CEREBROSPINAL FLUID PRESSURE RESPONSE TO UPPER CERVICAL VERTEBRAL MOTION AND DISPLACEMENT IN THE ANESTHETIZED RAT

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ABSTRACT

Objective: This study examined whether aligned or off-axis (subluxated) static and dynamic vertebral displacement within normal physiological ranges modulated cerebrospinal fluid pressure (CSF) as is considered to occur by some chiropractic theories.

Methods: Cerebrospinal fluid pressure pressure was measured via a subarachnoid catheter implanted at the lumbar level in 12 anesthetized adult male Wistar rats. A computer-driven manipulator was used to impose 3 motion patterns on the C2 vertebra: (i) dynamic oscillatory displacement (24° peak-to-peak 1.0 and 2.0 Hz), (ii) static rotary (ramp 20° at 10° per second and hold for 4 minutes) displacement about both the normal and an offset axis of rotation, and (iii) a spinal manipulative thrust displacement (200° per second; 12° peak-to-peak).

Results: The CSF pressure at rest for all rats ranged from 4.5 to 9.1 mm Hg, with a mean (± SD) of 6.3 ± 1.4 mm Hg. Of the imposed movements, only an offset ramp and hold displacement resulted in a significant ($P < .05$) difference between the CSF pressure before (6.1 ± 0.7 mm Hg) and during the imposed movement (6.6 ± 0.7 mm Hg). None of the interventions were associated with significant changes in the powers of the principal peaks of the CSF pressure power spectrum.

Conclusions: The results of this study suggest that static or dynamic displacement of an upper cervical vertebra within the limits of tissue integrity do not induce physiologically important changes in absolute CSF pressure or pressure dynamics in anesthetized rats. (J Manipulative Physiol Ther 2010;33:355-361)

Key Indexing Terms: *Chiropractic; Cerebrospinal Fluid; Neck; Rat; Spinal Cord*

Doctors of chiropractic/chiropractors have proposed that mechanical dysfunction of the vertebral motion segment, sometimes referred to by them as a vertebral subluxation or vertebral subluxation complex, results in signs and symptoms that can be resolved by the use of spinal manipulative therapy (SMT).[1] One hypothesis suggests that vertebral malposition less than a dislocation (subluxation) causes symptomatology by compromising cerebrospinal fluid (CSF) flow.[2] Certainly the pressure environment of the spinal cord critically influences neurological function, and so, under experimental conditions, relatively small absolute alterations in CSF pressure may have profound implications for how the spinal cord responds to insult.[3,4] However, it remains to be determined if vertebral position and/or motion within physiological limits alter CSF pressure and, furthermore, if SMT influences CSF pressure.

In this article we report a study, in an animal model, that characterizes the changes in CSF pressure and CSF dynamics during and after both slow and rapid movements of the upper cervical vertebral column. Using a computer-driven manipulator attached directly to the spinous process of the second cervical vertebra (C2), we have modeled vertebral movements on the temporal features of therapeutic SMT and whiplash events that have similar temporal profiles.[5,6] Furthermore, we have modeled altered motion on that known to occur subsequent to a whiplash event.[5] The animal model used in this investigation was the anesthetized adult rat. In both structural and functional terms, the upper cervical region of the rat is similar to that of

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the human[7] and has been used to model a number of biomechanical disturbances of the cervical spine (for example, see Choo et al[8] and Quinn and Winkelstein[9]).

Methods

Nonrecovery experiments were performed on 12 urethane-anesthetized young adult (8-12 weeks) male Wistar rats (310-440 g). All procedures were approved by the University of Newcastle animal care and ethics committee and conformed to the Australian National Health and Medical Research Council Code for Practice for the use of animals in experiments.

Surgical Preparation

Each rat was anesthetized by intraperitoneal injection of urethane (1.3 g/kg), tracheotomized and intubated, and initially allowed to ventilate spontaneously. A carotid artery and jugular vein were cannulated to monitor blood pressure (BP) and heart rate, and for the administration of supplementary anesthetic, respectively. Five animals in 1 subgroup were ventilated (tidal volume 1.5-1.8 mL) at rates of between 80 and 90 breaths per minute using a small animal ventilator (Small Animal Ventilator Model 683, Harvard Apparatus, South Natick, MA) with a spirometer (MLT1L Spirometer, ADInstruments, Sydney, Australia) to monitor ventilatory flow.

