

Cranial Manipulation Can Alter Sleep Latency and Sympathetic Nerve Activity in Humans: A Pilot Study

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ABSTRACT

Objective: To determine if cranial manipulation is associated with altered sleep latency. Furthermore, we investigated the effects of cranial manipulation on muscle sympathetic nerve activity (MSNA) as a potential mechanism for altered sleep latency.

Design: Randomized block design with repeated measures.

Setting: The Integrative Physiology and Manipulative Medicine Departments, University of North Texas Health Science Center, Fort Worth, TX.

Subjects: Twenty (20) healthy volunteers (12 male, 8 female; age range, 22–35 years) participated in this investigation.

Interventions: Subjects were exposed to 3 randomly ordered treatments: compression of the fourth ventricle (CV4), CV4 sham (simple touch), and control (no treatment).

Outcome measures: Sleep latency was assessed during each of the treatments in 11 subjects, using the standard Multiple Sleep Latency Test protocol. Conversely, directly recorded efferent MSNA was measured during each of the treatments in the remaining 9 subjects, using standard microneurographic technique.

Results: Sleep latency during the CV4 trial was decreased when compared to both the CV4 sham or control trials ($p < 0.05$). MSNA during the CV4-induced temporary halt of the cranial rhythmic impulse (stillpoint) was decreased when compared to prestillpoint MSNA ($p < 0.01$). During the CV4 sham and control trials MSNA was not different between CV4 time-matched measurements ($p > 0.05$). Moreover, the change in MSNA prestillpoint to stillpoint during the CV4 trial was different compared to the CV4 sham and control trials ($p < 0.05$). However, this change in MSNA was similar between the CV4 sham and control trials ($p > 0.80$).

Conclusions: The current study is the first to demonstrate that cranial manipulation, specifically the CV4 technique, can alter sleep latency and directly measured MSNA in healthy humans. These findings provide important insight into the possible physiologic effects of cranial manipulation. However, the mechanisms behind these changes remain unclear.

INTRODUCTION

Osteopathic physicians have practiced alternative, manual medicine for over than 100 years. Cranial manipulation is a subset of manual medicine, which in recent years has been used more and more by practitioners of manual

medicine (Chaitow, 1997). An integral component of cranial manipulation is the existence of cranial bone motion (Sutherland, 1939). The motive force behind this motion is referred to as the primary respiratory mechanism (PRM) and is described as an oscillation with a frequency of 10–14 cycles per minute (cpm) (Chaitow, 1999; Lay, 1997). Subtle

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cranial motion produced by the PRM is palpable by experienced practitioners and is referred to as the cranial rhythmic impulse (CRI).

One of the more popular cranial manipulative techniques, compression of the fourth ventricle (CV4), attempts to positively influence body physiologic functioning by modifying the rate of the CRI. During this technique the practitioner attempts to halt the CRI (stillpoint) temporarily with the expectation that various aspects of physiologic functioning will move toward normalization (Magoun, 1976). Subsequently, we have observed and others have suggested that the CV4 technique is profoundly relaxing, often causing patients to fall asleep during the treatment. Therefore, we have postulated that use of the CV4 technique may decrease sleep latency.

The autonomic nervous system plays an important role in the regulation of sleep/wake cycles (Moldofsky and Luk, 2003). For example, recent data demonstrated a decrease in sleep latency (more rapid onset of sleep) in norepinephrine-deficient mice compared to normal controls (Hunsley and Palmiter, 2003). Furthermore, Gronfier et al. (1999) demonstrated that low neuroendocrine activity is "a prerequisite" for an increase in slow wave EEG activity in humans. Interestingly, it has been postulated that the CV4-induced stillpoint is associated with decreased sympathetic tone. However, most of the data suggesting that the CV4 technique produces decreased sympathetic tone are limited and anecdotal. For example, Magoun (1976) demonstrated a decrease, compared to baseline, in electrical skin resistance after 3 minutes of CV4. He concluded that decrease in electrical skin resistance was an indication of a decrease in sympathetic nerve activity. Although this conclusion may be accurate, it would only be an estimation of skin sympathetic nerve activity, which is primarily involved in temperature regulation, and not an estimation of muscle sympathetic nerve activity (MSNA), which is a better marker of global sympathetic activity.

