



THE PROMISE
OSTEOPATHY'S PROMISE TO CHILDREN



Foundations of Osteopathy in the Cranial Field

Evidence Supportive of the Theory and Clinical Benefits

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Disclosures:

I am a paid consultant for Osteopathy's Promise to Children, the accredited sponsor of this CME activity.

Learning Objectives:

After viewing the power-point presentation and participating in the presentation, the participant will be able to:

1. Describe the research related to the 5-Phenomena of the Primary Respiratory Mechanism (PRM).
2. Discuss the research supportive of cranial bone motion and clinical benefit of OCF.
3. Describe areas of future research related to the practice of OCF.

Evidence-Based Medicine Research

OMT and OCF

Licciardone JC, Brimhall AK, King LN. Osteopathic manipulative treatment for low back pain: a systematic review and meta-analysis of randomized controlled trials. *BMC Musculoskelet Disord.* 2005;6:43.

These studies comprised the systematic review and meta-analysis

Andersson GBJ, Luente T, Davis AM, et al. A comparison of osteopathic spinal manipulation with standard care for patients with low back pain. *N Engl J Med.* 1999;341:1426-1431.

Burton AK, Tillotson KM, Cleary J. Single-blind randomized controlled trial of chemonucleolysis and manipulation in the treatment of symptomatic lumbar disc herniation. *Eur Spine J.* 2000;9:202-207.

Cleary C, Fox JP Menopausal symptoms; an osteopathic investigation. *Complement Ther Med.* 1994;2:181-186

Gibson T, Greahme R, Harkness J et al. Controlled comparison of short-wave diathermy treatment with osteopathic treatment in non-specific low back pain. *Lancet.* 1985; I: 1258-1261.

Hoehler FK, Tobis JS, Buerger AA. Spinal manipulation for low back pain. *J Am Med Assoc.* 1981;245:1835-1838.

Licciardone JC, Stoll ST, Fulda KG, et al. Osteopathic manipulative treatment for chronic low back pain: a randomized controlled trial. *Spine.* 2003;28:1355-1362.

OMT and Chronic Low Back Pain

Licciardone JC, Brimhall AK, King LN: Osteopathic manipulative treatment for low back pain: a systematic review and meta-analysis of randomized controlled trials. *BMC Musculoskelet Disord* 2005., 6:

This figure from – Licciardone JC. Osteopathic research: elephants, enigmas, and evidence. *Osteo Med Primary Care* 2007 1:7

Osteopathic Medicine and Primary Care 2007, 1:7

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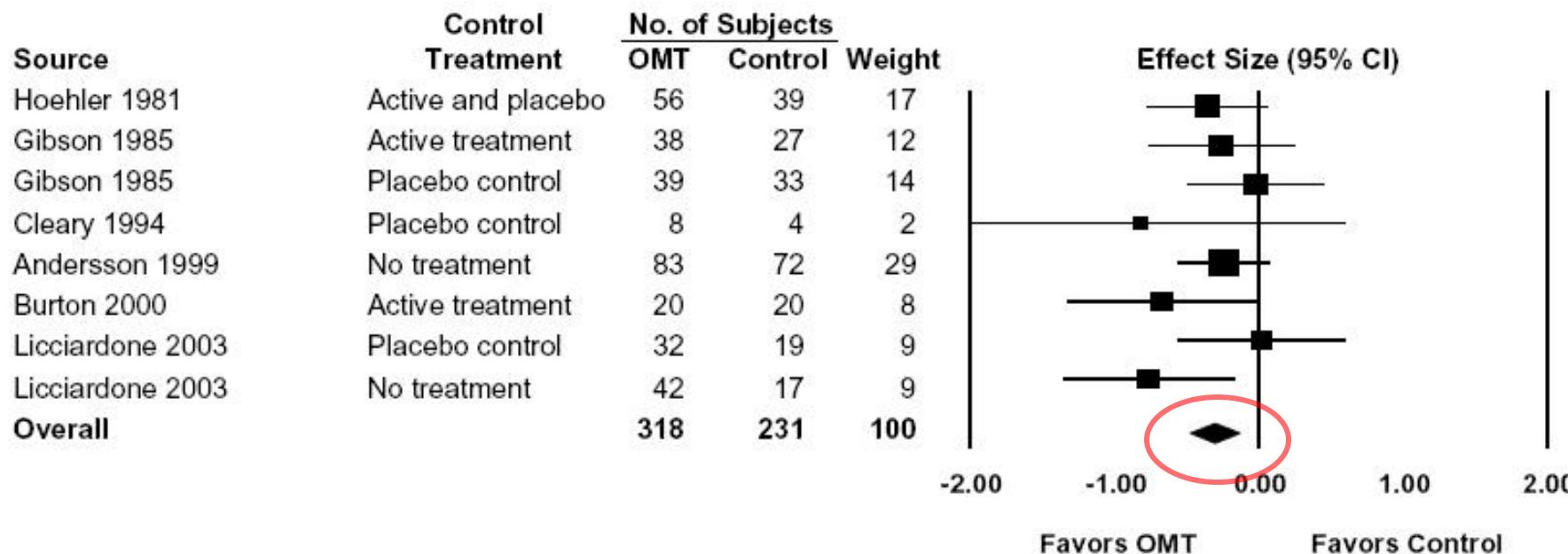


Figure 3

Meta-analysis results for osteopathic manipulative treatment (OMT) of low back pain. The overall effect size was -0.30 (95% confidence interval [CI], -0.47 – -0.13; $P = .001$). Source citations are available in reference 5.

Newborns and Children

Neonatal ICU

Cerritelli F, Pizzolorusso G, Ciardelli F, La Mola E, Cozzolino V, Renzeti C, D'Incecco C, Fusilli P, Sabatino G, Barlafante G. Effect of osteopathic manipulative treatment on length of stay in a population of preterm infants: **a randomized controlled trial**. *BMC Pediatrics*. 2013;13:65.

