years of age. Appropriate intervention is essential to prevent progressive disability with rapid loss of strength and function in affected individuals.

Assessing the impact of targeted continuing education training on improving dental hygienists' HPV-related knowledge

PRESENTER

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COLLEGE/SCHOOL

Faculty/Staff

ABSTRACT TOPIC

General Public Health

ABSTRACT

Background: Human papillomavirus (HPV) is the most prevalent sexually transmitted infection in the United States and is attributable to various cancers. Approximately 70% of oropharyngeal cancer diagnoses are linked with an HPV infection. HPV vaccination is an effective prevention method that can protect against multiple high-risk strains including those directly associated with oropharyngeal cancer. Given the connection between HPV and oropharyngeal cancer and the frequency of dental visits compared to annual primary care visits, dental hygienists are uniquely positioned to help reduce the risk of HPV infection among their patients through vaccine education and promotion. The goal of this project is to evaluate the impact of a continuing education (CE) training on dental hygienists' knowledge about HPV and the HPV vaccine.

Methods: This study used pre- and post-test survey design to collect data from dental hygienists. The CE training was presented at the Southwest Dental Conference on August 26th, 2022, in Dallas, Texas. Prior to the training, all attendees were asked to complete an online survey assessing their knowledge about HPV and the HPV vaccine. Knowledge questions included modes of transmission, types and sites of HPV-related cancers, and vaccine recommendations and indication. For example, "HPV is transmitted through skin-to-skin contact" was asked as a true or false question. With a total of 18 questions on the knowledge scale, participants were awarded 1 point per correct answer and no points for incorrect answers. Higher averages indicated higher knowledge, with 18 being the highest possible score. Following the 45-minute CE, participants completed a second online survey assessing their knowledge. Data were analyzed in SPSS using t-tests to assess for changes from pre-test to post-test. A p-value of <0.05 was considered statistically significant.

Results: While a total of 453 oral health providers were registered, only practicing dental hygienists (n=112) who had matched pre- and post-surveys were included in this analysis. Out of 18 items, the average number of correct responses pre-CE was 13.7 (SD=2.7), which was significantly higher following the CE (16.8 correct, SD=1.0; p<0.001). The item with the most significant knowledge increase pertained to the type of vaccine available for HPV (a virus-like particle vaccine, 39.1% pre-CE; 92.0% post-CE, p<0.001). Additional items with increases in knowledge included the various types of cancers directly linked to HPV such as anal cancer (54.9% pre-CE; 99.1% post-CE, p<0.001) and penile cancer (50.4% pre-CE; 97.3% post-CE, p<0.001).

Conclusions: The HPV vaccine is an FDA-approved form of cancer prevention, and the best predictor of HPV vaccination uptake is recommendation from a healthcare provider. The CE training resulted in increased knowledge regarding HPV-related cancers and the HPV vaccine, indicating a need for similar trainings that can help dental hygienists make stronger, more informed vaccination recommendations to their patients. Equipping dental hygienists with the most up-to-date knowledge, effective communication skills, and confidence to promote HPV vaccination among their patients could greatly reduce the number of missed clinical opportunities to recommend and refer for the HPV vaccine.

EXTERNAL FUNDING SOURCE

The University of Texas MD Anderson Cancer Center

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A Modified Kidney Perfusion System for Improved Data Acquisition and Assessment of Renal Function and Metabolism

PRESENTER

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COLLEGE/SCHOOL

Dual Degree

ABSTRACT TOPIC

Integrative Physiology

ABSTRACT

Purpose: In the United States, there are over 88,000 candidates on the waitlist for kidney donation as of December 2022 with less than 42,000 transplant procedures being recorded in the same year. Coinciding with this continued disparity has been a growing interest in the technology to preserve and improve the function of kidneys for transplantation, most notably machine perfusion (MP). Studies have shown that MP is superior to static cold storage, the most common method of kidney preservation used globally, which has allowed transplant programs to expand the current donor pool by use of marginal donor kidneys. Despite these advancements, machine perfusion technology used clinically is limited in its use for obtaining critical information regarding the real-time assessment of renal function, fluid dynamics, and metabolism. Here we discuss the development of a modified kidney perfusion system that allows for enhanced data acquisition of perfusion parameters, renal arterial and venous sampling, and organ monitoring within a controlled environment.

Methods: The modified kidney perfusion system was assembled to house and monitor a singular organ. The organ is placed in a chamber that allows for maximal cooling to 2°C - 6°C or temperature regulation up to room temperature. Renal artery and vein cannulation allow for accurate perfusate sampling in different parts of the system without disruption of organ perfusion. Continuous monitoring of pressure, flow, and resistance is performed using pressure and flow transducers in line with the polyethylene tubing. In line with the system includes an air trap to prevent gas emboli, modifiable filter, and screen for large particulate matter. A specialized rotor allows for pulsatile perfusion into the kidney while a servomotor is used to set a desired pressure or flow into the system. Values for flow, pressure, resistance are recorded in real time using Spike2 software and the corresponding waveforms displayed in the program.