Subcutaneous needle electrodes were inserted to monitor the electrocardiogram. Body temperature was monitored via a rectal probe (Model 43TA; Yellow Springs Instrument Company, Yellow Springs, OH) and maintained at 37.0°C to 37.5°C using a heating blanket (K-20-D, American Pharmaseal Company, Valencia, CA) and infrared lamp.

A catheter (PE10, Atom Medical, Tokyo) was introduced into the lower lumbar subarachnoid space, as described previously,[10,11] for continuous measurement of lumbar CSF pressure. A data acquisition system (MacLab 8S, ADInstruments) connected to a computer was used to record (electrocardiogram, BP, and CSF pressure at 2000 Hz; chest excursion and ventilatory flow at 200 Hz) and analyze (Chart ver 4.1.1, ADInstruments) data.

Vertebral Displacements

Displacements of C2 vertebra were induced as described previously by us.[12] In brief, the head of the rat was fixed in a stereotaxic device (model 51800, Stoelting, Wood Dale, IL), the T1 spinous process was clamped, and the C2 spinous process was attached to a computer-driven manipulator while maintaining the posture of the rat's head and neck.[12] This permitted precise regulation of the rate (±1°/s), magnitude (±1°), and timing (±0.5 milliseconds) of the displacement of C2 while allowing freedom for coupled motion in the cervical (C1-C7) vertebral column. Once attached, the manipulator

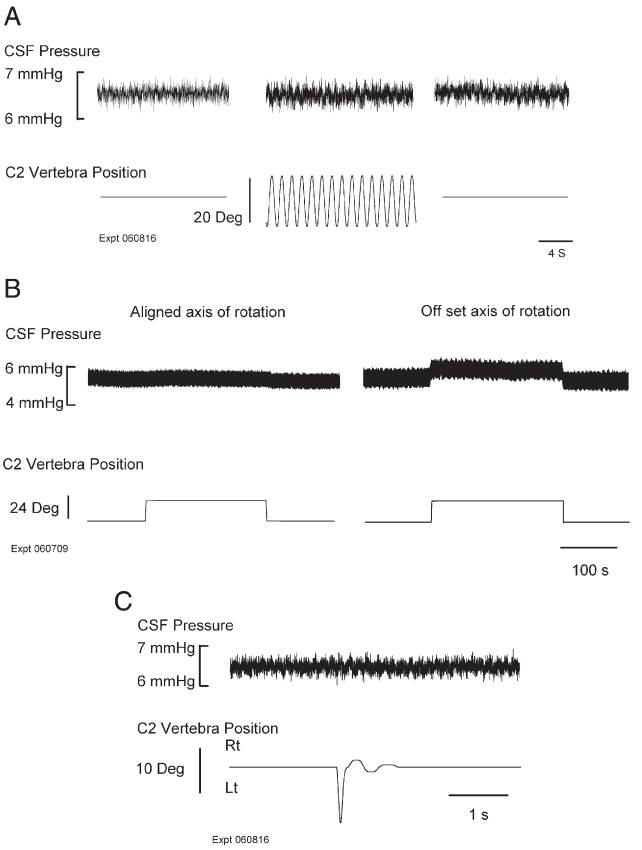

Fig 1. *This figure shows the CSF pressure (top panels) recorded from the subarachnoid space of the lumbar region of a spontaneously breathing anaesthetized rat and the position of its C2 vertebra (lower panels). A, No displacement of C2 (left panel), 1 Hz sinusoidal rotation of C2 (middle panel), and no displacement of C2 immediately after sinusoidal rotation (right panel) are shown. B, The CSF pressure before, during, and after a ramp and hold rotation of an aligned C2 vertebra (left panel) and the CSF pressure when the ramp and hold rotation is repeated with C2 rotation offset laterally 10 mm (right panel) are shown. C, The CSF pressure before, during, and after a rapid rotation of C2 are shown.*

was used to slowly rotate the C2 vertebra while observing the vertebral motion with a dissecting microscope (10×) to ensure that vertebral alignment had not been offset during the attachment of the manipulator. Subsequent imposed symmetrical motion of C2 about the longitudinal (rostrocaudal) axis of the vertebral column is referred to in this study as aligned vertebral rotation.