The present investigation was designed to determine if the CV4 technique is associated with altered sleep latency. Furthermore, as a potential mechanism for altered sleep latency, we investigated the effects of the CV4-induced stillpoint on MSNA. We hypothesized that the CV4 technique decreases sleep latency and the CV4-induced stillpoint is associated with decreased MSNA.

METHODS

Subjects

This study was approved by the University of North Texas Health Science Center Institutional Review Board. Twenty (20) healthy volunteers (12 male, 8 female; age range, 22–35 years) participated in this investigation. After giving informed consent, each subject completed a medical

history questionnaire. All subjects were nonsmokers, reported no history of cardiovascular, pulmonary, or neurologic disease, and were not currently using medications other than oral contraceptives. Female subjects all tested negative for pregnancy and were not tested during menses, to eliminate potential confounding effects of menses on fluid metabolism, blood volume, and cardiovascular function. Subjects were asked to abstain from vigorous exercise and alcohol for 24 hours and caffeine for 12 hours before the start of the study. Also, subjects were asked to maintain their usual sleep habits (i.e., to avoid sleep deprivation) during the week prior to participation in the study.

Sleep latency

Sleep latency was determined using standard Multiple Sleep Latency Test protocols (Carskadon et al., 1986). Participants were monitored as follows: electroencephalography (EEG), C3 or C4 and O1 or O2; electro-oculography (EOG), right horizontal or oblique, left horizontal or oblique, and vertical; and electromyography (EMG), mental/submental. Once the monitors had been placed, and the participant was lying on the table, the recording devices were calibrated. Following calibration, participants were told: "Please lie quietly, keep your eyes closed, and try to fall asleep," at which time the lights were turned out (signaling the beginning of the test). The test was terminated after 30 minutes even if the participant had not fallen asleep. Sleep onset was defined as 3 epochs of stage 1 or 1 epoch of stage 2 sleep as scored by an independent sleep expert who was blinded to treatment group. Sleep latency was measured as the time from lights out to sleep onset as defined above. Also, total percent sleep time during each trial is reported.

MSNA

Postganglionic MSNA was directly measured from the peroneal nerve at the popliteal fossa using standard microneurographic techniques (Valbo et al., 1979). MSNA is reported as total activity/minute as described previously by Smith et al. (1996).

Cardiovascular measurements

Heart rate (HR) was measured with standard limb-lead ECG. Arterial blood pressure (BP) was measured noninvasively with photoplethysmography at the finger (Finapres blood pressure monitor 2300, Ohmeda, Englewood, CO). This method has been shown to be a reliable and valid measure of arterial BP (Imholz et al., 1988; Parati et al., 1989).

Experimental protocols

These studies were performed with subjects in the supine position in a laboratory with an ambient temperature of 23°–24°C. Prior to the day of the experiment, subjects were

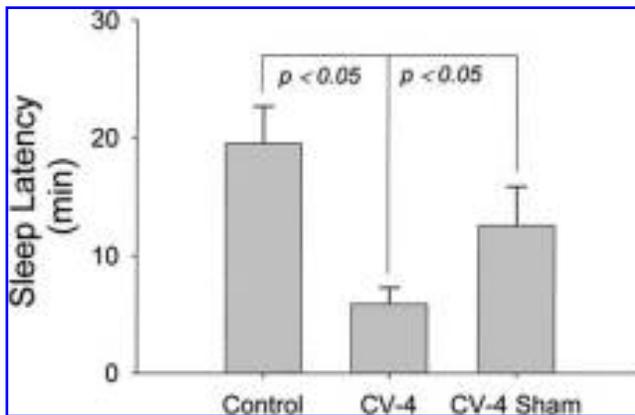


FIG. 1. Comparison of sleep latency between CV4, CV4 sham, and control groups ($n = 11$). CV4 = compression of the fourth ventricle; CV4 sham = simple touch; control = no treatment.

brought to the laboratory; during this visit, subjects were familiarized with the laboratory, completed all necessary paperwork (consent form and medical questionnaire), and were randomly assigned to either the sleep latency group ($n = 11$) or the MSNA group ($n = 9$).