Results & Conclusion: The limitations of machine perfusion technology currently used clinically hinder the ability to obtain data for interpretation of pre-transplant renal function. This modified kidney perfusion system improves upon many of these limitations and provides entirely new methods to gain insight on kidney function. Assessment of renal metabolite production and injury markers can be obtained from multiple sites throughout the perfusion circuit and instantaneous recording of both pressure and flow waveforms throughout the duration of machine perfusion.

EXTERNAL FUNDING SOURCE

Dallas Southwest Osteopathic Physicians Foundation

ORAL PRESENTATION

Brain mitochondrial dysfunction in postpartum preeclamptic rodents

PRESENTER

Kylie Jones

AUTHOR(S)

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COLLEGE/SCHOOL

School of Biomedical Sciences

ABSTRACT TOPIC

Integrative Physiology

ABSTRACT

Purpose: Pre-eclampsia (PE), new-onset hypertension during pregnancy, impacts 3-8% of all births in the USA yearly and causes significant neurological damage to the mother during and after pregnancy. Studies show postpartum PE women to have increased risks of hypertension (HTN) and cerebrovascular dysfunction (CVD). Although the cause of HTN and cerebral damage is unknown, mitochondrial dysfunction (mtDys) may play a role. MtDys includes reduced mitochondria-specific antioxidants, raised mitochondrial reactive-oxygen species, changes in mitochondrial fission and fusion proteins, and reduced efficiency of the electron transport chain (ETC). Previous studies in our lab indicate associations between cardiac mtDys and the reduced uterine perfusion pressure (RUPP) rat model of PE with HTN at 10 weeks postpartum (PMID: 34727994). However, cerebral mtDys has not been examined in RUPP rats postpartum. This study aims to examine cerebral mitochondrial functional proteins in hypertensive RUPP postpartum rats at six weeks. We hypothesize that RUPP postpartum rats will have lower amounts of cerebral mitochondrial functional proteins compared to control (CON) postpartum rats.

Methods: We divided pregnant Sprague Dawley rats into two groups: CON normal pregnant (NP, n = 4) and RUPP (n = 4). Then, the RUPP surgery was performed on gestational day 14. Pregnant rats gave birth naturally and weaned for three weeks. Six weeks after giving birth, rats were euthanized for brain collections to measure functional proteins via Western Blot analysis, including ETC complexes (Complexes I-V), fusion proteins (OPA-1 and MFN-2), fission protein (DRP-1), and mitochondria-specific antioxidant (MnSOD).

Results: In the brain, RUPP postpartum rats have significantly reduced Complex I proteins compared to NP postpartum rats (91 ± 2.27 vs. 100 ± 2.45 IU/protein/CON %, $p < 0.05$) with slight decreases in Complexes II (93 ± 4.14 % vs. 100 ± 7.57 IU/protein/CON %, ns), III (91 ± 3.18 vs. 100 ± 6.11 IU/protein/CON %, ns), IV (86 ± 11.25 vs. 100 ± 7.95 IU/protein/CON %, ns), and V (92 ± 3.99 vs. 100 ± 6.33 IU/protein/CON %, ns). RUPP and NP postpartum rats have no significant differences in fusion proteins OPA-1 (102 ± 2.56 vs. 100 ± 2.02 IU/protein/CON %, ns) and MFN-2 (106 ± 18.25 vs. 100 ± 14.35 IU/protein/CON %, ns). Fission protein DRP-1 has an increase in RUPP postpartum rats compared to NP postpartum rats (111 ± 6.92 vs. 100 ± 4.55 IU/protein/CON %, ns). RUPP postpartum rats have significantly decreased MnSOD in comparison to NP postpartum rats (89 ± 2.00 vs. 100 ± 2.45 IU/protein/CON %, $p < 0.05$).

Conclusion: RUPP postpartum rats have cerebral mtDys indicated by decreased ETC complexes, especially Complex I. RUPP postpartum rat brains have reduced MnSOD, which suggests elevated mitochondrial oxidative stress. Furthermore, raised mitochondrial fission in the brain supports the presence of mitochondrial damage and mtDys. Future studies will examine the role of cerebral mtDys in causing HTN and CVD in RUPP postpartum rats. This study is clinically relevant because our findings provide a possible mechanism for the pathophysiology of CVD in postpartum PE women and novel targets for cerebral mitochondrial therapy.

EXTERNAL FUNDING SOURCE

AHA 18CDA34110264

IACUC NUMBER
IACUC-2021-0037

T cell alterations in a mouse model of neglect-related early life stress

PRESENTER

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ABSTRACT TOPIC

Immunology

ABSTRACT

Exposure to severe or chronically stressful life events during childhood—referred to as early life stress (ELS)—is associated with negative effects on health across the life course. Neglect is a significant source of ELS during childhood and accounts for over 75% of maltreatment-related child abuse in the United States. Animal models of ELS emulate the nature of childhood neglect through scheduled separation. A major challenge in studying the impact of stress on immune competency has been the difficulty of developing a reliable mouse model. The thymus is responsible for producing self-tolerant T cells and is critical for adaptive immunity. Developing T cells can be identified based on CD4/CD8 expression status which corresponds to defined stages in thymocyte maturation. We developed a novel murine model of neglect-related ELS based on the maternal separation with early weaning (MSEW) paradigm featuring scheduled dam-pup separation and early weaning to a high carbohydrate diet. This study investigates the effect of ELS on surface markers for thymic T cell development and distribution. Pups were produced by in-house breeding and subjected to one of two distinct ELS conditions: (1) daily dam-pup separation with early weaning (MSEW) or (2) the early weaning condition alone (EW) at postnatal day (PD) 14. Control pups were maintained on the dam's milk to the standard wean date (PD21). Tissues were collected at PD21 after euthanasia. Flow cytometry revealed significant differences in the distribution of PD21 thymocytes between the double-positive CD4+CD8+ (DP) and single-positive (SP) compartments. Our data indicate that neglect-related ELS can disrupt the baseline distribution of developing T cells within defined thymic compartments and suggests ELS exposure may have downstream ramifications on T cell immunity.