Initially 110 patients were **randomized**, 55 to experimental group (standard care plus osteopathic evaluation and intervention) and 55 to control group (standard care plus osteopathic evaluation only).

The osteopathic intervention took place twice a week and consisted of 20 minutes of myofascial release, balanced ligamentous/membranous tension, **cranial and indirect fluidic and v-spread**.

The study was single-blind in that the osteopaths knew and recorded what they provided in the intervention. For the **control group**, the osteopaths did approximately **10 minutes of evaluation and then just stood in front of the incubators for the remainder of the 20 minutes**.

Cerritelli et al 2013

The mean LOS for the experimental group was **26.1±16.4** days and control group **31.3±20.2** days for a difference of 5.9 days (**p < 0.03**).

Table 3 Results of ordinary least square regression for cost estimates

	Costs (2012€)		
	Estimate	95% C.I.	p>x2
Male	576.14	-173.65 , 1325.93	0.13
Gestational Age	-120.76	-371.79 , 130.27	0.34
Birth Weight (gr)	0.49	-0.43 , 1.43	0.28
LOS	78.96	38.17 , 119.75	<0.001
OMT	-2,724.91	-3,491.73 , -1,958.09	<0.001

The weight gain was not significant (**p < 0.06**).

Table 2 Results of multivariate linear regression

	LOS (days)			Av. daily weight gain (gr)		
	β	95% C.I.	Pr(> t)	β	95% C.I.	Pr(> t)
Male	-1.899	-3.930 , 0.127	0.07	0.708	-3.067 , 4.483	0.71
Gestational Age	-3.373	-3.916 , 2.830	<0.001	-0.338	-1.344 , 0.668	0.51
Birth Weight (gr)	-0.014	-0.016 , -0.009	<0.001	-0.018	-0.022 , -0.014	<0.001
Milk Volume at Study Enrollment (mL)	0.002	-0.004 , 0.009	0.44	0.059	0.045 , 0.072	<0.001
OMT	-5.906	-7.944 , -3.869	<0.001	3.707	-0.065 , 7.479	0.06

Cerritelli F, Pizzolorusso G, Renzetti C, Cozzolino V, D'Orazio M, Lupacchini M, Marinelli B, Accorsi A, Lucci C, Lancellotti J, Ballobio S, Castelli C, Molteni D, Besana R, Tubaldi L, Perri FP, Fusilli P, D'Incecco C, Barlafante G. A multicenter, randomized controlled trial of osteopathic manipulative treatment on preterms. *Plos One*. 2015;10(5):e0127370.

3 different NICUs in central Italy

N = 695 Study Group N = 352 Control Group N = 342

LOS: Study Group 13.8 ± 8.1 Control Group N = 17.5
± 14.4 (*P < 0.001*)

Weight gain analysis showed no difference between the groups

Cost saving determined to be 1,586 € (*P < 0.001*)

Systematic Review and Meta-Analysis

Lanaro D, Ruffini N, Manzotti A, Lista G. Osteopathic manipulative treatment showed reduction of length of stay and costs in preterm infants. *Medicine*. 2017;96(12):1-8.

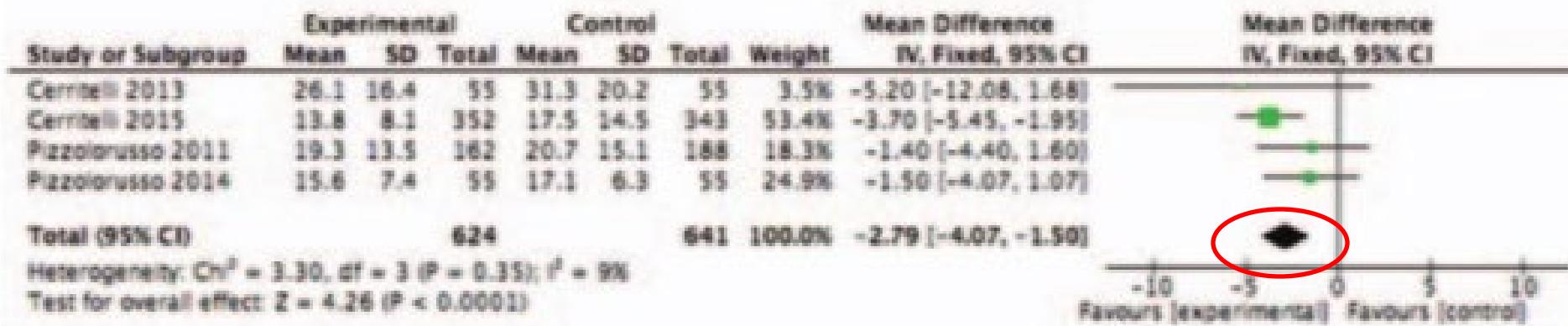


Table 2
Summary of results of meta-analysis.

