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Hypothesis: Compression of the fourth ventricle decreases sleep latency independent of therapeutic touch. **Methods:** Subjects participated in CV-4 treatment, sham treatment, and control. Order was randomized. Electrocardiogram and electroencephalogram tracings, heart rate, and blood pressure were recorded. After the treatments, data were collected for 30 minutes. Data were collected during the control for 30 minutes. After the first two treatments, subjects had a one hour recovery period. **Results:** The ANOVA showed a difference between groups ($F = 28.462$, power = .998, $p < .001$). Pairwise comparison showed sleep latency was shorter for CV-4 than sham or control. There was no difference between sham and control. For total percent sleep, an ANOVA showed a difference between groups ($F = 20.5$, power = .982, $p = .001$). Pairwise comparison revealed differences between control and CV-4, control and sham, but not CV-4 and sham. **Conclusions:** CV-4 shortens sleep latency independent of light touch.

EFFECTS OF COMPRESSION OF THE FOURTH VENTRICLE ON SLEEP LATENCY

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CHAPTER I

INTRODUCTION

Osteopathic medicine, since its inception during the 19th century, has claimed an interrelationship between structure and function. In other words, a change in structure creates a physiologic change in the function of a system, multiple systems, or the whole patient. The onset of sleep is one physiologic change proposed through the manipulation of the cranial structure. Osteopathic physicians have postulated that a technique called the compression of the fourth ventricle (CV-4) can affect the structures adjacent to the floor of the fourth ventricle and thereby alter systemic function via these brainstem structures. Included in the proposed effects is the hypothesis that the CV-4 may cause a relaxed state or even induce sleep. However, no data have been collected to support this claim. These claims are anecdotal, and based on a few case reports.

CHAPTER II

BACKGROUND

History of Osteopathic Medicine

Osteopathic Manipulative Medicine (OMM) is the cornerstone of the unique nature of osteopathic medicine. While other differences in philosophy and treatment also separate osteopathy from allopathic and naturopathic medicine, manipulation is the tool used by osteopathic physicians that makes osteopathy distinct. The foundation for OMM came as a result of observation and reasoning by osteopathy's founder, Andrew Taylor Still, M.D.[1] Through years of practicing frontier medicine in the 19th century, he concluded medicine practiced at that time was ineffective and even dangerous. So, through his study of anatomy, physics, chemistry, biology, philosophy, as well as the experience of several life events, he concluded there is a strong link between structure and function. Through manipulation of the structure, he deduced one could improve a patient's function. He concluded man was created with all of the remedies for diseases within him. Rather than focusing on the organism (bacteria, virus, etc.), Still and early osteopaths focused on the host. In other words, instead of treating a diseased patient with drugs or treatments to destroy the organism, osteopaths focused on finding and treating the weakness of the host.[1] Therefore, he set out to find and treat the cause, not the effect. The cause is a structural defect at some level (microscopically or macroscopically), making the host susceptible to an invading organism.

Prior to the introduction of many modern medications including antibiotics, osteopathic physicians succeeded in treating patients with a wide variety of ailments.[1] One of the more famous studies showing the success of osteopathic treatment during the early 20th century was done during the flu epidemic of 1918.[1] This study showed that patients treated by osteopaths had fewer cases of secondary pneumonia. Mortality rates were lower for patients treated osteopathically than those treated allopathically. Manipulative medicine was the only tool used to treat these patients. In addition to the use of manipulation, osteopathic physicians occasionally used other treatments including the use of medications available at that time, use of herbal and homeopathic remedies, application of salves, and performing surgery. Early students of osteopathy focused their attention on manipulation to treat the underlying disruption in structure that caused or allowed the patient to become diseased.[1] In the early osteopathic schools, the curriculum emphasized anatomy and the other basic sciences. The major difference in allopathic and osteopathic curricula was the absence of pharmacology in osteopathic education. It was not until the late 1920's that pharmacology entered the curriculum. Along with the understanding of anatomy, students learned mechanisms of disease with an emphasis on the philosophy that a disruption of structure caused the disruption of function. Unfortunately, the profession's ability to systematically defend this philosophy was not achieved, and after over 125 years of the practice of osteopathic medicine, much of what is being taught as fact in osteopathic schools has yet to be defended with sound scientific evidence.[1]

Osteopathy in the Cranial Field

While many osteopathic and allopathic physicians and basic scientists within the medical community find the use of all manipulative medicine techniques controversial due to lack of evidence, one set of techniques referred to as osteopathy in the cranial field, or cranial manipulation, is much more controversial than all other techniques. Osteopathy in the cranial field was first studied and explained by Warner Garner Sutherland, D.O. He concluded that the remaining sutures of the cranium must maintain a function since they do not fuse like other sutures.[1] Like joints of the body that remain separated, the separation of the cranial bones must allow the bones of the cranium to move. In addition, disruption of the motion of the cranium could theoretically disrupt the function of the rest of the body. Osteopathy in the cranial field includes a plethora of treatments used for a host of diagnoses. Entire books have been written describing possible findings and how to best treat. Nevertheless, a basic understanding of anatomy and the proposed mechanisms of cranial motion, such as the primary respiratory mechanism and cranial rhythmic impulse, allows the reader to comprehend the possible connection between cranial manipulation and sleep.

The Primary Respiratory Mechanism:

Sutherland assumed that the cranium moved since the sutures of the cranium remain throughout life. This assumption forced him to study more fully the structure of the cranium and related structures. Through further study of the cranium, he described a tidal motion of the cranium that he referred to as the cranial rhythmic impulse (CRI).