Sleep latency group protocol

On the day of the experiment, subjects were monitored for measurement of HR, BP, EEG, EOG, and EMG. After the monitors were in place, 5 minutes of baseline data were recorded while the subject lay quietly in the supine position. Subjects then underwent a sleep latency test (described above) during each of 3 (CV4, CV4 sham, and control) randomly ordered treatments. During the first 5–7 minutes of the CV4 and CV4 sham trials, subjects were exposed to cranial manipulation or touch. Conversely, during the control trial the subject was not exposed to cranial manipulation or touch. Each trial was separated by a 1-hour recovery period, during which subjects were allowed to use the restroom and move around the laboratory *ad lib*. Also, subjects were blinded to which trial was the CV4 or CV4 sham treatment, and the same practitioner performed the CV4 and CV4 sham treatments for individual subjects.

MSNA group protocol

On the day of the experiment, subjects were monitored for measurement of HR, BP, and MSNA. After the monitors were in place, 5 minutes of baseline data were recorded while the subject lay quietly in the supine position. Subjects then were exposed to each of three randomly ordered treatments (CV4, CV4 sham, and control). During the CV4 and CV4 Sham trials, subjects were exposed to cranial manipulation and touch, respectively. Conversely, during the control trial, the subject was not exposed to cranial manipulation or touch. Each trial was separated by a 30-minute recovery period, during which the subjects remained in the

supine position. Also, subjects were blinded to which trial was the CV4 or CV4 sham treatment, and the same practitioner performed the CV4 and CV4 sham treatments for individual subjects.

Cranial manipulation

CV4 trial. While sitting at the head of the table, the practitioner contacted the participant's occiput (lateral to the external occipital protuberances, but medial to the occipitomastoid suture) with his or her thenar eminences. Once the practitioner detected the CRI, the practitioner resisted the flexion phase of the CRI and exaggerated the extension phase. This compressive pressure was maintained until the CRI stopped, and the stillpoint was reached. The stillpoint was held until the CRI returned, at which point the compressive pressure was slowly released. Finally, the practitioner's hands were gently removed and the participant's head was placed on the table.

CV4 sham trial. While sitting at the head of the table, the practitioner lightly contacted the occiput without cradling the participant's head. This position was maintained throughout the entire treatment. At the end of the sham treatment (~5 minutes) the practitioner slowly let the participant's head down on the table.

Data analysis

All statistical analyses were performed at a significance level of $\alpha = 0.05$. Comparison of sleep latency and percent total sleep during the CV4, CV sham, and control trials were analyzed using one-way ANOVA with repeated measures. MSNA, HR, and BP during the CV4 trial reflect mean values obtained over 30-second measurement periods prior to and during the CV4-induced stillpoint. Similarly, during the CV4 sham and control trials, MSNA, HR, and BP reflect mean

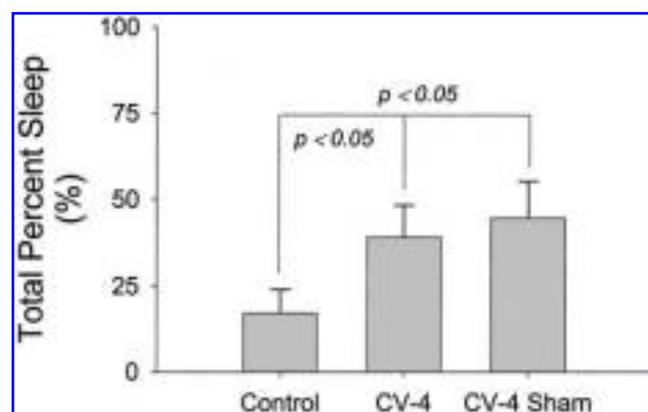


FIG. 2. Comparison of total percent sleep between CV4, CV4 sham, and control groups ($n = 11$). CV4 = compression of the fourth ventricle; CV4 sham = simple touch; control = no treatment.