An offset ramp and hold rotational displacement was used to model vertebral subluxation. Thus, rats were positioned as already described, and then the manipulator, while still attached by a lever arm to C2, was displaced laterally by 10 mm, offsetting the imposed axis of rotation either to the left or right of the neutral position. The attachment of the computer-driven manipulator to the C2 spinous process incorporated a friction clutch mechanism that prevented displacement of the C2 vertebra beyond its physiological range of motion in any plane. Consequently,

rotation about the longitudinal axis imposed by the manipulator resulted in coupled dorsal-ventral and lateral motion offset to the longitudinal axis but within the physiological range (see Discussion).

The computer was programed to produce, as described in detail below, 3 types of displacement of the C2 vertebra: (i) a dynamic oscillatory rotational displacement, (ii) a static ramp and hold displacement, and (iii) a rapid displacement modeled on the force time curve for a high-velocity SMT procedure.[5]

Dynamic Oscillatory Displacements

In 4 animals, 24° peak-to-peak sinusoidal rotational displacements about the longitudinal axis (12° left and 12° right) were induced at both 1.0 and 2.0 Hz (Fig 1A, lower middle panel). Each trial consisted of 4-minute recordings (i) preceding, (ii) during, and (iii) after sinusoidal displacement. Recordings were only undertaken in animals exhibiting a stable anesthetic plane with a systolic BP higher than 80 mm Hg and stable spontaneous ventilation.

Mean CSF pressure and mean arterial pressure (MAP) were calculated for each of the three 4-minute epochs and tested for statistically significant differences (see Statistical Analysis below). These 4-minute blocks of data were also analyzed for power spectra, capturing a minimum of 260 respiratory cycles even at the slowest rate of mechanical ventilation. Power spectra were generated using 64K or 128K fast Fourier transforms with a Hamming window (Chart ver 4.1.1, ADInstruments). Data were analyzed as follows: peak frequencies in CSF pressure power spectra were examined for concordance with peak frequencies in the power spectra of the respiratory cycle, the frequency of the imposed vertebral oscillation (1 or 2 Hz), and a low-frequency peak that did not correspond to heart rate or respiratory rate but which has previously been reported to coincide with a low-frequency oscillation in BP.[11] The powers of these 3 peaks were examined, as described below under Statistical Analysis, for differences in their predisplacement, during displacement, and postdisplacement powers.

Static Displacements

The effect of C2 static vertebral displacement on CSF pressure was examined in 4 animals with both spontaneous and mechanical ventilation. The ramp and hold displacement consisted of the C2 vertebra being rotated to 20° at 10° per second about its normal longitudinal axis or an offset axis, held in this rotational displacement for 4 minutes, and then returned to its original position (Fig 1B, left lower panel). For trials in which the manipulator was offset laterally by 10 mm to model vertebral subluxation, the animals were mechanically ventilated continuously to ensure that respiration was not compromised by the displacement of the cervical vertebrae.

Mean CSF pressure and MAP were calculated for each of the 4-minute epochs predisplacement, during displacement, and postdisplacement and tested for statistically significant differences (see Statistical Analysis below). In addition, the three 4-minute epochs of CSF pressure data were subjected to power spectrum analysis, comparing the powers of the peaks that corresponded to the respiratory rate and the low-frequency oscillation in BP.

Spinal Manipulative Thrust Displacements

In 7 animals, a rapid rotation of the C2 vertebra was induced to model the vertebral displacement associated with the most commonly used spinal manipulative thrust procedure.[13] This displacement was modeled on the thrust characteristics of SMT as actually performed by chiropractors.[6,14] The initial vertebral movement involved a rapid (up to 200°/s) rotational displacement (12° peak) of the C2 spinous process, to the left or right, followed by a 3-cycle dampened sinusoid rotation. The initial displacement had a time-to-peak-displacement of 60 milliseconds with a return to midposition (neutral) by 140 milliseconds followed by the dampened sinusoidal oscillation, which ended so that the modeled manipulative thrust displacement had a total duration of 740 milliseconds (Fig 1C, lower panel). Mean CSF pressure and MAP were compared for the 10 seconds predisplacement and postdisplacement. Power spectra of CSF pressure were compared for the 4-minute epochs predisplacement and postdisplacement. At least 8 minutes separated successive displacements when performed in the same animal.