The movement of the cranium was central to his understanding of the sutures. In addition to the sutures, he postulated that the movement of the cranium via the sutures was to allow for fluctuation of the cerebrospinal fluid, the brain, and other central nervous system components. All three of these, the sutures, central nervous system, and cerebrospinal fluid, functioned as a unit he termed the primary respiratory mechanism.[1] He proposed four features of this primary respiratory mechanism. The four features are: (1) fluctuation of the cerebrospinal fluid, (2) the relationship of the reciprocal tension membrane, (3) motility of the central nervous system, and finally (4) the articular mobility of the cranial bones and of the sacrum between the ilia.[2] Sutherland called this the primary respiratory mechanism because he proposed that the vital structures that allowed for life (pulmonary respiration, circulation, digestion, and elimination of waste) were all located in the floor of the fourth ventricle and depended on the function of the central nervous system. Primary refers not to order but to importance. Pulmonary respiration is obviously important, but the drive for this respiration is controlled by Sutherland's primary respiration. Respiration refers to the exchange of gasses and other metabolites at the cellular level. Mechanism refers to the motion of the cranium and its contents as well as the sacrum. Compromise of this motion through a disruption in the structure of either the cranium or the sacrum dilutes the vitality of the patient.[1]

Independent of osteopathic principles, primary respiration was also described by Crisera. Through an understanding of cellular biology, Crisera recognized the contractile and expansile properties at the intracellular level. This motion then translated into contraction and expansion of the entire living organism. He found this true in the most

simple and most complex living beings. At the heart of this rhythmic motion is the folding and unfolding of the DNA to allow for expression of the particular genes. Crisera postulated that this rhythmic motion moved both intracellularly and intercellulary via the cytoskelatal system. Through the idea of tensegrity (tensional integrity), harmonic motion can be translated to structures far from its origin. Tensegrity is a structural system that, although composed of disjointed compressive elements, also has uninterrupted tension cables that interact to relay mechanical information from one place to another. A suspension bridge represents a tensegrity structure. Scientists have described the cytoskelatal structure of the cells as a tensegrity structure.[3] Furthermore, the macrostructure of the body with its network of skeletal, muscular, ligamentous, tendinous and fascial connections is considered a tensegrity structure.[3]

Through further study, Crisera concluded that control of primary respiration is found in the central nervous system, specifically in the most rudimentary portion of the brain called the reticular formation. Communication from the central nervous system to all of the cells of the body is accomplished through the peripheral nervous system along electrochemical gradients. The drive for life is maintained through this primary respiration. He concluded that growth, maintenance, anabolism, catabolism, locomotion, reproduction, and other vital bodily and mental functions all stem from this rhythmic motion.[3]

While practitioners of osteopathy in the cranial field maintain they do feel a fluctuation of the structures of the cranium, others hold strongly to the more accepted belief that there is no movement of the bones of the cranium. Nevertheless, several

investigators have shown that there is movement of the cranial bones. In one National Aeronautic and Space Administration study, it was concluded that there was significant cranial (skull) movement with altered intracranial pressure. Using cadavers (less than 48 hours postmortem) saline was introduced to the lateral ventricle via a burr hole in the cranium. The saline acted to increase intracranial pressure. This pressure was measured by a fiber-optic, transducer-tipped catheter placed in the epidural space. To measure cranial motion, an ultrasound transducer was used to measure the distance between the temporal bones. Changes in distance were calculated from frequency changes in the ultrasound.[4] In another NASA study, the same measurement device was used to determine intracranial pressure and cranial mobility after head down tilt test with monkeys. The investigators stated that the cranium is slightly compliant, and that increased intracranial pressure causes measurable cranial movement across the sagittal suture.[5] Furthermore, in another study using computed tomography (CT), investigators concluded there are peristaltic movements of the cerebrospinal fluid throughout the ventricular system. In addition, they noted there are changes in brain parenchyma that have a measurable, consistent rate.[6] However, it is unknown what physiological significance these dynamics of the cranium or cerebrospinal fluid may have.

Cranial Rhythmic Impulse:

The rate of movement of the cranium and related structures is called the cranial rhythmic impulse. There appear to be two observed rhythms. One rhythm has a rate of between 6 and 14 cycles per minute (cpm), while another observed rate has 0.6 – 2.5

cpm.[7] Both of these rhythms have been recorded and studied by a number of physicians practicing osteopathy in the cranial field. Investigators used palpation, kinematic film, doppler studies, and tomography as modalities to study cranial rhythmic impulse rate.[7]

Many theories have been formed and studied as to the origin of the cranial rhythmic impulse. Production of the cerebrospinal fluid in the choroid plexus supported by both neurological and mechanical influences, relation to the cardiovascular and respiratory rhythms, lymphatic contractility, and entrainment of various harmonic frequencies from various rhythms of both patient and observer are among the theories that explain the cranial rhythmic impulse.[7]

The Traube-Hering-Mayer oscillation is one of the logical and more studied theories relating to the cranial rhythmic impulse. There are two different observed rates. These are referred to as the fast tide and slow tide.[2] To explain these two rates, it has been proposed that the two are the same as the two rates of the Traube-Hering-Mayer oscillations. Traube and Hering both recognized a fluctuation in pulse pressure with the frequency of respiration that persisted after respiration ended. The rate of this oscillation is between 6 and 10 cpm and is related to baroreflex activity. Mayer later identified a much slower oscillation ranging from 0.5 to 2.5 cpm and is associated with thermal regulation.[2, 8, 9] These oscillations result from the interactions between the sympathetic and parasympathetic components of the autonomic nervous system and the effects of the renin-angiotensin system on the cardiovascular system. The Traube-Hering-Mayer oscillation emanates from the floor of the fourth ventricle in the nucleus tractus solitarius along with the humoral effects of the renin-angiotensin system. Lateral pressor areas in

the nucleus tractus solitarius are responsible for vasoconstriction. The lateral pressor areas of the nucleus tractus solitarius are responsible for vasodilation. Both of these exhibit inherent automaticity via the autonomic nervous system.[10]

