Effects of Compression of the 4th Ventricle (CV4) Treatment on Medical Student Anxiety

Edward Goering, DO; Maranda Herner, DO; Meagan Smith, DO; Mary Galka, OMS-IV; Samuel Kammerzell, DO; Kaitlin Best, DO; Pamela Anderson, DO; and Michelle Steinauer, PhD

ORIGINAL RESEARCH

Abstract

Introduction: This study explores the effects of one Compression of the 4th Ventricle (CV4) treatment performed by experienced osteopathic physicians on reactive anxiety in healthy medical students. Anxiety was assessed with heart rate, blood pressure, and the Hamilton Anxiety Scale (HAM-A).

Methods: Western University of Health Sciences IRB #15/IRB/113 was obtained for this single blind study. Volunteer first and second year medical students naïve to Osteopathic Cranial Manipulative Medicine, both in curriculum and as a patient, were recruited for this two-day study. Students were de-identified and demographic information was collected. On the first day, all 64 students received a sham treatment. Eight practitioners agreed on CV4 and sham techniques (mastoid cranial hold). In the CV4 technique, the operator's thenar eminences contact the lateral angles of the occiput, and the operator encouraged the extension phase and discouraged the flexion phase of the CRI. Compression continued until a still point was reached in each student as identified by the practitioner. Students were evaluated before and after treatment using heart rate, blood pressure, and the Hamilton Anxiety Rating Scale (HAM-A).

Results: No significant difference was found in demographics of the two groups. A significant difference between sham and CV4 treatments was found for heart rate (p=0.036), but not for systolic or diastolic blood pressure (p=0.446 and p=0.799, respectively). Average heart rate reduction of CV4 group was 3.11 and of sham group was 1.12, with p=0.036 (Mann Whitney U = 1271). Heart rate increased in a few students after both CV4 and sham treatments. Average HAM-A score for students before and after CV4 treatment were 21.9 and 18.3, with an average net reduction of 3.58 compared to the sham's 2.77, but results were not found to be statistically significant (p=0.09, U=1172).

Conclusion: A statistically significant average reduction in heart rate, but not in blood pressure or HAM-A scores, was found after CV4 treatment compared to sham treatment. More studies with larger samples are needed to further investigate the effects of CV4.

From the Western University of Health Sciences-College of Osteopathic Medicine of the Pacific Northwest Campus

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Correspondence address:
Edward K Goering DO DVM MSHPE
Western University of Health Sciences-College of Osteopathic Medicine of the Pacific Northwest Campus
200 Mullins Drive
Lebanon, OR 97355
(541) 259-0218
egoering@westernu.edu

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Introduction

The prevalence of anxiety in the United States is estimated to be 1 in 4 adults.[1] According to the *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition) (*DSM-5*), generalized anxiety disorder is defined as "excessive anxiety about a number of events or activities that are difficult to control and interfere with psychosocial functioning."[2] The global impact of anxiety among medical students was recently estimated to be 28%, higher than the national average.[3] The prevalence rates of anxiety among medical students in training is a global issue and is largely felt to be due to the academic pressures of a challenging curricula during training. This study's primary objective was to see if a single treatment with the compression of the 4th ventricle technique impacted the reactive anxiety of medical students in their first and second years of medical school.[4]

The compression of the 4th ventricle (CV4) technique is a manual medicine technique within osteopathic cranial manipulative medicine. This modality was developed by William Garner Sutherland, DO, who defined alternations in motion of the cranial bones,