EXTERNAL FUNDING SOURCE

NIA T32 AG020494; NIMHD 5U54MD006882-10

IACUC NUMBER

2022-0024

Postpartum preeclamptic rats have hypertension and elevated cerebral oxidative stress

PRESENTER

AUTHOR(S)

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School of Biomedical Sciences

ABSTRACT TOPIC

Integrative Physiology

ABSTRACT

Background: Postpartum (PP) preeclamptic (PE) women have an increased risk for developing hypertension (HTN), cerebrovascular diseases, and chronic kidney diseases later in life. The timing and mechanisms that contribute to a rise in blood pressure (BP), cerebrovascular and kidney dysfunction in PP PE women is unknown and the focus of this study. Previous studies in our lab (PMID: 34727994) indicate PP PE rats at 10 weeks have HTN and decreased antioxidant capacity (AC). Our current study examines BP and oxidative stress (OS) in PP PE rats at an earlier time point, 6 weeks (PP6). Understanding changes in cerebral and renal OS may reveal the pathophysiology of HTN, cerebrovascular, and renal disease development in PP PE women. We hypothesize that BP, renal, and cerebral OS will increase in PP6 PE rats.

Methods: Pregnant Sprague Dawley rats were divided into 2 groups: control (CON) normal pregnant rats, and PE rats, derived from the surgically induced placental ischemic (reduced uterine perfusion pressure) model of PE. All rats gave birth and weaned for 3 weeks. At PP6, BP was measured via carotid catheterization. Brain and kidney tissues were collected to measure OS (HSP-1, Cu/ZnSOD, and MnSOD proteins and AC) through colorimetric assays and western blots.

Results: PP6 PE vs CON rats, BP was elevated (128 ± 6 vs 106 ± 4 mmHg, $p < 0.05$) and AC was decreased in systemic circulation (28.5 ± 5.1 vs 36.9 ± 4.5 mM Trolox/mg protein, ns). In the brain, both HSP-1 and Cu/ZnSOD were unchanged between PP6 PE and CON rats, while the levels of MnSOD (88.9 ± 2.0 vs 100 ± 2.5 IU/protein/CON %, $p < 0.05$) and AC were decreased (619.1 ± 179.2 vs 850.2 ± 50.3 mM Trolox/mg protein, ns) in PP6 PE vs CON rats. In the kidney, HSP-1 decreased (88.7 ± 3.0 vs 100 ± 4.0 IU/protein/CON %, ns) in PP6 PE vs CON, while Cu/ZnSOD levels remained unchanged. However, kidney MnSOD levels significantly increased (124.3 ± 8.0 vs 100 ± 2.7 IU/protein/CON %, $p < 0.05$) alongside an increase in AC (791.0 ± 165.4 vs 587.0 ± 64.5 mM Trolox/mg protein, ns) in PP6 PE vs CON rats.

Conclusion: PP6 PE rats have HTN and increased cerebral OS. Despite changes in the brain, kidneys appear to be protected from OS due to a decrease in a reactive OS protein (HSP-1) and increases in antioxidant capacity and protein (MnSOD). Future studies will determine the relationship between brain OS, HTN, and cerebral damage/dysfunction to PP PE rats. Furthermore, future studies will be designed to elucidate the protective mechanisms of the kidney in PP6 PE rats. Findings of this study are clinically relevant and could be used to improve the maternal health of women after PE pregnancies. In addition, therapy designed to target organ specific OS may be helpful in preventing HTN, cerebrovascular, and chronic kidney diseases later in life for women who have experienced PE.

EXTERNAL FUNDING SOURCE

This research was supported by the American Heart Association Early Career Development Awards [AHA 18CDA34110264 (Cunningham)].

IACUC NUMBER
IACUC-2021-0037

Sex and age differences in social and cognitive function in offspring exposed to late gestational hypoxia

PRESENTER

AUTHOR(S)

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ABSTRACT TOPIC

Neuroscience

ABSTRACT

Background: Gestational sleep apnea affects 8-26% of pregnancies and can increase the risk for autism spectrum disorder (ASD) in offspring. ASD is a neurodevelopmental disorder associated with social dysfunction, repetitive behaviors, anxiety, and cognitive impairment. To examine the relationship between gestational sleep apnea and ASD, we used a chronic intermittent hypoxia (CIH) protocol between gestational days (GD) 15-19 in pregnant rats to model gestational sleep apnea during the third trimester of pregnancy. We hypothesized that late gestational CIH would produce sex- and age-specific social, mood, and cognitive impairments in offspring.