Blood Pressure Challenge

In 7 animals, the effects of acute BP changes on CSF pressure were investigated. Blood pressure changes were induced by pinching a paw with a hemostat for 10 seconds. Blood pressure and CSF pressure were averaged over 1-second intervals for the 10 seconds before and after onset of the pinch. These values were then compared to the average BP and CSF pressure for the entire 10 seconds before onset of the pinch. The concurrent changes from mean values in BP and CSF pressure, both before and during the pinch, were plotted against one another, a linear regression line (with 99% confidence interval) was fitted using the least squares method, and the coefficients of determination (r^2) were calculated for these 2 epochs.

At the conclusion of the data collection, each rat was euthanized by intravenous overdose of urethane (3.0 g/kg).

Statistical Analysis

Statistical analyses of the respective null hypotheses were performed using the software package SigmaStat V2.03 (SPSS Inc, Chicago, IL). All data were first tested for normality using the Kolmogorov-Smirnov test (with Lilliefors' correction). If normally distributed, the paired *t*

test was used to assess the level of significance of differences in CSF pressure and MAP, or power spectrum of the CSF measured before and after the respective stimuli. One-way analysis of variance was used when comparing the values for the prestimulus, stimulus, and poststimulus periods. When data were not normally distributed, the Wilcoxon signed rank test was used instead of the *t* test, and the Friedman Repeated Measures Analysis of Variance on Ranks was used in place of the one-way analysis of variance. A probability of $P < .05$ was considered to be significant.

Results

The CSF pressure at rest ranged from 4.5 to 9.1 mm Hg (n = 11 rats) with a mean (± SD) pressure of 6.3 ± 1.4 mm Hg. There was no significant difference ($P = .317$) between the mean CSF pressure of ventilated (5.7 ± 1.1 mm Hg) and nonventilated (6.3 ± 1.4 mm Hg) preparations.

Dynamic Oscillatory Displacements

There were no differences between mean CSF pressures (at 1 Hz, $P = .594$; at 2 Hz, $P = .303$) or MAP (at 1 Hz, $P = .247$; at 2 Hz, $P = .309$) before, during, or after oscillatory sinusoidal displacements (Fig 1A). Furthermore, there were no changes in the powers of the frequency peaks corresponding to the respiratory cycle (at 1 Hz, $P = .635$; at 2 Hz, $P = .819$), the low-frequency oscillation in BP (at 1 Hz, $P = .212$; at 2 Hz, $P = .324$), or the frequency of the imposed oscillation (at 1 Hz, $P = .125$; at 2 Hz, $P = .125$).

Static Displacements

With aligned vertebral rotation, in both spontaneously ventilating (11 trials in 4 animals) and mechanically ventilated animals (10 trials in 4 animals), there were no differences between mean CSF pressures ($P = .808$ for each; cf, Fig 2A) or the MAP ($P = .143$ and $P = .137$, respectively) in the 4-minute epochs before, during, or after ramp and hold displacements. However, when the axis of rotation was offset (9 trials in 4 animals), mean CSF pressure increased significantly (Fig 2B) ($P < .001$) during displacement (eg, Fig 1B, upper right panel), without any concomitant change in MAP ($P = .569$).

With aligned vertebral rotation, there were no changes in CSF pressure power spectra regardless of whether ventilation was spontaneous (11 trials in 4 animals; $P = .190$) or mechanically assisted (10 trials in 4 animals; $P = .097$). Furthermore, there was no change in the power of the frequency peak associated with low-frequency oscillation in BP when the rats breathed spontaneously ($P = .058$) or were mechanically ventilated ($P = .156$).