Outcome	No of studies included in the meta-analysis (no of patients)	Mean effect of OMT on preterm infants versus usual care group (95% CI)	P
LOS (days)	5 (1306)	Decrease in preterm infants treated by OMT by 2.71 (95% CI -3.99, -1.43)	<0.001
Cost (Euros)	3 (915)	Preterm infants costs decreased in the OMT group (-1545.66 €; -1888.03, -1203.29€)	<0.0001
Subgroup analysis: LOS (days) <32 weeks	2 (118)	Decrease in preterm infants with severe prematurity treated with OMT (-8.64 days; 95% CI -13.46, -3.81 days)	<0.001
Subgroup analysis: LOS (days) >32; <35 weeks	3 (311)	Shorten in moderate preterm infants allocated to OMT group (-3.08 days; 95% CI -5.16, -0.99 days)	<0.01
Subgroup analysis: LOS (days) >35; <37 weeks	3 (477)	Diminish in late preterm infants treated by OMT (-2.21 days; 95% CI -3.63, -0.78 days)	<0.01

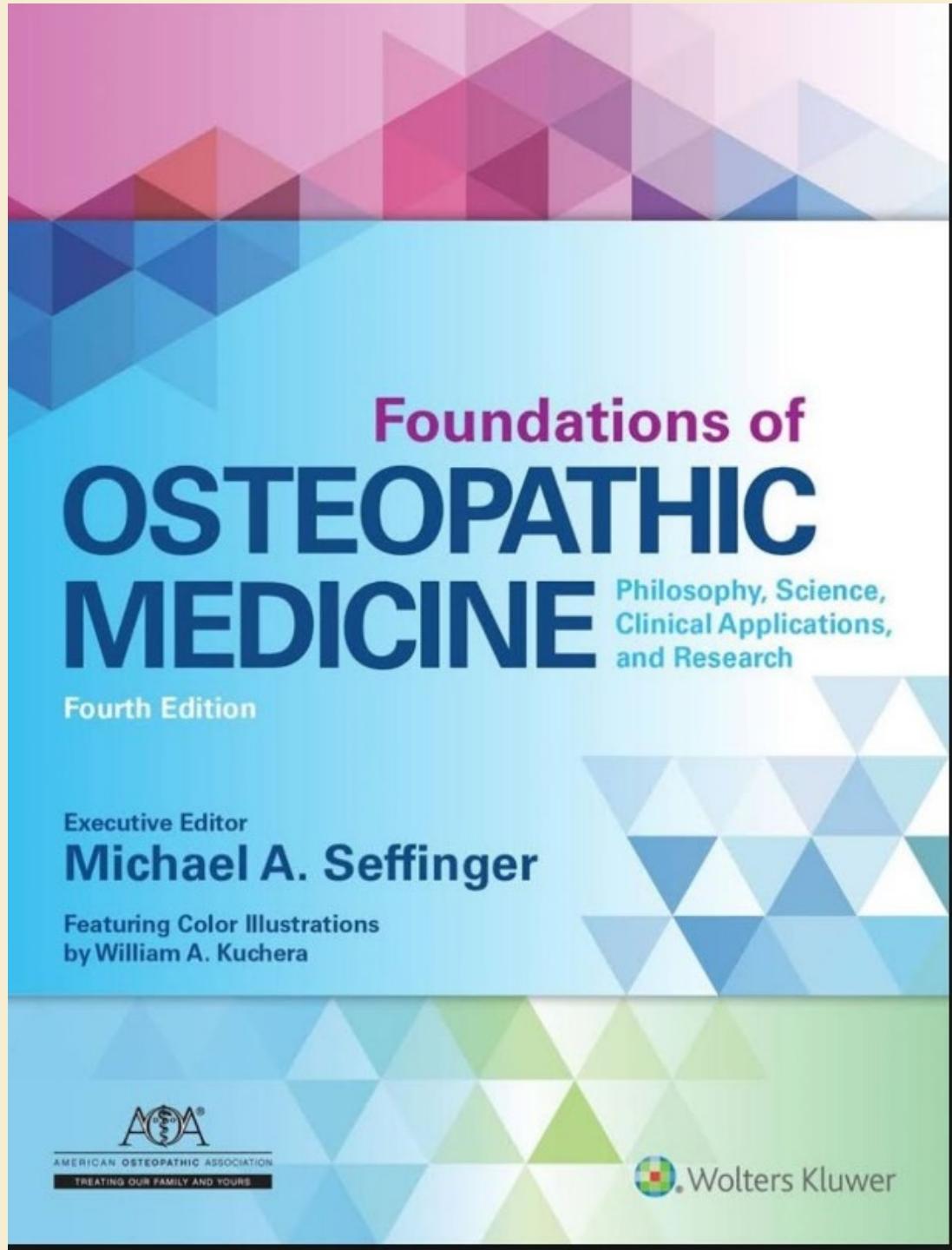
LOS = length of stay, OMT = osteopathic manipulative treatment.

Chapter 38

Osteopathic Cranial Manipulative Medicine

Working on the 5th Ed.

Due to be published
2024



Where did it all start?

Originally the OMT procedures you are studying were called

Osteopathy in the Cranial Field (OCF)



We like this one because of the emphasis on Osteopathy

Sometimes called Cranial Osteopathy.

Now the AOA approved term is OCMM.

William Garner Sutherland, D.O.



- 1873-1954
- Student of AT Still (~1900)
- The Cranial Bowl, published 1944

It has been said that Sutherland did for the head what Still did for the rest of the body.