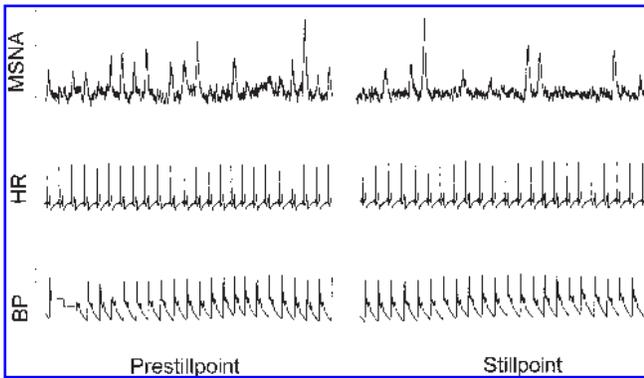


FIG. 3. Thirty-second sample tracing of muscle sympathetic nerve activity (MSNA), electrocardiogram ECG to show heart rate (HR), and blood pressure (BP) during the CV4 trial (n = 9). CV4 = compression of the fourth ventricle.

values obtained over 30 seconds during CV4 time-matched, prestillpoint and stillpoint measurement periods. MSNA, BP, and HR during the prestillpoint and stillpoint were compared using a paired-sample *t*-test. Comparison of the change in MSNA (prestillpoint to stillpoint) between CV4, CV4 sham, and control trials was analyzed using one-way ANOVA with repeated measures. When *F* values revealed differences, post hoc analysis was performed by pairwise comparison using the least significant difference method.

RESULTS

Effect of cranial manipulation on sleep latency

As hypothesized, a significant main effect for sleep latency between groups was observed ($p < 0.001$). Specific-

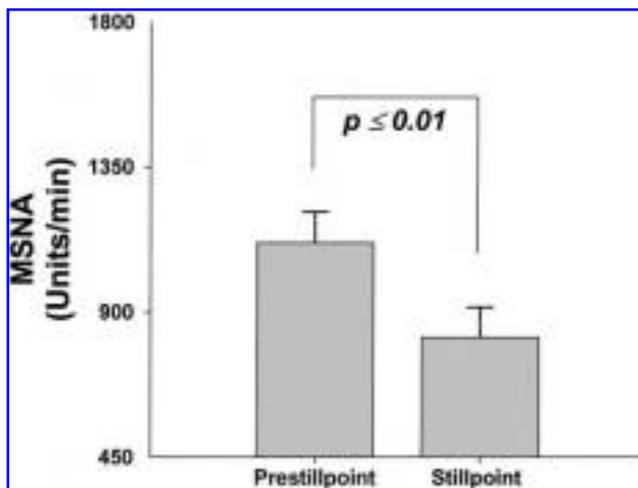


FIG. 4. Comparison of muscle sympathetic nerve activity (MSNA) between the prestillpoint and stillpoint during the CV4 trial (n = 9). CV4 = compression of the fourth ventricle.

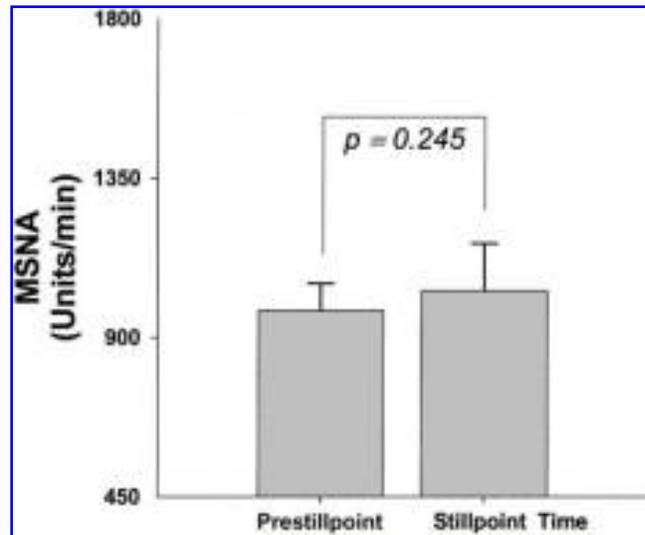


FIG. 5. Comparison of muscle sympathetic nerve activity (MSNA) between the CV4 trial time-matched prestillpoint and stillpoint during the CV4 sham trial (n = 9). CV4 = compression of the fourth ventricle; CV4 sham = simple touch.