Methods: Timed pregnant Long-Evans rats were exposed to CIH or room air normoxia from GD 15-19. Behavioral testing of offspring occurred during either puberty or young adulthood. To examine ASD phenotype, we quantified ASD-associated behaviors (social function, repetitive behaviors, anxiety-like behaviors, and spatial memory and learning), hippocampal activity (glutamatergic NMDA receptors, dopamine transporter, monoamine oxidase-A, neuronal activation, and neurogenesis), and circulating hormones in offspring.

Results: Late gestational CIH induced sex- and age-specific differences in social, repetitive and memory functions in offspring. These effects were mostly transient and present during puberty. In female pubertal offspring, CIH impaired social function, increased repetitive behaviors, suppressed circulating estradiol but did not impact memory. In contrast, CIH impaired spatial memory and suppressed circulating estradiol in pubertal male offspring but did not impact social or repetitive functions. Long term effects of gestational CIH were only observed in female offspring, wherein CIH induced social disengagement and suppression of circulating estradiol during puberty was maintained in young adulthood. No effects of gestational CIH were observed on anxiety-like behaviors, hippocampal activity, circulating testosterone, or circulating corticosterone, regardless of sex or age of offspring.

Conclusions: Our results indicate that hypoxia-associated pregnancy complications during the third trimester can increase the risk for ASD, such as pubertal social dysfunction, neuroendocrine suppression, and memory impairments. Current clinical recommendations support ASD screening for all children up to their 24-month checkup. Based on our findings, children from hypoxia-associated pregnancies should be screened for ASD throughout puberty.

EXTERNAL FUNDING SOURCE

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IACUC NUMBER

2018-0043

Intravitreal Endothelin-1 (ET-1) Injection Reduces Mitophagy in Retinal Ganglion Cells in MitoQC Mice

PRESENTER

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ABSTRACT TOPIC

Eye / Vision

ABSTRACT

Purpose: The peptide endothelin-1 (ET-1), and its receptors are upregulated in the aqueous humor and retina in animal models of experimentally induced ocular hypertension, and have been shown to have a causative role in retinal ganglion cell (RGC) neurodegeneration. The purpose of this experiment was to assess the role of mitophagy in RGC neurodegeneration following intravitreal ET-1 administration in MitoQC mice.

Methods: MitoQC mice (Gt(ROSA)26Sortm1(CAG-mCherry/GFP)Ganl on a C57BL/6 background) at the age of 3 months were used for the study. The mitochondria in these mice display both red and green fluorescence due to expression of a mCherry-GFP tag fused to the mitochondrial targeting sequence of an outer mitochondrial membrane protein, FIS1. When these mitochondria are trafficked to the lysosome for degradation, the green fluorescence is quenched, leaving only the red fluorescence. The MitoQC mice were intravitreally injected in both eyes with either ET-1 (1 nmole) or vehicle (water), and 72 hours following the injections the mice eyes were enucleated and retinal flat mounts were live-imaged using a Zeiss LSM 880 super resolution confocal microscope. Z-stack imaging was used to image the ganglion cell layer. For each Z layer, a threshold algorithm was used to define a region of interest (ROI) that included only areas with red fluorescence, after which red and green fluorescence were quantified for that ROI. Red/green fluorescence intensity was calculated and averaged per image. A red/green ratio larger than 1 is indicative of active mitophagy. This ratio was compared between ET-1 and vehicle-injected mice using a Mann-Whitney test (n=4 eyes per group).

Results: At 72 hours after injection with ET-1, the average red/green fluorescence ratio in the RGCs was 0.86, while the vehicle-injected mice had an average red/green ratio of 1.29. These ratios were significantly different ($P=0.0003$), and the smaller red/green ratio in the ET-1 group indicates lesser mitophagy than the vehicle group.

Conclusion: Mitophagy is known to be an important quality control mechanism for neuronal cell survival, and this study provides evidence that mitophagy is impaired by ET-1. The finding indicates that a decline in mitophagy may be associated with endothelin-mediated neurodegeneration in RGCs.

EXTERNAL FUNDING SOURCE

This study is funded by the National Institutes of Health R01 EY028179 and T32 AG020494

IACUC NUMBER

2020-0029

A new rodent model of preeclampsia: Pregnant daughters from hypertensive placental ischemic moms have hypertension

PRESENTER

AUTHOR(S)

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ABSTRACT TOPIC

Pediatrics & Women's Health

ABSTRACT

Purpose: Studies show that daughters from hypertensive pregnancies are twice as likely to have preeclampsia (PE), pregnancy-induced hypertension (HTN) in comparison to women born from a normal pregnancy. PE affects ~5-10% of all births in the USA and is the leading cause of intrauterine growth restriction (IUGR). PE is associated with oxidative stress (OS) and cerebral damage. The causes of PE are unknown but is influenced by genetic and environmental conditions. Studies show that pregnancies involving placental insufficiency and HTN create an adverse environment that can affect the IUGR baby's developmental programming and pregnancy outcomes.

This study aims to characterize the pregnancy of IUGR rat offspring from hypertensive placental ischemic moms. We hypothesize female rats born from pregnant hypertensive placental ischemic moms will have elevated blood pressure (BP) and OS.