In an attempt to relate the Traube-Hering-Mayer oscillations with the cranial rhythmic impulse, laser-Doppler blood velocity flometry measured the Traube-Hering-Mayer oscillation on patients while physicians, blinded to the Traube-Hering-Mayer measurements, related their findings on the cranial rhythmic impulse to the investigator recording information. There was a correlation between the two, suggesting that the two are related or possibly the same. The Traube-Hering oscillation is related to the fast tide, and the Mayer oscillation is related to the slow. The structures on the floor of the fourth ventricle provide these frequencies.[2, 8] The relation of the cranial rhythmic impulse to the Traube-Hering-Mayer oscillation implies there is a link between the primary respiratory mechanism and the sympathetic and parasympathetic components of the autonomic nervous system.[2, 8, 9] In addition, since the same pattern of the Traube-Hering-Mayer oscillation can be measured from other parts of the body, it follows that the primary respiratory mechanism which is detectible in the cranium and the sacrum may also be sensed in many or all regions of the body.[2] The role of the Traube-Hering-Mayer oscillation has been sufficiently discussed in other publications and is beyond the scope of this paper. Further discussion of the connection of the Traube-Hering-Mayer oscillation and the primary respiratory mechanism are also beyond the scope of this paper. Nevertheless, with an indication that the cranial rhythmic impulse and the Traube-

Hering-Mayer oscillation are one-in-the-same or at least related, there is evidence that physicians can feel a cranial rhythmic impulse that may have effects systemically.

The physician practicing osteopathy in the cranial field observes the movement of the structures in the head and the sacrum. While the cranial rhythmic impulse is also felt throughout the body, traditional cranial manipulation focuses primarily on the cranium and sacrum. After defining areas of dysfunction, the physician focuses his or her attention on restoring proper structure. Often, after restoring structure, the vitality or force of the primary respiratory mechanism may still be dampened.[1, 11] In order to restore the vitality of the primary respiratory mechanism and, thus, the movement of cerebrospinal fluid, a technique called the compression of the fourth ventricle (CV-4) is often used.[11]

Compression of the fourth ventricle (CV-4) technique:

Manipulation of the fourth ventricle is indirect, and the development of this technique was conceived from an understanding of the anatomy of the cranium. Compression of the fourth ventricle is accomplished via contact of the occiput. The shape of the occipital articulations with the parietal and temporal bones allows the physician to compress the lateral borders of the supraocciput medially.[11] This compression leads to an approximation of the lateral angles of the occiput. The proposed mechanism is that tension on the tentorium cerebelli results from the compression because of its attachments, drawing the tentorium more tightly on the cerebellum. The compression of the fourth ventricle is a result of the cerebellum rolling downward on the

roof of the pons and medulla. This compression on the ventricle increases hydrostatic pressure in the fourth ventricle facilitating dissipation of the CSF through and out of the ventricular system and central spinal canal.[11]

Concepts of Sleep Physiology

Sleep is a reversible state of unresponsiveness to and disengagement from the surrounding environment.[12] There are two separate states of sleep; non-rapid eye movement (NREM) and rapid eye movement (REM). These two are distinctly different and can be measured and distinguished by the electroencephalogram (EEG) and electro-oculography (EOG). The EEG pattern in NREM sleep is synchronous and has characteristic waveforms like sleep spindles, K complexes, and high-voltage slow waves. Within NREM sleep are four discernible stages of sleep labeled stages 1-4. These stages relate to the depth of sleep with arousal thresholds lowest at stage 1 and highest at stage 4. On EEG, each stage shows a slower wave. In other words, NREM sleep in general is slow wave compared to wakefulness and REM sleep. It is stages three and four that are most synonymous with slow wave sleep.[12] The brain during NREM sleep is considered relatively inactive, although actively regulating, and the body is movable. On the other hand, REM sleep does not have stages and is characterized by episodic bursts of rapid eye movements and muscle atonia. This stage of sleep is associated with vivid dreaming. The brain during REM sleep is highly active, while the body is paralyzed.

Onset of sleep is normally through sequential stages of NREM sleep.[12] The EEG pattern at the onset of sleep is a highly reliable finding in normal subjects. The EEG

changes from a rhythmic alpha pattern of 8 to 13 cycles per second (cps) to a relatively low-voltage, mixed frequency pattern (stage 1). While the EEG pattern indicates sleep, the subject may or may not perceive sleep at this transition point. Stage 2 sleep has characteristic patterns like the K complex and sleep spindle, and it is easily recognizable. Even during stage two sleep, patients may not perceive sleep. For this study, sleep onset was measured by changes in EEG leads C4/A1 and C3/A2 as described from wakefulness to stage 1, NREM sleep. This choice was made because scientists and physicians studying sleep concur that transition to stage 1 sleep is recognized as the beginning of sleep through EEG patterns.[12]

Sleep cycles:

Normal young adults experience cycles of sleep throughout the night. These cycles are from wakefulness to NREM to REM sleep. This pattern continues through the night with the exception of wakefulness after the first cycle. Exiting REM sleep to re-enter NREM sleep occurs at stage 2 sleep, not stage 1. Stages 3 and 4 are experienced less and less throughout the night, while stage 2 sleep lengthens and nearly consumes the entire NREM portion of the cycle. NREM sleep predominates each cycle early in the night, while REM sleep dominates the cycles in the last third of sleep.[12] Looking at percentages, NREM sleep comprises about 75% to 80% of sleep, and REM sleep comprises the remaining 20% to 25%. Each NREM-REM cycle lasts from 70 to 120 minutes with the early cycles being shorter. The average cycle is 90 to 110 minutes.[12]

Brain mapping in sleep:

In order to correlate sleep and the effects of the CV-4 technique, it is necessary to include a short discussion of brain function during sleep, specifically NREM light sleep. Both EEG and PET imaging have been used to develop understanding on the particular parts of the brain that are relatively active and inactive. Positron Emission Tomographic (PET) imaging, allows one to see the regional cerebral blood flow. During light NREM sleep (stages 1 and 2), regional cerebral blood flow decreased in the pons, cerebellum, thalamus, basal ganglia, hypothalamus, putamen, anterior cingulate gyrus, and left neocortical regions, inferior frontal gyrus, and the inferior parietal gyrus when compared to wakefulness.[13, 14] Activity is maintained in the reticular formation of the midbrain during light sleep but decreases significantly during the later stages of NREM sleep. Of the structures with decreased cerebral blood flow during light sleep, the midbrain, cerebellar vermis, caudate nucleus and thalamus had an even more significant decrease during deep sleep. In addition an increase in cerebral blood flow to the occipital lobes indicates increased activity in this area.[15]

Sleep and age:

We selected young, healthy adults for this study because age is the factor that most consistently affects sleep. Slow wave sleep is at its peak in young children and progressively lessens with age. In fact, by the age of 60, slow wave sleep may be completely absent in some people, particularly men.[12] Sleep cycles continue into old age, with ratios of NREM and REM sleep remaining the same. REM sleep is decreased in

patients with organic brain dysfunction.[12] As people age, they also experience an increased frequency of arousals. These may be extended periods of wakefulness in the night or transient, unrecognized, periods of arousal. While these are generalizations about the elderly, few stereotypes can be made because sleep becomes increasingly interindividualized as people age.[12]

Relaxation

Stage 1 NREM sleep is often described as relaxed wakefulness. Although there are obvious changes in the EEG pattern, patients remain somewhat aware of their surroundings and are easily aroused as compared with NREM stages 2-4 and REM sleep.[12] Because patients report deep relaxation after cranial manipulation, specifically the CV-4, a description of relaxation is included.

Relaxation, described as loosening, or release of tension from muscles, precludes the onset of sleep.[12] With the capabilities of magnetic resonance imaging (MRI) and positron emission tomography (PET), we now know more about changes in the central nervous system associated with relaxation. The relaxation response (described below) originates in the hypothalamus and leads to a decreased arousal in the central nervous system.[16, 17] Images of the brain during and after meditation (clearing of the mind), which leads to a relaxed state, show that there is decreased electrocortical arousal.[18] In addition, PET imaging was used to investigate areas of brain activity during relaxation alone, biofeedback with relaxation, and two controls. During relaxation alone, imaging showed heightened activity in the left anterior cingulate, globus pallidus, and parietal

cortex. Biofeedback with relaxation also showed cerebellar vermal activity and further increased anterior cingulate activity. Interestingly, left anterior cingulate activity decreased once relaxation was achieved and did discriminate between relaxation and control.[19] The anterior cingulate is a region of the limbic cortex implicated in cognitive and emotional processing. This area has also been implicated in autonomic arousal.[19] It was noted in a study using PET imaging that the anterior cingulate maintained the same cerebral blood flow from sleep to wakefulness.[20] Additionally, EEG topography during sleep showed a sleep-wake-dependent homeostatic control in the centro-parietal brain region, also associated with relaxation.[21] Another PET imaging study on stage 1 sleep concluded that brain activity in stage 1 sleep is more similar to activity during altered conscious states such as a meditative or relaxation meditation state than it is to deeper levels of sleep.[15]

Relaxation techniques have been used to induce sleep. Studies on these techniques began in the 1920's and continue today.[12] Several relaxation techniques have been studied and described. With progressive relaxation, subjects contract and then relax the muscles in the body, starting with the toes and continuing all the way to the head. Electromyographic (EMG) biofeedback is used by physicians to induce physiologic relaxation. The frontalis muscles are monitored with an EMG recording, and the patient is given feedback on their level of tension. While being monitored patients are taught techniques such as deep breathing. Immediate feedback from the EMG allows the physician and patient to determine what best relaxes him or her.[12] In a study comparing

these two relaxation techniques, they both decreased sleep latency significantly, and one technique was no more effective than the other.[22]

Another relaxation technique extensively studied to determine its affects on insomnia, hypertension, anxiety, and many other disorders and diseases is the relaxation response technique created by Herbert Benson. This technique includes progressive relaxation, deep breathing, and some meditation techniques. The meditation techniques include repeating a single word or phrase in one's mind throughout the exercise and keeping the mind clear of any other thought. The author describes the technique as the physiologic antithesis of the stress response.[17] Studies of this technique show that stress-related diseases respond positively.[16, 23] It is effective in reducing hypertension, insomnia, anxiety, pain, and the use of medications.[16] In one study, patients with borderline or labile hypertension practiced the relaxation response technique for five weeks. During that time, the patients reported less anxiety and somatic symptoms. However, after five weeks of not practicing the technique, the patients were questioned again, and psychological and somatic variables returned to baseline.[23]

CHAPTER III

SPECIFIC AIM

The aim of this study is to test the following hypothesis: the use of cranial manipulation, specifically compression of the fourth ventricle (CV-4), decreases sleep latency independent of distracted light touch. This study is the first systematic investigation to test the hypothesis that the CV-4 decreases sleep latency.