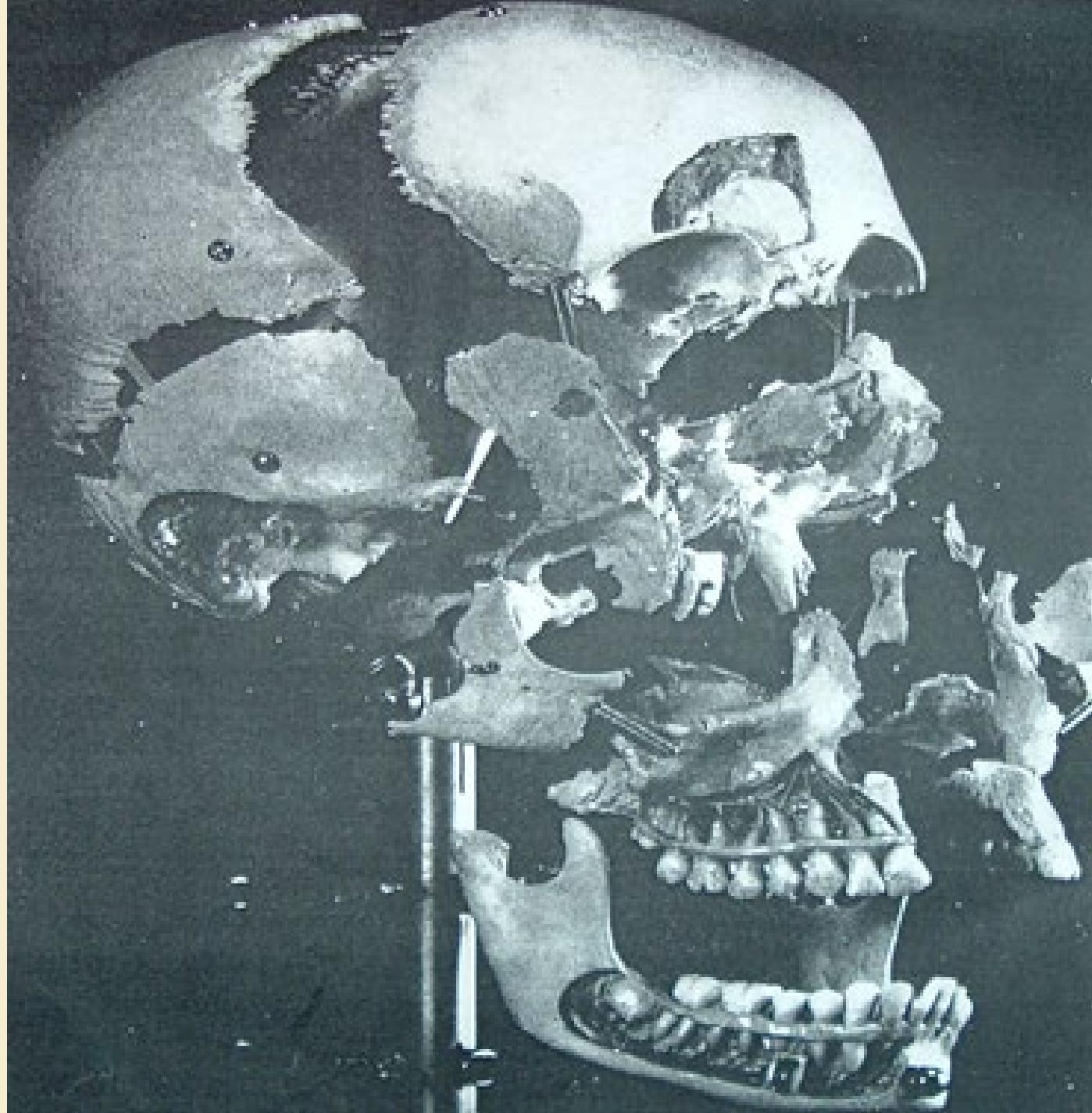


William G. Sutherland, D.O., D.Sc. (hon.)
signing the charter incorporating the SCTF



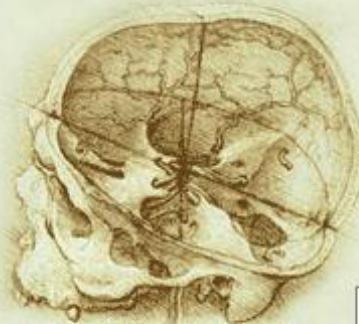
Beauchêne Disarticulated Skull

If nothing else in this course you should become aware of both the strength and fragility of the skull's structure which may inform your ability to assess and treat cranial trauma.



Circa 1953





The Osteopathic Cranial Academy



HOME OSTEOPATHY RESEARCH BOOKS CURRICULUM MEMBERSHIP CONTACT US

RESEARCH

Intro to Research

CNS Motility

CSF Fluctuation

Dural Mobility

Cranial Bone Mobility

Sacral Motion

Clinical Research

Glossary of Terms

Download In-Depth
Research Article



Research

Research supporting Osteopathy in the Cranial Field (OCF) had been well established in the scientific literature long before William Garner Sutherland's first documentation of the Primary Respiratory Mechanism in the late 1920's.^{1,2,3,4} Like Dr. Still, Dr. Sutherland based his concepts on systematic observation, private research, and the published science and philosophy of his time.

In 1914 Louisa Burns DO began her landmark osteopathic research.⁵ Since then, the osteopathic profession has continued to pursue disciplined research concerning osteopathic principles.^{6,7} A significant body of research produced by independent scientists and other health care professions has also proven supportive of OCF.⁸

Today, research supportive of the cranial concept is flourishing. Recent technological advances and increased funding have enabled research scientists to further study the fundamental principles of OCF.

Research supporting OCF can be classified into three basic categories:

1. Explaining the underlying physiology (how things work). Dr. Sutherland described **five phenomena** as the basic premise for OCF. Links are provided below to explore relevant research.
 - a. **The inherent motility of the brain and spinal cord.**
 - b. **The fluctuation of cerebrospinal fluid.**
 - c. **The mobility of intracranial and intraspinal membranes.**
 - d. **The articular mobility of the cranial bones.**
 - e. **The involuntary mobility of the sacrum between the ilia.**
2. Confirming the **positive clinical effects of treatment.**
3. Verifying **palpatory reliability**

OCF has been substantiated by a sound body of scientific and clinical research. Further research is important for the continued understanding and confirmation of osteopathic principles and practice.



Primary Respiratory Mechanism has five phenomena:

1. The motility (inherent rhythmic motion) of the brain and spinal cord.
2. The fluctuation of the cerebrospinal fluid (CSF) that bathes and nourishes the brain and spinal cord.
3. The mobility of intracranial and intraspinal membranes. This entire membranous structure acts as a unit and is called a “Reciprocal Tension Membrane.”
4. The articular mobility of the cranial bones.
5. The involuntary motion of the sacrum between the ilia.