Performing the ramp and hold in the offset configuration did not modulate the power of the frequency peak associated with ventilation (n = 9 trials; $P = .107$) or the low-frequency oscillation in BP (n = 9 trials; $P = .053$).

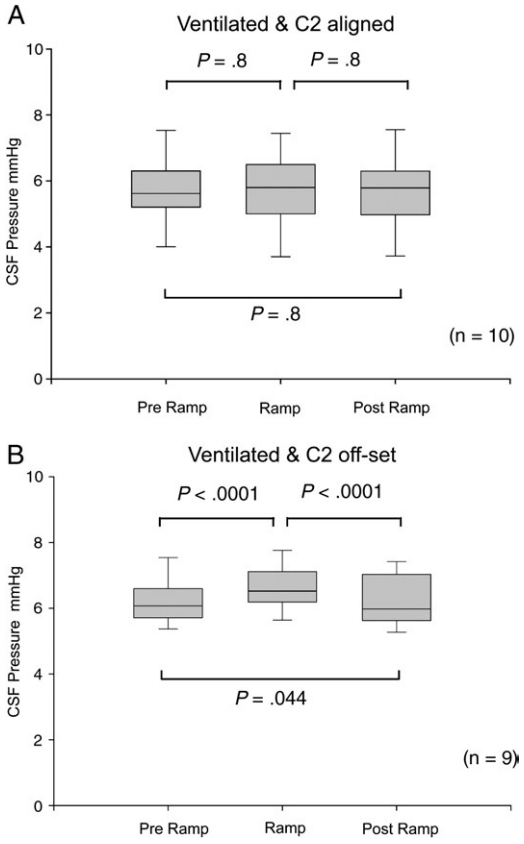

Fig 2. *Box plots showing the median (line), 25th and 75th percentiles (box), and 95% confidence intervals (horizontal bars) of the CSF pressure for the 4 minutes preceding (Pre Ramp), during (Ramp), and subsequent (Post Ramp) to an aligned (A) and offset (B) ramp and hold rotation of C2, both in mechanically ventilated animals. Results of statistical tests for differences have been listed.*

Rapid Low-Amplitude Displacements

In none of 26 trials in 7 animals did rapid, low-amplitude C2 displacement result in a detectable fluctuation in CSF pressure at the lumbar level. There were no significant differences in the mean CSF pressure ($P = .887$) or MAP ($P = .095$) for the 10-second epochs before and after the displacements (Fig 1C).

Analysis of power spectra before and after the rapid low-amplitude displacement revealed no changes in the powers of the peaks corresponding to the respiratory cycle (frequency range, 1.007-1.678 Hz; $P = .574$) or the peaks corresponding to the low-frequency oscillation in BP (frequency range, 0.024-0.092 Hz; $P = .689$).

Blood Pressure Challenge

Before onset of noxious pinching, small second-by-second changes in MAP appeared to exert little influence on second-by-second changes in CSF pressure (Fig 3 filled circles; $r^2 = 0.015$; $P = .05$). On the other hand, after onset

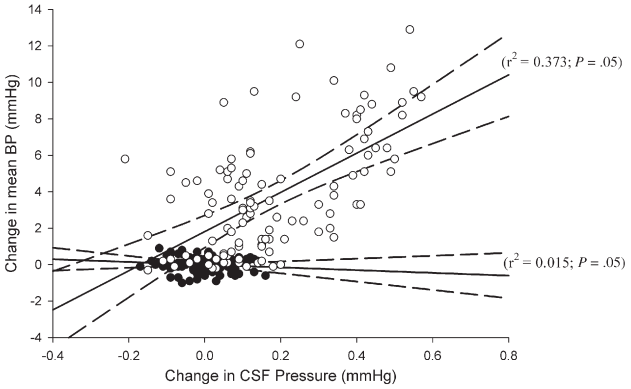

Fig 3. *Plot of the change (over 1-second intervals) in mean BP against change in CSF pressure for 10 seconds immediately preceding (filled circles) and during (open circles) noxious pinch of the hind paw. Linear regression (solid lines) and 99% confidence intervals (dashed lines) have been fitted to the data and the coefficient of determination (r^2 and P = .05) reported for each fit.*

of noxious pinching, there were more pronounced increases in MAP (<12.9 mm Hg in 10 seconds), which were more closely correlated (Fig 3 open circles; $r^2 = 0.373$; $P = .05$) with increases in CSF pressure.