CHAPTER IV

METHODS

Eleven healthy adults (7 male, 4 female) with a mean age of 25.5 years of age and ranging from 22 to 35 years of age were studied for each of the described protocols. Each subject underwent a standard medical history and physical. Before participating in the study, each subject gave informed written consent. There were no exclusions based on gender, race, color or religious affiliation. None of the female subjects were pregnant at the time of the study. Female subjects were not studied during or within two days of menses to eliminate potential confounding effects of menses on fluid metabolism, blood volume, and cardiovascular function. Each of the eleven subjects completed the study.

For this study, sleep latency was defined as the elapsed time from the end of each trial until the first of three consecutive epochs of stage 1 sleep or the first of any other stage.

Experimental Protocol

The following procedures were used to test the hypothesis that the osteopathic manipulative technique, CV-4, decreases sleep latency. Each subject took part in the CV-4 treatment, sham treatment, and a control. In order to control for an order effect in analysis, the order of trials was randomized. For consistency, all patients were tested in the afternoon (between the hours of 1:00 pm and 6:00 pm). In addition, to insure normal

sleep patterns, subjects were asked to abstain from caffeine, alcohol, and medications during the periods of study and were studied in the post-absorptive state. Participants reported to the laboratory and were instrumented for the measurement of a limb lead electrocardiogram (ECG), electroencephalogram (EEG), and beat-to-beat blood pressure measured at the finger (photoplethysmography, Finapres). Once instrumented, baseline data were gathered for five minutes. At the end of baseline, the subject received either a sham CV-4 treatment, a CV-4 treatment, or participated in a control period. After the sham or CV-4 treatment was completed, data was collected for 30 minutes, and during the control period, the subject was monitored for 30 minutes. Each subject participated in each of these trials. After the first trial was completed, the subject had a recovery period lasting one hour. At the end of the recovery period, the subject then underwent the second trial followed by a second recovery period, and finally, the last trial. Data were only collected during the trials and not during the recovery periods.

Compression of the fourth ventricle (CV-4):

In the dimly lit laboratory, the investigator sat at the head of the table, with arms resting on the table. With fingers interlocked, the investigator contacted the participant's occiput (lateral to the external occipital protuberances, but medial to the occipitomastoid suture) with his thenar eminences. Once the investigator could detect the patient's cranial motion, he applied very slight, constant pressure exaggerating the extension phase of cranial motion. When the participant's occiput attempted to enter the flexion phase of cranial motion, the investigator resisted this movement. This compressive pressure was

focused toward the fourth ventricle of the brain and was maintained until the cranial rhythm rested (still point). The still point was held until the cranial rhythm fluctuations returned, at which point the compressive pressure was slowly released. After this was accomplished, the investigator's hands were gently removed and the participant's head was placed gently on the table.

CV-4 Sham:

In the dimly lit laboratory, the investigator sat at the head of the table, with arms resting on the table. He then lightly contacted the patient's occiput with his fingertips (without cradling the participant's head), and maintained this position for the entire time of the treatment. Time of sham treatment was between 7 and 10 minutes, which is approximately equivalent to the time it takes to do a CV-4. At the end of the sham treatment, the investigator slowly removed his hands, leaving the participant's head lying on the table.

Control:

In the dimly lit laboratory, the patient laid on the treatment table. The participant was instructed to attempt to fall asleep.

Data Collection

Heart Rate was obtained from a standard limb lead ECG by placing four electrodes on the torso for recording at the left arm, left leg, right arm, and right leg.

Sleep was measured using EEG leads (C_4/A_1; C_3/A_2) to detect the time from lights out to the onset of stage 1 sleep. Total sleep including all stages was also recorded. Up to 30 minutes of data were recorded following each of the trials.

Statistical Analyses

An ANOVA with repeated measures was performed on sleep onset data. When a significant main effect was observed, a pairwise comparison was obtained to compare CV-4 treatment, non-treatment (control), and sham treatment with dependent outcome variables sleep latency. Total percent sleep (minutes slept/minutes measured after trial ended or control began) was also analyzed using an ANOVA with repeated measures. A pairwise comparison was obtained to compare CV-4 treatment, control, and sham treatment since a significant main effect was observed. Statistical significance was defined at an alpha level of 0.05.

CHAPTER V

RESULTS

Table 1 shows the pairwise comparison for sleep onset between groups. Figure 1 shows the estimated marginal means for all three groups and sleep onset. Sleep onset time following CV-4 treatment, CV-4 sham treatment, and control (no treatment), following initial ANOVA, repeated measures design, showed a difference between groups ($F = 28.462$, power = .998, $p < .001$). Pairwise comparison further showed that sleep latency was shorter for CV-4 than either sham or control, while there was no statistically significant difference between sham and control.

Table 2 shows the pairwise comparison for total percent sleep between groups and Figure 2 shows the estimated marginal means. With regards to total percent sleep, the ANOVA also showed a difference between groups ($F = 20.5$, power = .982, $p = .001$). Pairwise comparison revealed a difference between control and CV-4. In addition, there was difference between control and sham. No difference was found between CV-4 and sham.