Osteopathic Cranial Manipulative Medicine (OCF/OCMM)

- “A system of diagnosis and treatment by an osteopathic practitioner using the primary respiratory mechanism and balanced membranous tension.”
- ECOP 2019 Glossary of Osteopathic Terminology

In previous editions of this presentation I used to say 4 phenomena were not controversial, one was still – sort of, was....^{controversial}

- The inherent rhythmic motion of the brain and spinal cord.
- The fluctuation of the cerebrospinal fluid (CSF) that bathes and nourishes the brain and spinal cord.
- The shifting tensions of the membranous envelope (dura mater) surrounding the brain and spinal cord.
- **Articular mobility of the cranial bones** – I contend is no longer controversial.
- Involuntary mobility of sacrum between the ilia

Here is a very brief overview of evidence supporting the previously non-controversial PRM phenomena

The inherent rhythmic motion of the brain and spinal cord

Grietz D, Wirestam R, Franck A, et al. Pulsatile brain movement and associated hydrodynamics studied by magnetic resonance phase imaging: The Monro-Kellie doctrine revisited. *Neuroradiology* 1992; 34:370-380.

Describe motion in certain areas in the range of 1.0 mm to 1.5 mm.

Poncelet BP, Wedeen VJ, Weisskoff RM. Brain parenchyma motion: measurement with cine echo-planar MR imaging. *Radiology* 1992; 185:645-651.

Brain motion consists of a single displacement in systole followed by a slow return in diastole with velocities ≤ 2 mm/sec.

Associated with cardiac cycle

The fluctuation of the cerebrospinal fluid (CSF)

DuBolay GH, O'Connell J, Currie J, et al. Further investigations on pulsatile movements in the cerebrospinal fluid pathways. *Acta Radiol Diagnost* **1971**;13:496-523.

“The majority of workers throughout these seven decades have become convinced that the ‘cardiac’ CSF pressure rise measured in the ventricles, at the cisterna magna and in the lumbar theca, is caused by the rhythmic arterial input of blood to the cranial cavity.”

*In the Rule of the Artery courses we learn there is more to this phenomenon. Other rhythms may be at work. HR 60-80/min. CRI 6-12/min.

CSF fluctuation rates vary by area and condition of the person

Levy LM, DiChiro GD, McCollough DC, et al. Fixed spinal cord: Diagnosis with MR imaging. *Radiology* 1988;169:773-778.

In healthy Ss spinal CSF motion rate is 12.4 ± 2.92 mm/sec.

Ss with spinal dysraphism (spina bifida) 2.12 ± 1.69 mm/sec.

“The origin of cord pulsations is compatible with a direct transfer of motion from brain pulsations.”

The mobility of intracranial and intraspinal membranes.

(This entire membranous structure acts as a unit and is called a “Reciprocal Tension Membrane”)

The existence of this anatomy is not controversial.
“Mobility” has been shown.

Neurosurgeons talk about it all the time, just ask them when you do a rotation on a neurosurgery service.

Mobility of Intracranial and Intraspinal Membranes

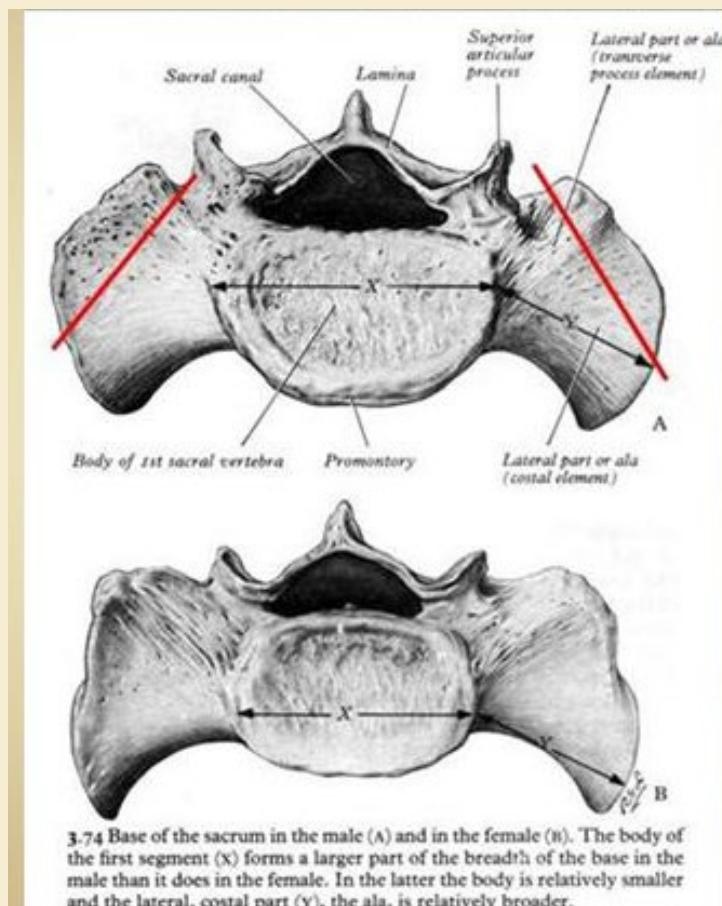
Kostopoulos DC, Keramidas G. Changes in elongation of falx cerebri during craniosacral therapy techniques applied on the skull of an embalmed cadaver. *J Craniomandibular Practice* 1992;10:9-12.