Methods: Pregnant Sprague Dawley moms are divided into 2 groups: normal pregnant (NP) and the reduced uterine perfusion pressure (RUPP) hypertensive placental ischemic rats. On day 14 of pregnancy, the RUPP surgery is performed to generate PE. All dams (NP and RUPP) give birth naturally and weaned for 3 weeks. Offspring were then separated by sex and mother's pregnancy status. ~10 weeks later, offspring were mated according to 4 groups: ♀NP x ♂NP (CON Preg, n=3), ♀NP x ♂RUPP (n=2), ♀RUPP x ♂NP (IUGR Preg, n=5), ♀RUPP x ♂RUPP (n=4). On day 19 of offspring pregnancy, BP was measured via carotid catheterization and the blood and brains were collected for analyses.

Results: IUGR Preg rats have elevated BP (116 ± 4.17 vs 100.6 ± 2.54 mmHg, $p < 0.02$) and 8-isoprostanes (439.2 ± 13.61 vs 381.3 ± 26.10 g, ns), decreased circulating antioxidant capacity (AC) (0.33 ± 0.01 vs 0.37 ± 0.01 mM Trolox/mg protein, $p < 0.01$), and reduced body weight (330.1 ± 5.24 vs 350.3 ± 10.82 g, ns) compared to CON Preg rats. IUGR Preg rats have larger brains, suggesting brain swelling (5.38 ± 0.10 vs 4.95 ± 0.19 g/1000g BW, $p < 0.04$). HSP-1 (186.1 ± 28.14 vs 100.0 ± 6.36 %HSP-1/protein/CON, $p < 0.04$) and H₂O₂ (25.76 ± 2.95 vs 15.81 ± 4.56 μM/mg protein, ns), markers of ROS, are increased in the brains of IUGR Preg vs. CON Preg rats. Cerebral AC was slightly reduced (260.0 ± 33.14 vs 292.3 ± 13.91 uM Trolox/mg protein) and MnSOD (antioxidant) amounts were decreased (87.96 ± 3.43 vs 100.0 ± 2.84 %MnSOD/protein/CON, $p < 0.63$).

Conclusion: IUGR Preg rats have increased systemic and cerebral OS, as well as larger brain sizes which may lead to cerebral damage. In summary, pregnant daughters from hypertensive placental ischemic moms show symptoms of a preeclamptic-like phenotype, thus creating a new model of PE. Future studies will determine the role of maternal PE status and OS in the development of HTN in pregnant IUGR offspring.

IACUC NUMBER

2021-0037

Induced Blood Flow Oscillations at 0.1 Hz Protects Oxygenation of Severely Ischemic Tissue

PRESENTER

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ABSTRACT TOPIC

Integrative Physiology

ABSTRACT

Purpose: Early interventions that improve vital organ perfusion will reduce the number of lives lost from blood loss injuries. We have shown that generating 10 second (~0.1 Hz) fluctuations or “oscillations” in arterial pressure and blood flow during simulated hemorrhage protects cerebral tissue oxygenation. Lower body negative pressure (LBNP) was used to both simulate hemorrhage, and induce the hemodynamic oscillations in these previous studies. However, the magnitude of cerebral tissue ischemia is limited to 20-30% with LBNP due to the onset of pre-syncopal symptoms. To examine the effect of 0.1 Hz hemodynamic oscillations on blood flow delivery and tissue oxygenation of severely ischemic tissues, we developed a limb ischemia model. Hypothesis: Oscillatory arterial pressure and blood flow will attenuate reductions in brachial artery blood flow and forearm tissue oxygenation in a severely ischemic limb.

Methods: Nine healthy human subjects (5M, 4F; 27.2 ± 4.1 y) completed two experimental protocols separated by ≥ 48 h. In both conditions, ischemia of the forearm was induced with a pneumatic cuff on the upper arm to decrease brachial artery (BA) blood velocity by ~70-80% from baseline. In the oscillation condition (OSC), 0.1 Hz oscillations in mean arterial pressure (MAP) and BA blood flow were then induced by inflating and deflating bilateral thigh cuffs every 10 seconds (0.1 Hz) throughout the forearm ischemia period. In the control condition (CON), the thigh cuffs were in place, but were inactive throughout the forearm ischemia period. BA blood flow was measured via duplex ultrasound, forearm muscle tissue oxygenation (SmO₂) was measured via near infrared spectroscopy, and arterial pressure was measured via finger photoplethysmography.