Table 1:
Pairwise Comparison of Sleep Onset between Groups

(I) Group	(J) Group	Mean Difference (I-J)	SE	Sig[a]	95% Confidence Interval for Difference[a] Lower Bound	Upper Bound
Control	CV-4	11.27	3.36	.007	3.79	18.75
	Sham	4.59	2.76	.128	-1.57	10.75
CV-4	Control	-11.27	3.36	.007	-18.75	-3.79
	Sham	-6.68	2.72	.034	-12.75	-.61
Sham	Control	-4.59	2.76	.128	-10.75	1.57
	CV-4	6.68	2.72	.034	.61	12.75

[a]Adjustment for multiple comparisons: Least Significant Difference

Table 1 Key:
(I) Group is compared with each of the two groups in (J) Group for Sleep Onset. Difference is shown between CV-4 and Control, and CV-4 and Sham, but no difference is shown between Sham and Control.

Figure 1:
Estimated Marginal Means for Groups and Sleep Latency

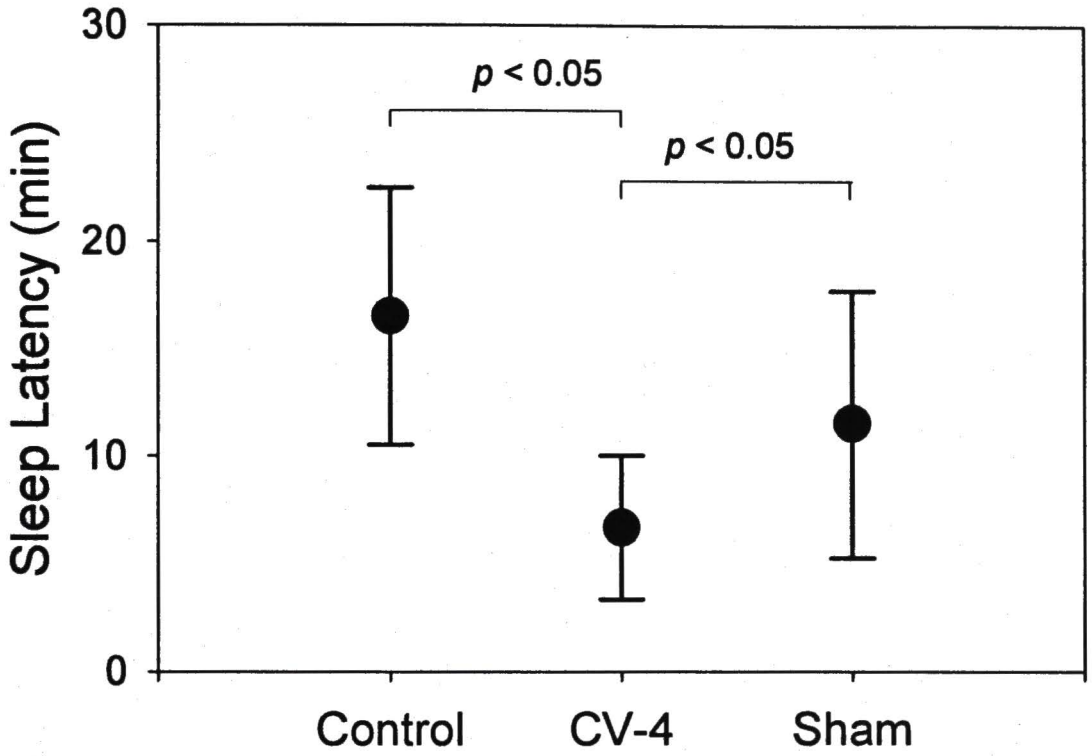

Figure 1 Legend:
The 95% confidence intervals for sleep onset measured in minutes are shown for each of the trials; control, CV-4 treatment, and sham.

Table 2:
Pairwise Comparison of Total Percent Sleep between Groups

(I) Group	(J) Group	Mean Difference (I-J)	SE	Sig[a]	95% Confidence Interval for Difference[a] Lower Bound	Upper Bound
Control	CV-4	-21.95	7.78	.018	-39.27	-4.62
	Sham	-27.41	10.57	.027	-50.96	-3.86
CV-4	Control	21.95	7.78	.018	4.62	39.27
	Sham	-5.46	8.03	.512	-23.36	12.43
Sham	Control	27.409	2.76	.027	3.86	50.96
	CV-4	5.46	2.72	.512	-12.43	23.36

[a]Adjustment for multiple comparisons: Least Significant Difference

Table 2 Key:
(I) Group is compared with each of the two groups in (J) Group for Total Percent Sleep. Difference is shown between CV-4 and Control, and Sham and Control, but no difference is shown between CV-4 and Sham.