- The brain tissue was removed leaving intact the three divisions of the dural membranes. Oscilloscope recorded piezoelectric element attached to falx cerebri. **Frontal lift = 1.44mm elongation and parietal lift = 1.08mm elongation.**
- This observable motion of dural membrane tissue by cranial bone pressure is also a demonstration of the continuity of cranial bone and dural-fascial structures.



The involuntary motion of the sacrum between the ilia

This is not disputed, Iliosacral motion has been established for many years. It would be hard to walk if not true.



3.74 Base of the sacrum in the male (A) and in the female (B). The body of the first segment (X) forms a larger part of the breadth of the base in the male than it does in the female. In the latter the body is relatively smaller and the lateral, costal part (Y), the ala, is relatively broader.

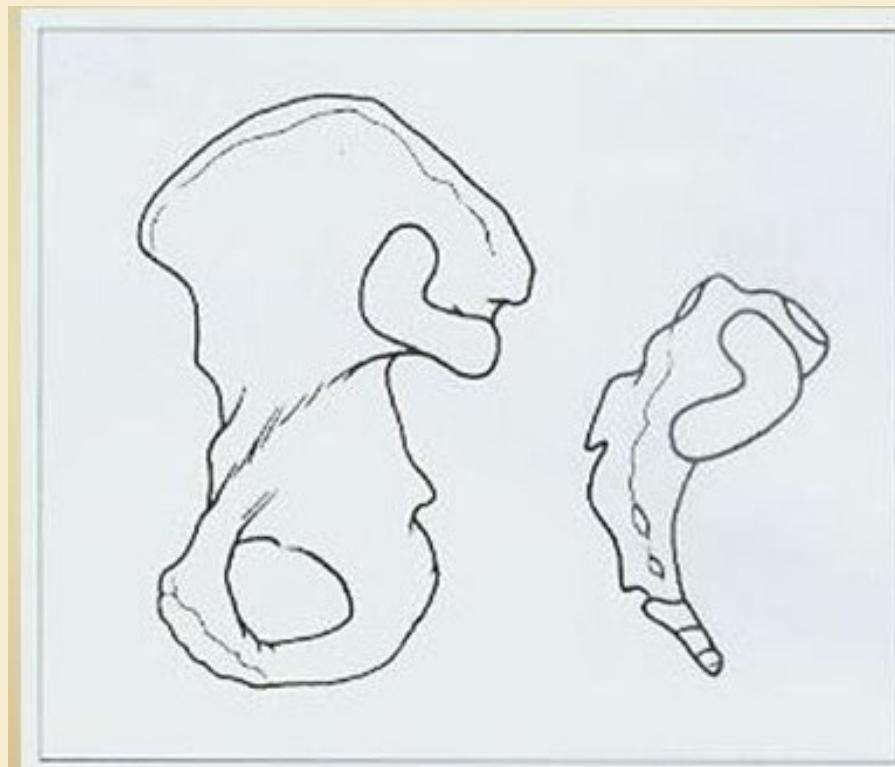


Fig. 3.50 Anatomic representation of the sacroiliac joint.

Before turning to the cranial bone motion:

To see all of the research I have presented demonstrating the validity of the Primary Respiratory Phenomena” I refer the participants to the *FOM 4e* OCMM chapter, as well as to **Chapter 6** by Glonek, Sergueef & Nelson, “Inherent Motion, Rhythms, and Oscillations.”

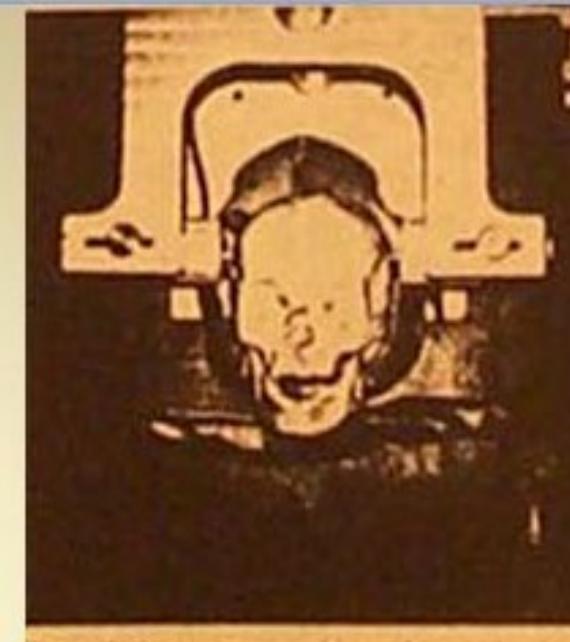
Chapter 6 gives the most comprehensive discussion of all the various “rhythms” commonly described in the practice of OCF.

Unless you are looking for it, one tends to go right by it to the chapters on the techniques.

Pioneering research on cranial bone motion

Frymann VM. A study of the rhythmic motions of the living cranium. *J Am Osteopath Assoc.* 1971;70:1-18.

Cranial motion was recorded simultaneously with thoracic respiration. Frymann concluded that a rhythmic pattern of cranial bone mobility exists and moves at a rate that is different than that of thoracic respiration.



Methodology

The skull device was inserted under sterile conditions approximately 1 mm into the outer plate of the calvaria. This point was approximately 6 cm above the external auditory meatus. A base reading was



FIG. 1. Head holder modified to incorporate two strain gauges on the concave surface of a plastic bridge.

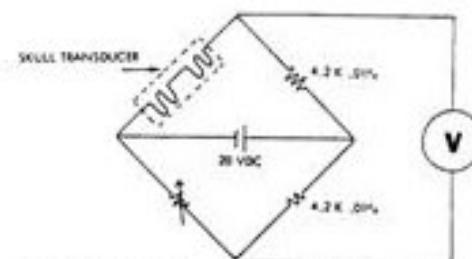


FIG. 2. Skull transducer as part of a Wheatstone bridge. V = voltmeter.