Results: The magnitude of forearm ischemia, indexed by the reduction in BA blood velocity, was matched between protocols (CON: -75.2 ± 8.4 % vs. OSC: -78.3 ± 7.8 %, $p=0.20$). Power spectral density of 0.1 Hz oscillations in MAP (CON: 19.4 ± 22.8 mmHg² vs. OSC: 716.8 ± 514.6 mmHg²; $p<0.001$) and BA blood velocity (CON: 0.7 ± 1.0 cm/s² vs. OSC: 10.6 ± 7.1 cm/s², $p=0.02$) were greater with oscillatory thigh cuff compression compared with the control condition. While oscillatory thigh cuff compression during forearm ischemia had no effect on absolute MAP (CON: 94.3 ± 6.6 mmHg vs. OSC: 94.4 ± 10.8 mmHg, $p=0.99$), BA blood flow (CON: 9.7 ± 5.8 ml/min vs. OSC: 9.5 ± 7.3 ml/min, $p=0.82$), or BA conductance (CON: 0.10 ± 0.06 ml/min/mmHg vs. OSC: 0.09 ± 0.06 ml/min/mmHg, $p=0.39$), the reduction in SmO₂ was attenuated (CON: -38.7 ± 8.3 % vs. OSC: -28.4 ± 9.7 %; $p=0.04$). These data provide further evidence for the use of 0.1 Hz hemodynamic oscillations as a therapeutic intervention for conditions associated with severe vital organ ischemia such as hemorrhage, stroke, myocardial infarction, and sepsis.

EXTERNAL FUNDING SOURCE

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IRB NUMBER

2021-067

MIEN1 promoter ablation provides novel evidence for colorectal cancer genome editing-based therapeutics.

PRESENTER

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School of Biomedical Sciences

ABSTRACT TOPIC

Cancer

ABSTRACT

Purpose: Colorectal cancer (CRC) is one of the leading causes of cancer associated mortalities worldwide. It starts with hyperproliferation of epithelial cells forming a polyp & leads to stages 3 & 4 which are associated with acquisition of metastasis. Chemotherapy majorly focuses on attenuating symptoms with no promising cure. Hence, studying the underlying mechanism of CRC progression & identifying novel therapeutic targets is critical for early diagnosis & treatment.

The process of metastasis involves a complex interplay of signaling pathways, where various proteins play crucial roles. One such important protein that aids the process of migration is Migration & Invasion ENhancer 1 (MIEN1). In CRC, MIEN1 expression is predominantly upregulated in cancerous tissue in comparison to normal colorectal tissue, which is closely associated with invasive behavior. But the exact mechanism involved in the process of metastasis is yet unexplored.

Methods: It is established that MIEN1 overexpression is a result of 17q12 chromosomal amplification, & such dysregulated expression is linked to the trans-regulation of its minimal promoter region. Therefore, we aim to investigate the effect of MIEN1 promoter ablation on CRC migration properties. CRISPR-Cas9 gene editing technology was used for deleting MIEN1 promoter region in the CRC cell line HT29. RNA seq & bioinformatics tools were employed to assess the transcriptomic consequences of genome-editing. Several DEGs discerned by RNA seq analysis were involved in different biological processes & molecular pathways such as cell adhesion, migration, invasion, & angiogenesis. Out of these the genes vital to CRC biogenesis were evaluated at both RNA & protein levels.

Results: We analyzed the effect of MIEN1 knock-out on CRC metastatic potential using functional assays such as wound healing, Matrigel invasion, hanging drop cell – cell adhesion, & found that migration potential of HT29 cells was significantly reduced in absence of MIEN1 protein. We also successfully demonstrated that MIEN1 deletion disrupts the cytoskeletal rearrangement by affecting F-actin reorganization using phalloidin staining. Confocal staining of different proteins participating in actin cytoskeleton rearrangement such as paxillin, FAK, MIEN1 gave us an insight about the role of MIEN1 in mediating phosphorylation of FAK at different phosphorylation sites such as Tyr 397 & 925. Immunoblotting analysis of an array of proteins further confirmed the role of MIEN1 in actin cytoskeleton dynamics.

Conclusion: MIEN1 is an important metastatic protein that is specifically overexpressed in cancerous cells. Taken together, our results prove that MIEN1 is involved in different signaling pathways responsible for CRC migration & its deletion leads to perturbation of several biological processes especially the actin cytoskeleton rearrangement, involved in metastasis. Hence, targeting MIEN1 would be a potentially effective therapeutic strategy for CRC patients.

Chronic Intermittent Hypoxia Increases Oxidative Stress and Impairs Spatial Memory in Male and Female Rats

PRESENTER

AUTHOR(S)

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ABSTRACT TOPIC

Pharmaceutical Sciences

ABSTRACT

Obstructive sleep apnea (OSA) is characterized by complex phenotypes and increased long-term risk of neurodegenerative disease. The impact of OSA in women is unknown due to sex differences in clinical presentation contributing to underdiagnosis. Using chronic intermittent hypoxia (CIH) to model OSA in rodents, our previous studies have shown CIH exposure increases oxidative stress and inflammation in male rats. However, the impact of CIH in female rats remains unclear. The objective of this study was to assess sex differences in CIH-mediated oxidative stress and rodent behaviors associated with neurodegenerative disease. Young adult male and female Long Evans and Sprague Dawley rats were exposed to CIH or normoxia for 14-15 days. Spatial memory and fine and gross motor skills were assessed. Plasma oxidative stress was measured and neuronal expression in the dorsal hippocampus was quantified. Female rats exhibited better spatial memory than males with increased neuronal expression in the CA1 region of the hippocampus. In both males and females, CIH impaired spatial memory and increased circulating oxidative stress. Yet, CIH increased CA1 neuronal expression in female rats only. CIH did not impact gross or fine motor skills, regardless of sex. Our preliminary findings indicate CIH increases oxidative stress and impairs spatial memory in males and females, but the impact of CIH on hippocampal neurons and region-specific contributions to spatial memory may be sexually dimorphic.