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sacrum, cerebrospinal fluid, brain, spinal cord, and reciprocal tension membranes as the Primary Respiratory Mechanism.[5,6] He proposed this mechanism can be palpated as biphasic fluctuations around the sphenobasilar synchondrosis (SBS), termed the cranial rhythmic impulse (CRI). He described flexion of the mechanism as the slight cephalad convexity or rise in the SBS and extension as a slight caudal fall in the SBS.[7,8] The CRI has also been described as the PRM manifested as a body-wide rhythmic motion. According to Dr. Sutherland, this mechanism is driven by a dynamic metabolic interchange at the cellular level, namely primary cellular respiration of gas exchange in the tissues.[7,9,10] CV4 has been proposed to help rebalance the autonomic nervous system, and by its close proximity to the vagus nerve, stimulate the parasympathetic response. The CV4 technique is felt to increase parasympathetic activity and decrease overall sympathetic tone.[9,11] It has been theorized the endocannabinoid system is activated as well, causing downregulation of the sympathetic arm of the autonomic nervous system.[9,12] Reported effects of the CV4 technique are relaxation,[13] decreased sleep latency,[14] improved immunity and self-regulation,[6] as well as decrease in hypertension and improved heart rate variablity.[11]

Considering the above proposed effects, the objective of the present study is to evaluate the effects of the CV4 technique on the anxiety stress response experienced by previously undiagnosed first and second year medical students during the initiation of a robust medical school curriculum.

We hypothesized that one CV4 intervention performed by a practicing physician will cause a statistically significant difference in heart rate, blood pressure, or Hamilton Anxiety Scale (HAM-A) ratings after treatment in healthy medical students compared to sham control.

Methods

Participants

This single-blind study was conducted at Western University of Health Sciences COMP- Northwest Osteopathic Manipulation Lab on two different days in September and October 2016 (IRB #15/IRB/113). Medical students were recruited from the population at Western University COMP Northwest campus first and second year classes and were naive to osteopathic cranial manipulative medicine. Consent and demographic information was collected prior to the intervention, however an osteopathic structural exam was not performed to identify somatic dysfunction prior to the study. Students were given an identification number, which was used on all data throughout the study. No compensation or academic benefit was provided for the students' involvement in the study.

Exclusion criteria included previous knowledge of osteopathic cranial manipulation, current use of blood pressure, sympathomimetic, or anxiety medications, or caffeine consumption within six hours of the scheduled study time. Students were not asked to provide any information about anxiety, other mood disorders, or any other health information apart from attesting to not using the medications listed above.

To assess an objective measure of autonomic function as related to anxiety, heart rate and blood pressure measurements were evaluated. In 2011, at the European School of Osteopathy, Dr. Otman, then a fourth-year student, studied the effect of his performance of a CV4 technique on 20 students. He cited many potential areas of bias in his study, including the lack of experience of the practitioner, the practitioner being the author himself, and the subjects being osteopathic students aware of the aims of a CV4.[15] In this study, we invited experienced osteopathic physicians to perform the CV4 technique on students naive to cranial manipulation and attempted to minimize his described biases. The students had never experienced osteopathic cranial manipulative medicine, and knew nothing about the treatment, having not studied it yet within the curriculum. In addition, students were eliminated from participation if they were currently being treated for anxiety or were taking sympathomimetic drugs or BP medication.

The Hamilton Anxiety Scale (HAM-A) Survey was selected as a subjective measure of anxiety because it has shown to correlate well with other anxiety scales and holds acceptable inter-rater reliability. Additionally, it can be taken independently by each subject without a second party administrator.[16,17] The ability for the subject to take the survey without an administrator, as well as the inter-rater reliability led to the choice of HAM-A to evaluate anxiety in subjects.

Study Design

Subjects completed a HAM-A survey. Subjects then entered a room for a 30-second seated rest period before initial pre-treatment blood pressure and heart rate reading performed via pulse oximetry of the left index finger and automatic OMRON wrist or arm BP cuff. CV4 or sham was performed dependent on the arm of the study being tested. BP and HR were taken within 30 seconds of the practitioner removing their hands and while the patient was prone using the same pulse oximeter and OMRON wrist or arm BP cuff. A second HAM-A was administered outside the room. All students were randomly assigned to either the CV4 group or the sham group. All

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students who participated during the first study day underwent the CV4 treatment, and all students who participated the second day received the sham treatment. In total, 40 participants were present both days and received both treatment and sham.[6] The 2 study dates were separated by 1 month, and were selected to avoid proximity to curriculum tests.