Heifitz MD, Weiss M. Detection of skull expansion with increased intracranial pressure. *J Neurosurg* 1981;55:811-812.

Using a stain gauge device, they were able to demonstrate cranial vault expansion associated with an artificial rise in intracranial pressure (ICP) in two comatose patients.

Contemporary cranial bone research

Rasmussen TR, Meulengracht KC. Direct measurement of the rhythmic motions of the human head identifies a third rhythm. *J Bodyw Mov Ther.* 2021: doi [10.1016/j.jbmt.2020.08.018](https://doi.org/10.1016/j.jbmt.2020.08.018)

Introduction: Central to the osteopathic cranial field, and at the same time controversial, is the concept of a unique rhythmic movement believed to originate from a primary respiratory mechanism (**PRM**). Further, the PRM is reported to manifest as a cranial rhythmic impulse (**CRI**) on the living human skull. This study explores the rhythmic oscillations of the human head measured directly as physical movements. The aim is to **investigate the existence of a third rhythm** distinct from the head movements caused by respiratory breathing and arterial pulsing, in an objective and purely experimental study.

Experimental: In 50 healthy individuals, rhythmic oscillations of the head were measured in real-time for 42 min in a supine resting state without any intervention. A newly developed machine for tracking rhythmic movements was used for measurements.

Results: In all individuals, a third rhythm was distinguished as separate from the arterial and respiratory rhythm at all times. The third rhythm was observed as a dynamic physiological phenomenon with a narrow range in resting healthy individuals with a mean of 6.16 cycles/minute (4.25-7.07). The significant contribution to the amplitude of the measured movements was the respiratory breathing and this third rhythm, whereas the contribution from the arterial pulsing were minor.

Conclusion: The present study demonstrates the existence, and normative range of a third physical rhythm detected on the human head. Having developed an objective approach to studying this third rhythm might form the future basis for clinical and physiological studies of craniosacral function and dysfunction.

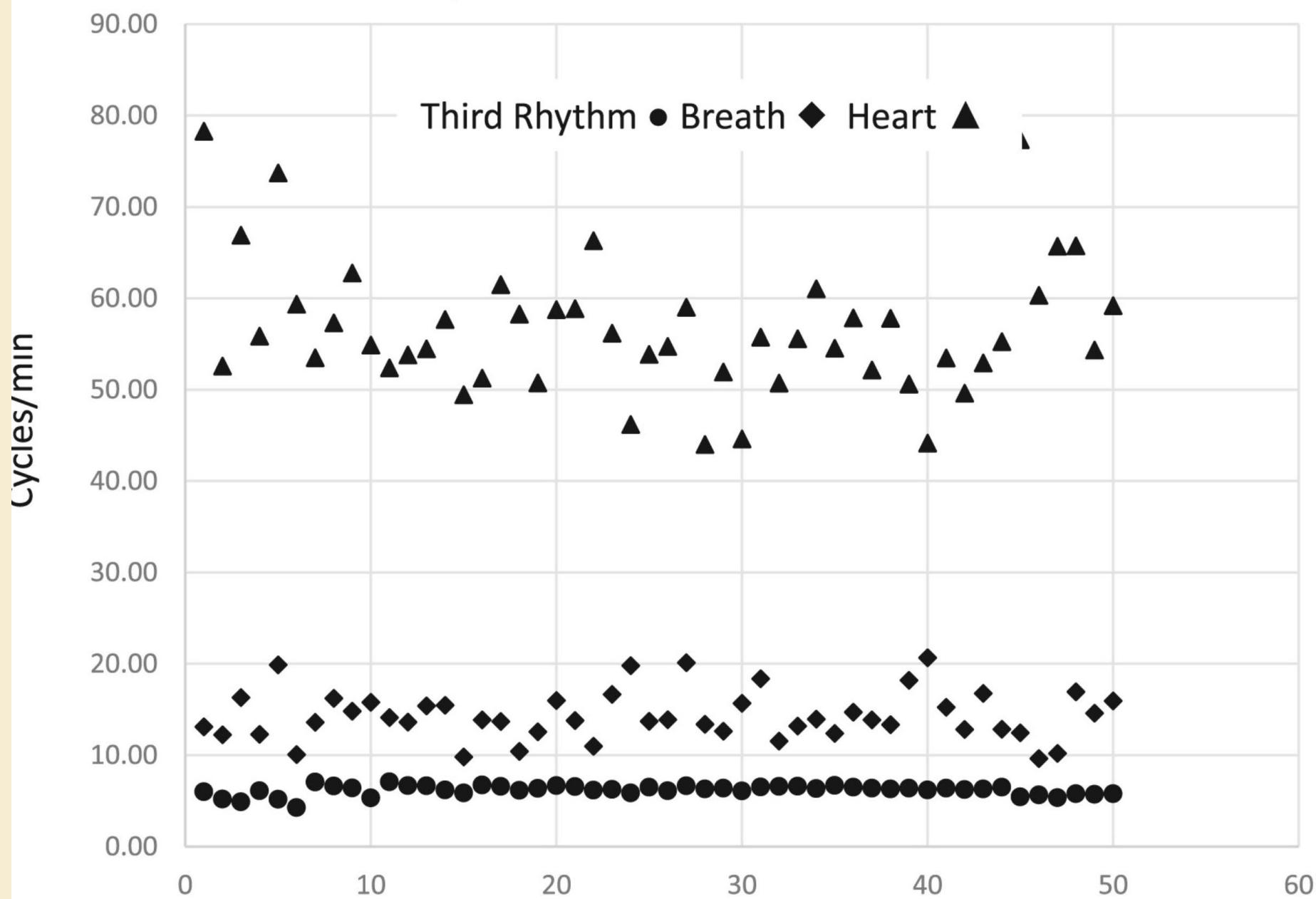


Figure 11. Actuator set-up with test person



The actuator measures movements on the wart-shaped part of the ear bone.