Discussion

Previous studies have shown that simultaneous CSF pressure recordings in the cisterna magna and level of the lumbar vertebral column in the same rat are within the same range[10] in contrast to intracranial pressure recordings, which are slightly higher than recordings from the cisterna magna.[15] The lumbar CSF pressures recorded at rest in this study are similar to previously published CSF pressures recorded at rest in the adult rat cisterna magna (mean, 6 ± 0.9 mm Hg)[15] and lumbar region (mean, 7.1 mm Hg; range, 6-8 mm Hg).[10] Furthermore, our lumbar CSF recordings showed variation with respiration that has previously been observed by others[10] and provides evidence that the CSF recordings in this study involved a closed CSF system.

Uniquely, however, this study examined the effects of static and dynamic vertebral displacements on mean CSF pressure and the 2 major CSF pressure oscillations—that at the respiratory rate and that at the rate of the low-frequency oscillation in BP. Experimental interventions involved (i) a dynamic sinusoidal oscillation; (ii) a static, ramp and hold displacement both with the vertebrae aligned and with the C2 vertebral axis of rotation offset to model an upper cervical subluxation; and (iii) a rapid low-amplitude displacement modeled on a clinical manipulative thrust.

Dynamic Oscillatory Displacements

Although there are no published data on the velocities of normal neck movements in the rat, the rates of oscillatory rotation of C2 used in this study appear to be at the lower end of the spectrum for voluntary neck movements in humans.[16] The dynamic oscillatory displacement produced neither a baseline shift in CSF pressure, nor any significant change in the powers of the 2 major frequency peaks of the power spectrum. Furthermore, there were no detectable oscillations in CSF pressure entrained to the imposed oscillations (1 and 2 Hz) of the C2 vertebra. These findings showed that the compliance of the subarachnoid space of the neuraxis is sufficient to effectively buffer any pressure or volume changes imposed by oscillatory movements of a single C2 vertebra within the range and rate limits used in this study.

Static Displacements

The aligned cervical ramp and hold displacement produced neither a baseline shift in CSF pressure, nor any significant change in the powers of the 2 major frequency peaks of the power spectrum. These findings confirm that the compliance of the subarachnoid space of the neuraxis is sufficient to effectively buffer the pressure and volume changes imposed by static displacement of C2 within the amplitude used in this study. However, a static offset ramp and hold displacement of C2, modeling subluxation, did induce a statistically significant increase in CSF pressure without a concomitant change in MAP. This suggests that the displacement of the vertebra caused a direct change in CSF pressure rather than a change mediated via altered BP.

An unambiguous definition or set of clinical determinants of subluxation have not yet emerged.[17,18] However, with regard to the model of upper cervical subluxation used in this study, frank malpositioning of the atlas on the axis is a well-documented phenomenon that alters not only gross static cervical positioning but also motion (see Takatori et al[19] and Yamazaki et al[20]). Furthermore, it has been shown in humans that whiplash injury alters the positioning of the instantaneous axis of rotation of the cervical vertebrae during movements.[5] Hence, in this study, upper cervical subluxation was modeled by offsetting the rostrocaudal axis of rotation of the C2 vertebra (the static component) and imposing a rotational displacement about this axis (the dynamic component).

The results obtained in this study suggest that with C2 set off-axis, rotational displacement compromised the subarachnoid space of the neuraxis so that it was not possible to buffer the pressure or volume changes imposed by displacement. Nonetheless, the powers of the 2 principal frequency peaks of the CSF power spectrum were unaffected.