cally, sleep onset was more rapid in the CV4 treatment group (5.9 ± 1.4 minutes) compared to the CV4 sham and control groups (12.6 ± 3.3 minutes and 17.2 ± 3.3 minutes, respectively) (Fig. 1). Additionally, a significant main effect for total percent sleep between groups was observed ($p < 0.01$). Both CV4 and CV4 sham groups spent a greater percentage of time in sleep ($39.1 \pm 9.2\%$ and $44.5 \pm 10.7\%$, respectively) compared to the control group ($17.1 \pm 6.8\%$;

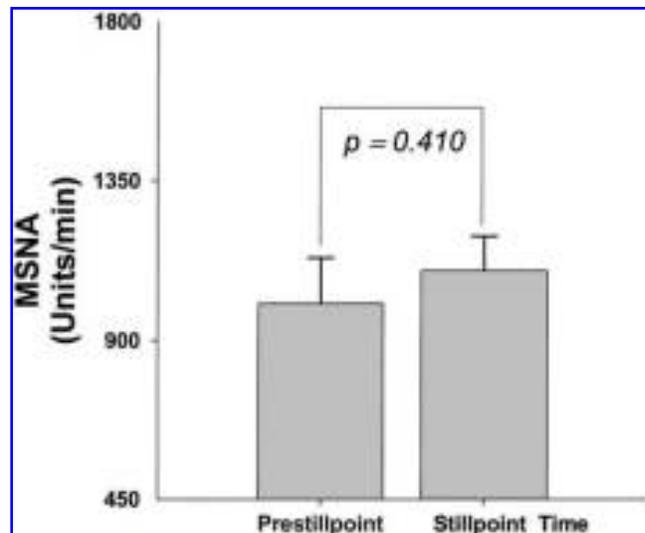


FIG. 6. Comparison of muscle sympathetic nerve activity (MSNA) between the CV4 trial time-matched prestillpoint and stillpoint during the control trial (n = 9). CV4 = compression of the fourth ventricle; control = no treatment.

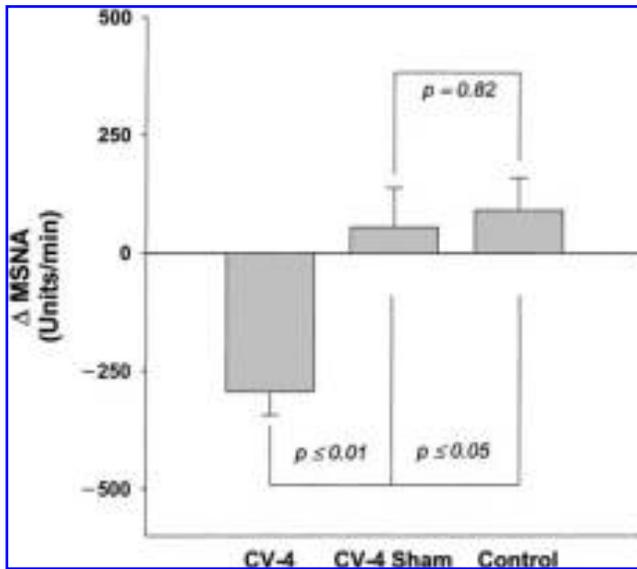


FIG. 7. Change in muscle sympathetic nerve activity (MSNA) from prestillpoint to stillpoint during CV4, CV4 sham, and control trials (n = 9). CV4 = compression of the fourth ventricle; CV4 sham = simple touch; control = no treatment.

$p < 0.05$) (Fig. 2). However, there was no difference in percent total sleep between the CV4 and CV4 sham groups.