EXTERNAL FUNDING SOURCE

AHA 22PRE-900431, NIH R01 NS0091359, T32 AG020494, AHA 22POST-903250

IACUC NUMBER

IACUC-2018-0043

Design of mini Cas9 proteins using computational tools

PRESENTER

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School of Biomedical Sciences

ABSTRACT TOPIC

Other

ABSTRACT

Purpose: Adeno-associated viral (AAV) vectors are routinely used for the delivery of CRISPR-Cas systems. These vectors can only package molecules up to ~4.7 kilobase pair (kbp) in size. The most widely used Cas protein is *Streptococcus pyogenes* Cas9 (SpCas9), which is comprised of 1368 amino acid (aa) residues and is 4.3 kbp in size. Therefore, delivery of the CRISPR-Cas9 and the guide RNA (gRNA) requires the use of two separate vectors, which decreases the overall effectiveness of the system. In this study we used computational tools to facilitate the design of mini *Neisseria Meningitidis* Cas9 (Nme1Cas9) nucleases, of 900 aa in length or less, that can be packed with its associated guide gRNA in a single vector. Nme1Cas9 is a promising system, given that in its wild-type conformation, it already is 286 aa residues smaller than the widely used SpCas9[LJ1]; and it has shown promising effectiveness in mammalian cells. Additionally, Nme1Cas9 also has a longer spacer derived guide sequence than other orthologs, and a longer protospacer adjacent motif (PAM[LJ2]) consensus, which reduces the propensity to off-target effects. For these reasons, Nme1Cas9 provides an ideal starting point for the development of engineered mini Cas9 protein, allowing us to exploit its natural features and optimize them with the use of computational tools including artificial intelligence (AI) and machine learning.

Methods: We used The Protein Data Bank (PDB) database, UniProt database, and ChEMBL database to obtain the sequences and crystal structures of Cas orthologs and their associated gRNA and DNA sequences. Next, we identified the known DNA and RNA interacting residues of Nme1Cas9 from the available literature. Sequence alignments were performed with CLUSTAL OMEGA. Structural visualizations and reductions were performed with ChimeraX and Yasara software. AlphaFold2 was used for 3D structure prediction and molecular dynamics (MD) simulations were used to determine the stability of designed proteins.

Results/Conclusions: We generated a library of mini Nme1Cas9 sequences that are less than 900 aa in length. The AI based modeling studies using the AlphaFold2 have shown similar folding of these mini Cas proteins compared to their original counterparts. MD simulations confirm their stability in the presence of DNA and gRNA. Further validation of the designed proteins and their experimental testing is under investigation at this point of the study.

Keywords: CRISPR-Cas9, Cas9, mini Cas9, Cas9 orthologs, AI.

EXTERNAL FUNDING SOURCE

Initiative to Maximize Student Diversity (IMSD)

Role of methylation in risk for cognitive impairment in Mexican Americans

PRESENTER

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AUTHOR(S)

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COLLEGE/SCHOOL

School of Biomedical Sciences

ABSTRACT TOPIC

Aging / Alzheimer

ABSTRACT

Purpose: Mexican Americans (MAs) are the largest aging (>65 years old) and growing US ethnic minority group, with a unique risk for cognitive impairment (CI) in comparison to non-Hispanic whites (NHWs). MAs have an earlier age of onset and a risk for CI that is largely metabolism related in contrast to NHWs who have a more inflammation-based risk for CI. CI is defined in this study as individuals diagnosed with either Alzheimer's disease (AD), or mild cognitive impairment (MCI) (a likely precursor to AD). Risk for CI is multifactorial and involves an epigenetic form of gene regulation called DNA methylation, which involves the addition of a methyl group to the cytosine base of DNA. DNA methylation patterns can be altered or possibly reversed through changes in environmental factors such as diet and lifestyle. Our aim was to identify differentially methylated sites of the genome associated with CI and determine DNA methylation profiles that are specific to MAs and NHWs.

Methods: Peripheral blood was drawn from 551 Texas Alzheimer's Research and Care Consortium participants (299 MAs and 252 NHWs) and DNA was typed on the Illumina Infinium MethylationEPIC chip array, assessing >850,000 CpG genomic sites. Participants were compared according to cognitive status (control versus CI(AD/MCI)) among each ethnic group. Beta values that represent relative degree of methylation were normalized using the Beta Mixture Quantile dilation (BMIQ) method. Differential methylation between control and CI was assessed using the Chip Analysis Methylation Pipeline (ChAMP), limma and cate packages within R studio.

Results: Two significant differentially methylated sites were associated with CI at an FDR-adjusted p-value threshold <0.05: cg13135255 in MAs and cg27002303 in NHWs. Three differentially methylated sites were suggestively associated with CI at an FDR-adjusted p-value threshold <0.1: cg01887506 and cg10607142 in MAs, and cg13529380 in NHWs. Four of the five significant and suggestively differentially methylated sites were hypermethylated in CI compared to normal controls, except for hypomethylated site cg13529380. The site most significantly associated with CI was cg13135255 within the CREBBP gene in MAs (FDR-adjusted p-value = 0.029). The CREBBP protein is a histone acetyltransferase, involved in epigenetic regulation, and plays a role in memory formation.