Rapid Low-Amplitude Displacements

The rapid displacement was not associated with any short-term change in mean CSF pressure or MAP, nor were

there any changes in the powers of the 2 major frequency peaks of the CSF pressure power spectrum. Furthermore, within the limits of sensitivity of these experiments, in no instance did the impulse delivered to C2 result in a detectable CSF pressure impulse in the lumbar subarachnoid space. Although this is in contrast to the significant changes in pressures (range, 50-80 mm Hg) recorded in the cervical vertebral canal during a whiplash event involving a porcine model,[21] the porcine model used a head displacement and our study used isolated vertebral movements about a head fixed in space. These contrasting results suggest that any CSF pressure changes occurring during a whiplash event are likely to be associated with a shift of fluid volume involving the cranium rather than the influence of vertebral displacement. This also suggests that when SMT is performed in a way that primarily involves upper cervical vertebral movements with limited head movements, that the procedure is unlikely to modulate the mean CSF pressure.

Blood Pressure Challenge

Averaging BP over 1-second intervals (thus, several cardiac cycles) before onset of noxious stimulation confirmed that relatively small, short-term changes in BP (less than 1 mm Hg) do not significantly influence mean CSF pressure. However, acute changes in MAP (<12.9 mm Hg in 10 seconds) induced concomitant increases in CSF pressure (Fig 3). Hence, when interpreting the mechanisms by which vertebral positioning or motion might impact CSF pressure, it is necessary to take into account acute fluctuations in MAP.

Study Implications

Small displacements of C2 about its normal axis of rotation do not translate into statistically significant changes in CSF pressure nor in the power spectra of the normal oscillations in CSF pressure. This pressure-buffering capacity of the neuraxis is robust to both static and dynamic aligned displacements.

However, an offset rotation of C2, which is a malposition less than a dislocation modeling vertebral subluxation, did induce a statistically significant change in mean CSF pressure. This occurred without changes in MAP or in the powers of the 2 major peaks in the CSF pressure power spectrum. Thus, the CSF pressure change accompanying offset rotation was likely due to a combination of a volume change in the subarachnoid space and compromise of the compliance of the system. The offset positioning of C2 applied in this study resulted in complex coupled motion of the adjacent cervical vertebrae, which was visible under the dissecting microscope. Because the instantaneous axis of rotation shifts throughout imposed movement, it is not possible to provide a single mathematical measure of the degree to which the axis of rotation of C2 was offset. Nonetheless, considering that the cross-sectional diameter of the vertebral canal of C2 in the young adult rat has previously been shown to average 4.13 mm (range, 3.37-4.65 mm),[7] offsetting the manipulator laterally by 10 mm, as was done in this study, should probably be regarded as modeling subluxation at the upper end of the amplitude spectrum. Nonetheless, the absolute levels of CSF pressure achieved with this offset rotation (mean, 6.6; range, 5.6-7.7 mm Hg) were still within the ranges of CSF pressures of, and not significantly different (P = .717) from, those seen in animals before aligned (mean, 5.7; range, 3.9-7.5 mm Hg) or offset (mean, 6.2; range, 5.4-7.5 mm Hg) rotation.

Conclusion

Collectively, the results of this study suggest that short (<1 second) and long (~4 minutes) duration aligned displacements of C2 do not affect mean CSF pressure or CSF pressure dynamics. Neither does off-axis rotational displacement of C2 affect CSF pressure dynamics. However, offset rotation of C2 may manifest as a change in mean CSF pressure, which is, nonetheless, within normal physiological limits.

Practical Applications

- Subtle vertebral malpositioning or aberrant motion (vertebral subluxation) is considered by some chiropractors to disturb function in the spinal cord. One proposed mechanism is that this aberrant position or motion compromises CSF flow and pressure, which in turn alters spinal cord function.
- Spinal manipulative therapy has also been hypothesized to influence CSF pressure.
- This study, performed in the anesthetized rat shows that relatively low- and high-velocity static and dynamic rotations of the C2 vertebra, when in alignment, do not modulate CSF pressure.
- Offsetting the axis of rotation of the C2 vertebra, while not changing CSF dynamics, can induce a small but statistically significant change in mean CSF pressure.