Effect of cranial manipulation on MSNA, HR, and BP

Figure 3 is a representative tracing from one subject during the CV4 trial comparing MSNA during the prestillpoint and stillpoint. Consistent with our hypothesis, MSNA during the CV4-induced stillpoint was decreased when compared to prestillpoint MSNA; $p = 0.01$ (Fig. 4). Conversely, during the CV4 sham and control trials, MSNA was not different between the CV4 time-matched prestillpoint and stillpoint measurements; $p > 0.05$ (Figs. 5 and 6). Furthermore, the change in MSNA prestillpoint to stillpoint during the CV4 trial was different compared to the CV4 sham and control trials; $p = 0.05$ (Fig. 7). However, this change in MSNA was similar between the CV4 sham and control trials; $p = 0.80$. Finally, HR and BP were not significantly different at any time points during all three trials; $p > 0.05$ (Table 1).

DISCUSSION

The primary findings of the present investigation are that cranial manipulation using the CV4 technique can decrease sleep latency independent of touch in humans. Also, the CV4-induced stillpoint is associated with decreased MSNA compared to prestillpoint MSNA and this response appears to be independent of touch in humans.

This investigation is the first to evaluate the effect of cranial manipulation on sleep onset. Specifically, we demonstrated that onset of sleep was more rapid following cranial manipulation using the CV4 technique, when compared to both sham treatment and no treatment. The mechanism for decreased sleep latency following cranial manipulation is not known. Recent research suggests that the autonomic nervous system plays an important role in sleep onset. Specifically, using power spectral analysis of heart rate, Gronfier et al. (1999) demonstrated that decreased sympathetic nervous system activity precedes and is likely a prerequisite for increasing slow wave EEG activity. Additionally, Hunsley and Palmiter (2003) established that norepinephrine-deficient mice have decreased sleep latency after mild stress when compared to controls. Together these studies suggest an important relationship between the sympathetic nervous system and sleep onset.

The current study demonstrated that the CV4-induced stillpoint is associated with a modest decrease in MSNA. This is consistent with previous data from Sergueef et al. (2002), who demonstrated that cranial manipulation alters autonomic nervous system activity. Specifically, they demonstrated that cranial manipulation alters the thermal (Mayer) and baro (Traube-Hering) signals from cranial bloodflow velocity recordings, both of which are mediated through sympathetic and parasympathetic nervous system activity. The mechanism for the decrease in MSNA during the CV4-induced stillpoint is not known. Similarly, how long MSNA remains decreased is not known, as the present study did not follow sympathetic nerve activity during recovery from treatment.

Possible limitations of our study include, first, the effect of circadian cycles on the sleep latency test. To control for possible confounding effects of circadian cycles, all patients were tested during the same time of day (between the hours of 1:00 PM and 6:00 PM). Second, our data assume the existence of the PRM. Because of the subtle nature of these

TABLE 1. COMPARISON OF MEAN HEART RATE (HR) AND BLOOD PRESSURE (BP) BETWEEN THE PRESTILLPOINT AND STILLPOINT DURING CV4, CV4 SHAM, AND CONTROL TRIALS (N = 9)

	CV4 trial		CV4 sham trial		Control trial	
	Prestillpoint	Stillpoint	Prestillpoint	Stillpoint	Prestillpoint	Stillpoint
HR	56 ± 4	57 ± 4	57 ± 4	56 ± 4	59 ± 4	57 ± 4
BP	90 ± 5	91 ± 4	92 ± 4	91 ± 4	92 ± 3	91 ± 3

CV4, compression of the fourth ventricle; CV4 sham, simple touch; control, no treatment.