Conclusion: This is the first study to report these specific CpG sites as either significantly or suggestively associated with CI among MAs and NHWs. These sites may be used in addition to other methylated sites to develop risk assessments that are ethnicity specific for CI. Following further validation and replication in other cohorts these sites may aid development of ethnic specific therapeutics that could deter or delay CI in the future.

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Acute sex difference in response to repeated mild traumatic brain injury in mice

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ABSTRACT TOPIC

Neuroscience

ABSTRACT

Background: Repetitive mild traumatic brain injury (rmTBI), such as that occurring in contact sports, is associated with the development of neurodegenerative diseases of aging. Severe TBI and repetitive concussions are associated with chronic traumatic encephalopathy (CTE), Alzheimer's disease (AD), and Parkinson's disease (PD), among others. However, less severe injuries may also lead to delayed neurological disfunction if repeated often and without sufficient rest time between injuries. Previously, we found that the progression of behavioral deficits in males and female mice differed from 5 to 15 weeks after 25 rmTBI. Both sexes showed motor deficits at 5 weeks, but only males showed affective and cognitive deficits at 15 weeks.

Purpose: This study tested the hypothesis that rmTBI neurological deficits in male mice will appear earlier after rmTBI than in female mice.

Methods: C57BL/6 male and female mice (8 wk old) were assigned to sham and rmTBI groups (n=20/group). Lightly anesthetized mice received 7 mild head injuries, once a day (M-F) using a weight drop model (75 g from 1 meter) that included a free fall with rotational injury. Five minutes after the final injury, mice were tested on a balance beam. Additional behavioral assessments began the following day.

Results: No sex differences in balance beam performance were observed 5 minutes after the final injury. There were no significant effects of rmTBI on vestibular motor function assessed with a rotarod; cognition assessed with the Morris water maze; or affective behavior assessed with the elevated plus maze. However, in the open field test there was a significant increase in total distance traveled in rmTBI mice ($F_{1,35} = 6.47$, $P=0.016$). Post-hoc analysis revealed that this effect was only significant in male mice (Fisher LSD, $P<0.05$), supporting the hypothesis that males exhibit earlier deficits than females.

Conclusion: At extended time points following rmTBI, both male and female mice develop motor deficits. However, up to 15 weeks after injury, only male mice experience cognitive and affective deficits. The current study reveals that male mice also display hyperactivity in the week after rmTBI that is not observed in female mice. Thus, sex differences in response to rmTBI are apparent both in the acute and chronic phase of injury and suggest that interventions to reduce brain injury may require different timing for males and females. Ongoing studies are examining potential differences in biochemical and histological responses in the brains of male and female mice.

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Computational Design of Compact CRISPR-Cas Enzymes of *Lachnospiraceae* bacterium Cas12a Utilizing Bioinformatic Tools

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ABSTRACT TOPIC

Molecular Genetics

ABSTRACT

Purpose: Nature has provided us with a popular genome editing tool known as the CRISPR (clustered regularly interspaced short palindromic repeats)-Cas system, which has shown promise in both plants and animals. The CRISPR-Cas system utilizes a guide RNA (gRNA) and specific proteins known as Cas proteins to facilitate its function. A major limitation of the CRISPR/Cas system and any gene therapy is how it's delivered within the organism. The most common "vehicle" for delivering gene therapies is adeno-associated viral vectors (AAVs), which have a maximum effective capacity of approximately 4.7 kb. The main issue with most Cas enzymes and other CRISPR components needed is that they are much bigger than this required maximum capacity. The most widely characterized CRISPR-Cas system is Cas9. However, the unique feature of Cas12a's ability to process its own crRNA arrays without the requirement for tracrRNA makes it a promising candidate as well. In other CRISPR-Cas systems, the RNA CRISPR components need to be synthesized and packaged into an AAV, whereas in the Cas12a family, some of these components are not needed. *Lachnospiraceae* bacterium Cas12a (LbCas12a) has increased activity when compared to other species of Cas12a enzymes. To address the aforementioned size issue, we have used various bioinformatic tools to computationally design compact-size proteins of LbCas12a with similar functionality and comparable efficiency.

Methods: The best available crystal structure of LbCas12a was chosen from the Protein Data Bank (PDB). A structure reduction process was carried out using Yasara and UCSF ChimeraX. The intermediate steps of this process were verified using the homology-based modeling tool SWISS-MODEL and AI-based modeling tool AlphaFold2 to ensure that the protein was still folding similarly to the original structure. Furthermore, the global and local structural features were analyzed, and the best candidate was subjected to molecular dynamics (MD) simulations along with gRNA and substrate DNA to determine its functional efficiency under realistic dynamic conditions and compared it with the original structure.

Results/Conclusions: A compact-size variant of LbCas12a was generated, which is 292 residues smaller than the original crystal structure. This man-made miniature protein contains all the regions that are needed for DNA cleavage activity. MD simulations confirm its stability in the presence of DNA and gRNA. Further validation of the designed protein and experimental testing is under investigation at this point of the study.