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References

1. Keating JC. Philosophy in chiropractic. In: Haldeman S, editor. Principles and practice of chiropractic. 3rd ed. New York: McGraw-Hill; 2005. p. 77-97.
2. Mootz RD. Theoretic models of subluxation. In: Gatterman MI, editor. Foundations of chiropractic subluxation. 2nd ed. St Louis (MO): Elsevier Mosby; 2005. p. 228-44.
3. Wang YF, Gwathmey JK, Zhang G, et al. Cerebrospinal fluid may mediate CNS ischemic injury. Cerebrospinal Fluid Res 2005;2:7, doi:10.1186/1743-8454-2-7.
4. Benicio A, Moreira LF, Monaco BA, et al. Comparative study between ischemic preconditioning and cerebrospinal fluid drainage as methods of spinal cord protection in dogs. Braz J Cardiovasc Surg 2007;22:15-23.
5. Kaneoka K, Ono K, Inami S, Hayashi K. Motion analysis of cervical vertebrae during whiplash loading. Spine 1999;24: 763-9.
6. Herzog W, Conway PJ, Kawchuk GN, Zhang Y, Hasler EM. Forces exerted during spinal manipulative therapy. Spine 1993;180:1206-12.
7. Flynn JR, Bolton PS. Measurement of the vertebral canal dimensions of the neck of the rat with a comparison to the human. Anat Rec 2007;7:893-9.
8. Choo AM, Liu J, Lam CK, Dvorak M, Tetzlaff W, Oxland TR. Contusion, dislocation and distraction: primary hemorrhage and membrane permeability in distinct mechanisms of spinal injury. J Neurosurg Spine 2007;6:255-66.
9. Quinn KP, Winkelstein BA. Cervical facet capsular ligament yield defines the threshold for injury and persistent joint-mediated neck pain. J Biomech 2007;40:2299-306.
10. Kusaka G, Calvert JW, Smelley C, Nada A, Zhang JH. New lumbar method for monitoring cerebrospinal fluid pressure in rats. J Neurosci Methods 2004;135:121-7.
11. Budgell BS, Bolton PS. Cerebrospinal fluid pressure in the anaesthetized rat. J Manipulative Physiol Ther 2007;30: 351-60.
12. Bolton P, Budgell B, Kimpton A. Influence of innocuous cervical vertebral movement on the efferent innervation of the adrenal gland in the rat. Auton Neurosci 2006;124:103-11.
13. Christensen MG, Kollasch MW. Job analysis of chiropractic 2005. Colorado: National Board of Chiropractic Examiners; 2005. p. 135.
14. Graham BA, Clausen P, Bolton PS. A descriptive study of the force and displacement profiles of the toggle-recoil spinal manipulative procedure (adjustment) as performed by chiropractors. Man Ther 2010;15:74-9.
15. Zweinenberg M, Gong Q-Z, Lee LL, Berman RF, Lyeth BG. ICP monitoring in the rat: comparison of monitoring in the ventricle, brain parenchyma, and cisterna magna. J Neurotrauma 1999;16:1095-102.
16. Grossman GE, Leigh RJ, Abel LA, Lanska DJ, Thurston SE. Frequency and velocity of rotational head perturbations during locomotion. ExpBrain Res 1988;70:470-6.
17. Monckeberg JE, Tome CV, Matias A, Alonso A, Vasquez J, Zubieta JL. CT scan study of atlantoaxial rotatory mobility in asymptomatic adult subjects: a basis for better understanding C1-C2 rotatory fixation and subluxation. Spine 2009;34: 1292-5.
18. Leboeuf-Yde C. How real is the subluxation? A research perspective. J Manipulative Physiol Ther 1998;21:492-4.
19. Takatori R, Tokunaga D, Inoue N, Hase H, Harada T, Suzuki H, Ito H, Nishimura T, An HS, Kubo T. In vivo segmental motion of the cervical spine in rheumatoid arthritis patients with atlantoaxial subluxation. Clin Exp Rheumatol 2008;26: 442-8.
20. Yamazaki M, Someya Y, Aramomi M, Masaki Y, Okawa H, Koda M. Infection-related atlanto-axial subluxation (Grisel syndrome) in an adult with Down syndrome. Spine 2008;33: E156-160.
21. Örtengren T, Hansson H-A, Lövsud P, Svensson MY, Suneson A, Säljö A. Membrane leakage in spinal ganglion nerve cells induced by experimental whiplash extension motion: a study in pigs. J Neurotrauma 1996;13:171-80.