Procedures

CV4 treatments were performed by 7 physicians experienced in cranial osteopathic manipulation. Consensus training on CV4 technique delivery via the occiput was completed prior to the study. In the CV4 technique, the operator's thenar eminences contact the lateral angles of the occiput just medial to the occipitomastoid suture, and the operator encourages the extension phase of the cranial rhythmic impulse by gently compressing the lateral angles of the occiput and discourages the flexion phase. Compression is continued for a few minutes until a softening is felt in the suboccipital area, thoracic diaphragmatic breaths become more even, and there is an "idling of the motor" known as the still point.[6,7] This treatment lasted for approximately 5 minutes.

The sham treatment consisted of the physicians using a mastoid cranial hold for 5 minutes without treatment intervention.

Blood pressure was measured with arm or wrist OMRON blood pressure cuffs, all taken on the left arm. Heart rate was measured with pulse oximeters. Subjects rested for approximately 30 seconds before blood pressure and heart rate measurements were collected.

Statistical Analysis

Contingency table analysis using Fisher's Exact test and Pearson Chi Squared Test was used to assess group differences in gender and race. T- and Mann-Whitney U-tests were used to analyze the mean age between the 2 study groups. Changes in heart rate, blood pressure, and HAM-A scores were assessed using the Mann-Whitney U-test since the distributions were non-normal.

For all comparisons, P<.05 was considered statistically significant, and 95% CIs were calculated. Data was analyzed with Graph Pad Prism 7.0 and VassarStats.

	CV4		Sham	
	Count	Percent	Count	Percent
Male	28	45%	18.0	29%
Caucasian	51	82%	42	79%
Hispanic	2	3%	3	6%
Asian	8	13%	6	11%
Other	1	2%	2	4%
Average Age	25.0		25.4	

Table 1. *Participant demographics.*

Results

Of the 77 medical students recruited for this study, 64 received a single CV4 treatment while 53 received a sham treatment (40 received both). The demographic parameters of the two study populations (CV4 and sham) did not differ significantly (age: p=0.5456 gender: p=0.2551; race: p= 0.8037). The CV4 and sham groups were self-reported as: 45% and 29% male, 82% and 79% Caucasian, 3% and 6% Hispanic, and 13% and 11% Asian with average age of 25.0 and 25.4, respectively (shown in Table 1). A T-test with Welch's correction for unequal standard deviation for age yielded p=0.5456 (T=0.6064, df=106.8) and the Mann-Whitney U-Test (two tailed) for non-normal distribution showed p=0.6373 (U=1611). For gender, VassarStats contingency table was used to calculate Fisher's Exact Test (p=0.2551) and Pearson Chi-Square (x2 = 1.49, p=0.2222). The predominant race was Caucasian but again, no difference existed between treatment groups based on VassarStats Pearson Chi-Square p= 0.8037 (x2 =0.99, df=3). (See Table 1 Participant demographics.)

There was a statistically significant reduction in heart rate of the CV4 group (3.11 bpm) and the sham group (1.12 bpm) (U =1271, p = 0.0364). The sham group contained 6 data points that were apparent outliers, 3 showing a large increase in heart rate and 3 showing a large reduction in heart rate. (See Figure 1a.) To examine the effects of these outliers on the data, the statistical test was rerun after the outliers were removed. The difference was still significant (U=1085, p = 0.025). (See Figure 1b.) This suggests the patients with the large changes in the control group are not driving the underlying pattern. If only the 3 instances of the large increases in heart rate are removed (this response is unexpected in either group), the results are no longer significant (U = 1271, p = 0.0952).