Figure 2:
Estimated Marginal Means for Groups and Total Percent Sleep

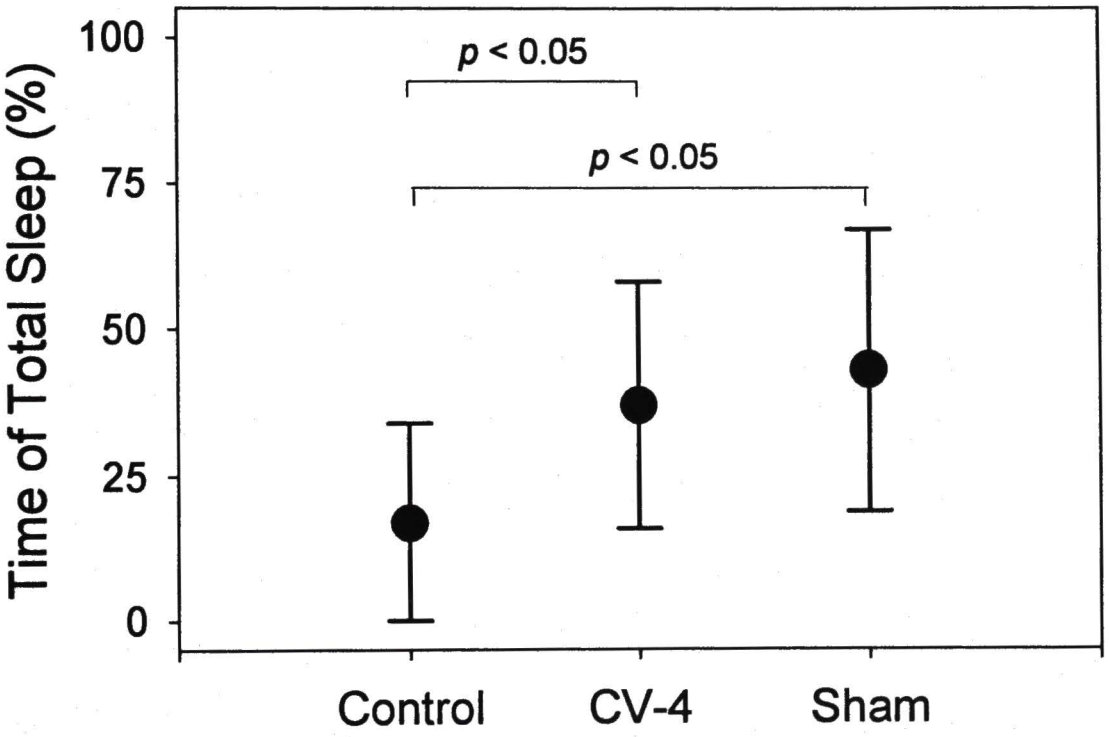

Figure 2 Legend:
The 95% confidence intervals for total percent sleep are shown for each of the trials; control, CV-4 treatemt, and sham. A lower percentage indicates the group of subjects slept less of the total time recorded following each trial.

CHAPTER VI

DISCUSSION

The primary goal of this study was to determine if cranial manipulation using the CV-4 technique shortened sleep latency when compared to a sham treatment or control. The data suggest there is an effect on sleep onset due to the cranial manipulation independent of distracted light touch (sham treatment). Total percent sleep, however, did not show a difference between CV-4 and sham. These differences and the potential significance are discussed below.

Uses and claimed effects of the CV-4

Physicians have used the compression of the fourth ventricle technique for a variety of problems and have recorded some of the responses patients commonly have. Magoun states that after several minutes of light medial compression of the lateral angles of the occiput, there is a softening of the suboccipital area and increased warmth in the area. Additional patient responses might include a moistened forehead, more even and deeper diaphragmatic contractions resulting in a slowed respiratory rate, and occasional deep relaxed sighs.[11] Physicians practicing osteopathy in the cranial field report a spontaneous deep sighing respiration and other respiratory changes with the use of cranial manipulation.[2] These responses mimic expressions made by deeply relaxed individuals just prior to sleep. Physicians often report that patients are left in a deeply relaxed state

or asleep following the CV-4.[11] Historical uses of this technique include augmentation of anesthesia, normalizing ligamentous and membranous tone, relief of acute respiratory distress secondary to asthma, decrease in localized edema from trauma, arthritis, and fracture, decrease in extremity paresthesias, relief of headaches, relief of sinus and nasal congestion due to infection, reduction of blood pressure, balancing of the autonomic nervous and neuroendocrine systems, and normalization of the psyche.[11] Cooper and Kilmore suggested that the CV-4 may affect peripheral circulation.[24] However, they did not indicate what effect there was, and with only eight subjects, no definitive data were obtained to support this claim. In a similar study, CV-4 and touch alone were used on patients to determine if there was an autonomically induced cardiopulmonary response. The preliminary findings of this pilot study suggested that there is a parasympathetic responsiveness to the CV-4 compared to touch.[25] Postdate gravida women were given a cranial treatment using the CV-4 technique to determine if this technique could induce labor. The results of this pilot study suggest that the CV-4 technique may initiate uterine contractions in this population.[26] Finally, the claim that headache relief is obtainable with the CV-4 was studied. In particular, patients with tension-type headaches were randomly given a CV-4, positional relaxation, or no treatment (rest). Analysis of patient responses showed that patients receiving the CV-4 had less pain than the other two groups following the treatment.[27]

Anatomy of the fourth ventricle and related structures

In order to more fully understand the logic of the CV-4, a more thorough comprehension of the fourth ventricle and related structures is necessary. The fourth ventricle is a complex structure found in the midbrain and cerebellum. In the sagittal section, the ventricle is triangular and protrudes into the cerebellum posteriorly. The floor of the fourth ventricle is a rhomboidal shaped structure continuous with the central canal of the spinal cord. It also is continuous with the subarachnoid space via the foramen of Luschka at the level of the inferior cerebellar peduncles. These peduncles form the anterior and rostral boundries of the lateral recess of the fourth ventricle. The third and fourth ventricles communicate via the aqueduct of the midbrain (also called the aqueduct of Sylvius). For completion, the lateral and third ventricles are connected by the foramina of Monro.[28] It is important to recognize the fourth ventricle is continuous with both the more rostral ventricles and the central canal of the spinal cord. There are many important structures related to the floor of the fourth ventricle that are keys in communication between the cerebrum, cerebellum, and spinal cord. In addition, there are several nuclei of cranial nerves which come in contact with the floor of the fourth ventricle.[28]

The clinical results produced by the compression of the fourth ventricle are hypothetically related to the structures of the floor of the fourth ventricle. One of these structures is the nucleus tractus solitarius.[2] The nucleus tractus solitarius is the primay relay station for most peripheral afferent inputs and also serves as a critical integration structure for most autonomic actions related to the brainstem and higher brain centers.[28]