phenomena, their very existence is an issue of debate (Ferre and Barbin, 1991; Norton, 2000). However, though the underlying mechanism of the PRM remains unclear, there is considerable research to document the existence of the PRM, recently reviewed by Nelson (2002). Also, similar to the findings of Sergueef et al. (2002), our data demonstrated a quantitative difference between cranial manipulation and simple palpation. These findings suggest that cranial manipulation can alter physiology; however, the mechanisms explaining these changes remain unclear. Third, our data assume the existence of the practitioner-perceived stillpoint. However, the current study demonstrated a decrease in MSNA during the practitioner-perceived stillpoint and no difference in time-matched measurement of MSNA during the CV4 sham and control trials. Therefore, it seems reasonable to assume that the practitioner-perceived stillpoint represents an actual phenomenon. Fourth, measurement of MSNA and sleep latency was not performed in the same subjects. This limits our ability to draw a clear mechanistic link between decreased MSNA and sleep latency during cranial manipulations. Nevertheless, current research has demonstrated an apparent relationship between the autonomic nervous system and sleep onset. Therefore, the decreases in MSNA and sleep latency demonstrated in the current study are likely related. However, further research is needed to confirm this assumption.

In conclusion, the current study is the first to demonstrate that cranial manipulation, specifically the CV4 technique, can alter sleep latency and directly measured MSNA in healthy humans. These findings provide important insight into the possible physiological effects of cranial manipulation. However, the mechanisms behind these changes remain unclear.

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REFERENCES

Carskadon MA, Dement WC, Mitler MM, Roth T, Westbrook PR, Keenan S. Guidelines for the Multiple Sleep Latency Test (MSLT): A standard measure of sleepiness. *Sleep* 1986;9:519–524.

Chaitow L. Cranial manipulation re-examined. *Int J Altern Complement Med* 1997;15:28–32.

Chaitow L. *Cranial Manipulation Theory and Practice: Osseous and Soft Tissue Approaches*. Toronto: Churchill Livingstone, 1999.

Ferre JC, Barbin JY. The osteopathic cranial concept: Fact or fiction? *Surg Radiol Anat* 1991;13:165–170.

Gronfier C, Simon C, Piquard F, Ehrhart J, Brandenberger G. Neuroendocrine processes underlying ultradian sleep regulation in man. *J Clin Endocrinol Metab* 1999;84:2686–2690.

Hunsley MS, Palmiter RD. Norepinephrine-deficient mice exhibit normal sleep-wake states but have shorter sleep latency after mild stress and low doses of amphetamine. *Sleep* 2003;26:521–526.

Imholz BP, van Montfrans GA, Settels JJ, van der Hoeven GM, Karemaker JM, Wieling W. Continuous non-invasive blood pressure monitoring: reliability of Finapres device during the Valsalva manoeuvre. *Cardiovasc Res* 1988;22:390–397.

Lay E. Cranial Field. In: Ward RC, ed. *Foundations for Osteopathic Medicine*. Baltimore: Williams and Wilkins, 1997:901–913.

Magoun HI. *Osteopathy in the Cranial Field*. Kirksville, MO: Journal Printing Company, 1976.

Moldofsky H, Luk WP. Sleep Regulation and the Autonomic Nervous System. In: Bolis CL, Licinio J, Govoni S, eds. *Handbook of the Autonomic Nervous System in Health and Disease*. New York: Marcel Dekker, 2003:635–654.

Nelson KE. The primary respiratory mechanism. *AAO Journal* 2002;12:24–33.

Norton JM. Dig on [letter to the editor]. *AAO Journal* 2000;10:16–17.

Parati G, Casadei R, Groppelli A, Di Rienzo M, Mancia G. Comparison of finger and intra-arterial blood pressure monitoring at rest and during laboratory testing. *Hypertension* 1989;13:647–655.

Sergueef N, Nelson KE, Glonek T. The effect of cranial manipulation on the Traube-Hering-Mayer oscillation as measured by laser-Doppler flowmetry. *Altern Ther Health Med* 2002;8:74–76.

Smith ML, Niedermaier ON, Hardy SM, Decker MJ, Strohl KP. Role of hypoxemia in sleep apnea-induced sympathoexcitation. *J Auton Nerv Syst* 1996;56:184–190.

Sutherland W. *The Cranial Bowl*. Mankato, MN: Free Press, 1939.

Vallbo AB, Hagbarth KE, Torebjork HE, Wallin BG. Somatosensory, proprioceptive, and sympathetic activity in human peripheral nerves. *Physiol Rev* 1979;59:919–957.

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