Average systolic blood pressure reduction of the CV4 and sham group was 6.92 and 7.31, respectively, with no significant difference between the two groups, p=0.4456 (U=1557). The average reduction in diastolic blood pressure was 2.74 for the CV4 group and 2.76 for the sham group, p=0.7987 (U=1537).

The pre-treatment HAM-A scores of the CV4 group and the sham group were 21.9 and 21.3, respectively, with no significant difference

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between them (U=1299, p=0.2560). A score of 17 or less indicates mild anxiety, and a score between 18 and 24 indicates mild to moderate anxiety, and a score between 25 and 30 indicates moderate to severe anxiety, which puts the averages of 21.9 for the CV4 group and 21.3 for the sham group with mild to moderate anxiety. Based on these measures, 11 subjects who received the CV4 treatment and 12 subjects who received the sham treatment would be classified as exhibiting symptoms of mild anxiety. The average reduction in HAM-A score was 3.58 for the CV4 group and 2.77 for the sham group. Although the CV4 had a larger reduction, the difference in reduction was not statistically significant (U=1172, p=0.09).

Comment

This study assessed whether a single CV4 treatment delivered by an experienced osteopathic clinician reduced medical students' perceived reactive anxiety symptoms during the initiation of medical school curriculum. While a significant difference was found between CV4 and sham treatments for post-treatment heart rate reductions, the reduction was minimal, with changes of 3 bpm in CV4 group and 1 bpm in sham. This invites the question of clinical significance since a healthy adult heart rate ranges from 60 to 100 bpm. Interestingly, a few students experienced increases in heart rate post-treatment in both CV4 and sham groups. This may reflect the students' discomfort with being in a study, unease with undergoing a treatment, unexpected stimulatory distraction from around the room or not adhering to the 6-hour caffeine window. It is also a possible spurious effect of these individuals. These unexpected increases in HR confounded the data collection. Additionally, it is impossible to tell the effect of resting quietly on those students demonstrating a HR change as there was not a resting arm of the study, however greater decrease in the treatment group would favor autonomic nervous system downregulation. A further study could clarify this effect by adding a third "resting quietly" arm as an additional control group.

No significant differences were seen in systolic and diastolic blood pressure changes in this study.

The HAM-A survey assessed anxiety as rated subjectively by the students. The CV4 group HAM-A scores dropped more than the sham group's, but the difference was not statistically significant. The lack of significant difference could reflect the inability of one CV4 treatment to address some of the long-term questions on the HAM-A survey by the end of one treatment, such as insomnia. Since HAM-A is a tool for clinical anxiety, some of the questions did not apply to this scenario.

Limitations and future study revision options

The findings of this study may indicate that CV4 is an effective tool for heart rate reduction, but not for self-perceived anxiety in medical students in the first and second years. The findings of the HAM-A showed an encouraging but insignificant reduction; further study with a larger sample size and subjects in different states of sympathetic/parasympathetic tone would be warranted to avoid both type I and II errors.

Limitations to this study include not having a 'resting arm' to determine if HR reduction was due to prone position for 5 minutes, use of both wrist and arm automatic blood pressure readings, and medical student bias.

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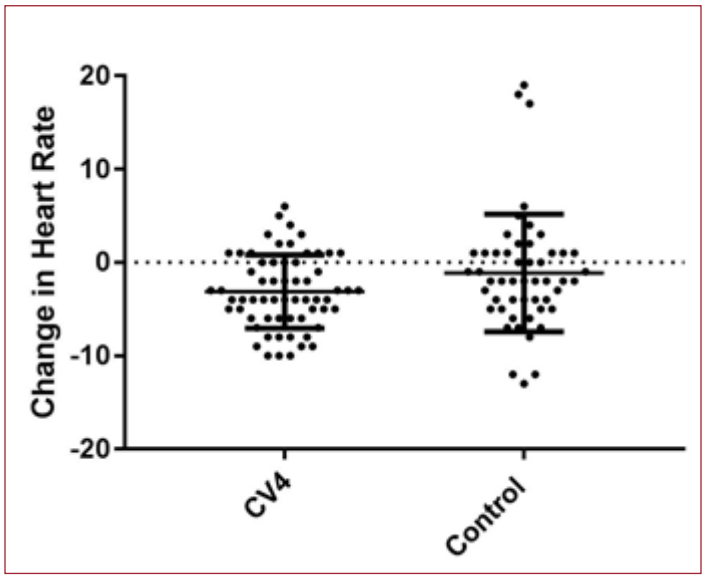