The nucleus tractus solitarius is believed to be where the vagal visceral afferent fibers end. The nucleus tractus solitarius is connected to the reticular formation which serves the reflex control of the cardiovascular, respiratory, and cardiac functions. This is via the noradrenergic dorsal medullary cell group that lies within the nucleus tractus solitarius, dorsal motor nucleus of the vagus and the adjoining parvocellular reticular area. Afferent fibers from the pneumotaxic center (the Kolliker-Fuse nucleus) end in an inspiratory center of the ventrolateral part of the nucleus tractus solitarius and a mixed expiratory-inspiratory center in the superficial ventrolateral reticular area. The spinal fibers of the Kolliker-Fuse inspiratory neurons in both centers monosynaptically project to the phrenic and intercostalis motor neurons. The axons of expiratory neurons end on lower motor neurons innervating intercostalis and abdominal musculature.[28] In addition, the Traube-Hering-Mayer oscillation emanates from the floor of the fourth ventricle in the nucleus tractus solitarius along with the humoral effects of the renin-angiotensin system. Medial pressor areas in this nucleus are responsible for vasoconstriction, and the lateral pressor areas are responsible for vasodilatation.[10] Both of these exhibit inherent automaticity.[10] An effect on this nucleus alone would explain many of the respiratory, cardiovascular, and autonomic effects of the CV-4.

In addition, the dorsal vagal nucleus is found on the floor of the fourth ventricle.[28] This nucleus has fine preganglionic parasympathetic fibers innervating non-striated muscle. Other nuclei in this location include the trigeminal, abducent, facial, dorsal cochlear, and hypoglossal nuclei. These nuclei include special sensory, special motor, gross motor, and autonomic functions. In comparing the claims made by patients

receiving the CV-4 and physicians performing it, many of the claims line up with the functions of the various structures mentioned.

Many structures of the floor of the fourth ventricle are part of the reticular formation. This reticular formation has long been associated with sleep.[29] Within the reticular formation adrenergic, serotoninergic, and cholinergic neurotransmitters are stored. More recent studies recognize the role of nitric oxide (NO) in sleep.[30, 31] In particular, NO released from the pedunculopontine tegmental nucleus is associated with REM sleep and the wake/sleep cycle.[31] A further anatomic proximity to the fourth ventricle that plays a role in sleep is the lateral column of the reticular nuclei. This nucleus abuts many of the structures already mentioned including the nucleus tractus solitarius, nucleus ambiguous, and dorsal motor nucleus of the vagus. The ventrolateral reticular area of the lateral column is involved in cardiovascular, respiratory, vasoreceptor and chemoreceptor reflexes. Additionally, both noradrenergic and adrenergic cell groups are located in this area.[28] Part of the reticular formation also includes the thalamus. The thalamus has long been associated with sleep.[12] Destruction of the anterior portion of the thalamus is associated with insomnia, while destruction of the posterior portion is associated with hypersomnolence.[12] A study of the reticular activating system of rats demonstrated that the thalamus produces nitric oxide in different amounts from the alert stage to the REM stage of sleep. Low levels are produced during alertness, and the greatest amounts are produced during REM sleep.[30] During NREM sleep, the thalamus produces moderate amounts of the gas. This information strengthens the association between the thalamus, hypothalamus, and sleep.[30, 32]

In conclusion, the structures related to the floor of the fourth ventricle and their connections to portions of the brain known to be related to sleep and relaxation may be related to the effects of the CV-4 technique's ability to shorten sleep latency or create a state of relaxation. In this study, findings support the hypothesis that cranial manipulation does shorten sleep-onset latency when compared to distracted light touch and no treatment. While there was no difference between CV-4 treatment and sham treatment for total percent sleep, the calming effects of the CV-4 treatment through the proposed mechanisms discussed, allowed the subjects of this study to fall asleep more quickly than the other two groups.

Limitations

In spite of everything discussed, sleep, in many aspects, remains a mystery to physicians and scientists. Much more is known about neurotransmitters involved in sleep, stages of sleep, brain activity during sleep, blood flow to and from the brain in sleep, effects of insomnia, and many of the causes of sleep disorders. On the other hand, the cause-and-effect relationships of sleep are still unclear. It is known that people who do not sleep must endure many difficult consequences, even death.[12] On the other hand, the effects of sleep on the body, brain, and psyche are still unclear. Scientists also know many structures in the central nervous system are related to sleep and damage to some of these structures may cause a disruption of normal sleep[12]. However, how these structures relate to one another and induce sleep, maintain sleep, and terminate sleep with wakefulness is somewhat ambiguous.

In light of the many unknowns about sleep, determining how the CV-4 may shorten sleep latency may be impossible. This study was not done to make this determination, but it is a logical question that needs further investigation. It is unknown what the CV-4 is doing to the structures on the floor of the fourth ventricle or the brainstem. While claims have been made that the CV-4 affects the reticular activating system, nothing in this study or any other studies to date can support this claim. The danger in this study is that those practicing cranial osteopathy and others will over interpret the results stating they prove that the CV-4 is creating a physiologic change in the central nervous system. Making such a statement is unreasonable since the physiology of sleep is not fully understood.

Summary

The CV-4 shortens sleep latency independent of distracted light touch and no treatment. The mechanism for this effect is not proposed and should not be assumed based on the findings of this study. Nevertheless, these data clearly demonstrate that this cranial manipulative technique can produce a state that favors progression to sleep. Future studies will be directed at the effects of the CV-4 technique on sleep latency and sleep architecture during the night. In addition, distinguishing whether this effect is related to direct effects on primary brain structures of sleep or indirectly by creating a state of enhanced relaxation will be studied.

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