Figure 1a. *Change in heart rate for experimental and control groups with outliers included.*

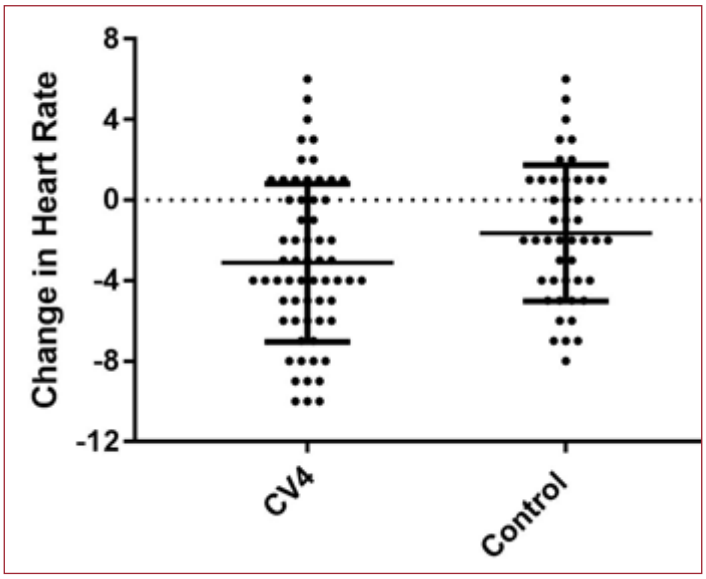

Figure 1b. *Change in heart rate for experimental and control groups with outliers excluded.*

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In addition, cross-over did not occur, as only some students participated in both study days, but a crossover would have better controlled for confounding factors. Of the 64 1st year students volunteering on the first day, only about 40 returned which may reflect schedule conflicts or other factors contributing to bias. Due to a high drop-out rate, 2nd year students were included for the second study day (the sham treatment) which confounded the study further. While both 1st and 2nd year class students were naive to cranial throughout this study and no difference was noted in the demographics of the two groups. The inclusion of 2nd years in only the sham treatment could have introduced unseen biases.

The sham was performed almost a month after the CV4 treatment. This may have allowed some natural "self-regulation" to occur among the study population. Finally, while all providers of both CV4 and sham were experienced licensed osteopathic physicians, there were different physicians performing the CV4 and sham arms. This could have introduced variation in the skill level and practice of the different physicians. Since the sham involved palpation but not treatment, there may have been some effect from human touch.[18]

Conclusion

A significant decrease in heart rate was found in healthy medical students after receiving a CV4 treatment compared to sham performed by an osteopathic physician. No significant difference was found in systolic or diastolic blood pressure reductions. While the CV4 group had a larger reduction in average Hamilton Anxiety Scale scores after treatment compared to sham, the difference was not significant. More studies are needed to support the data found and investigate populations with varied sympathetic/parasympathetic tone and those diagnosed with anxiety disorders. A larger study, with longer treatment allowances, more thorough and accurate measurements, and more controlled environments and study parameters can better illustrate a more accurate effect of a CV4 treatment on heart rate, blood pressure, and HAM-A scores. This study serves as a pilot to show proof of concept and to inspire further research on this topic. Future studies will be able to moderate the potential confounding factors and more clearly demonstrate the effects of the CV4 on anxiety.

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