Different Rhythmic Movements on the Human Skull



Research suggests cranial sutures can remain patent and may never fuse.

Sabini RC, Elkowitz DE. Significance of differences in patency among cranial sutures. *J Am Osteopath Assoc.* 2006;106(10):600-604.

The external morphology of the **coronal**, **sagittal** and **lambdoid sutures** was evaluated in **thirty-six human cadaver skulls**. Each suture was described using a modified grading scale (4 grades) to quantify the extent of sutural patency and obliteration. Four findings were observed:

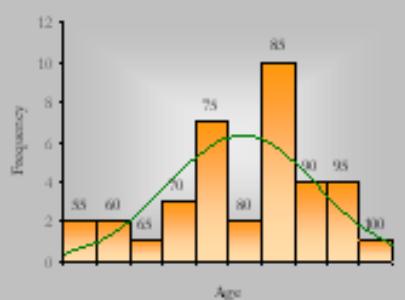
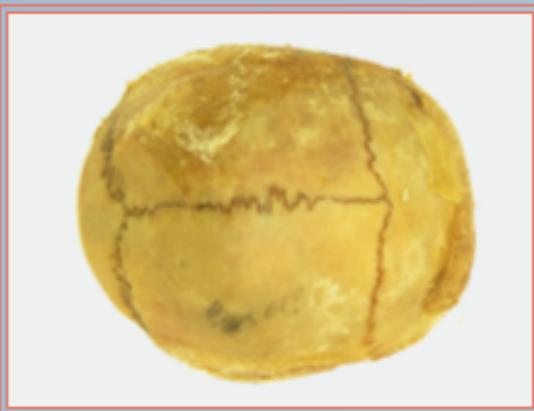


Figure 1. Sagittal Suture Grade I



Suture Grade	Degree of Sutural Closure
0	Open, not fused at any point
I	Fused, not obliterated at any point
II	<50% Obliterated
III	>50% Obliterated
IV	100% Obliterated

Figure 2. Sagittal Suture Grade II



Figure 3. Sagittal Suture Grade III



Figure 4. Sagittal Suture Grade IV



Results

- 1) all three sutures were intercorrelated**
- 2) the lambdoid suture was most likely to be patent and least likely to be obliterated when compared to the sagittal suture,[due to the larger number of muscles attached on the occiput than to area of the sagittal suture.**
- 3) no difference in suture grades was found between male and female cadavers and**
- 4) no significant difference was found between age and grading of the sutures.**

Sabini and Elkowitz go on to say, “The theory that external forces maintain suture patency and complexity can be supported by morphologic characteristics of facial sutures, which are more serrated and interdigitated and remain patent for longer periods of time.¹⁻³ This difference can be presumed to correlate with facial muscles necessary for speaking, mastication, and facial expression.”

1. Saito K, Shimizu Y, Ooya K. Age-related morphological changes in squamoujs and parietomastoid sutures of human cranium. *Cells Tissues Organs*. 2002;170:266-273.
2. Herring SW. Sutures – a tool in functional cranial analysis. *Acta Anat (Basel)*. 1972;83:222-247
3. Wagemans PA, van de Velde JP, Kuijpers-Jagtman AM. Sutures and forces: a review. *Am J Orthod Dentofacial Orthop*. 1988;94:129-141.



NASA Studies

Ballard RE, Wilson M, Hargens AR, et al. Noninvasive measurement of intracranial volume and pressure using ultrasound. *American Institute of Aeronautics and Astronautics Life Sciences and Space Medicine Conference*. Book of Abstracts, pp. 76-77, Houston, TX, 3-6 March 1996.

Ueno T, Ballard RE, Cantrell JH, Yost WT, Hargens AR. Noninvasive estimation of pulsatile intracranial pressure using ultrasound. 1996 *Research & Technology: Human Exploration and Development of Space Enterprise: Technology Applications to Human Health*. NASA Ames Research Center.

Ueno T, Ballard RE, Shuer LM, Yost WT, Cantrell JH, Hargens AR. Ultrasonic measurement of intracranial pressure waveforms. 1997. *Aeronautics & Space Transportation Technology Enterprise*. NASA Ames

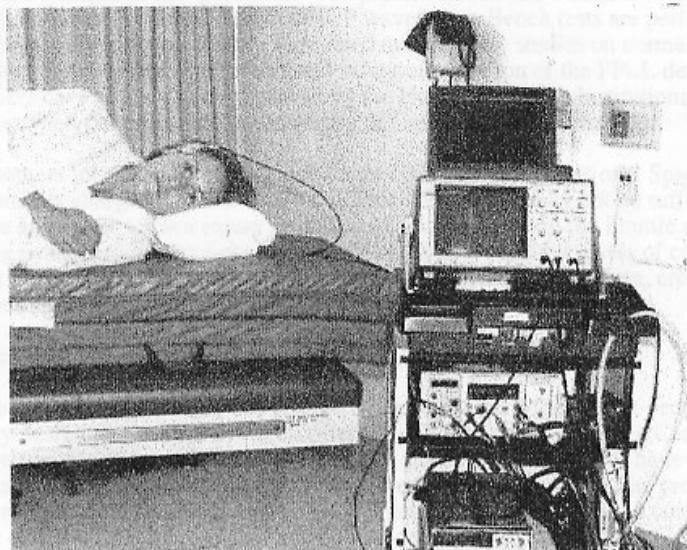
Ueno T, Ballard RE, Shuer LM, Yost WT, Cantrell, Hargens AR. Noninvasive measurement of pulsatile intracranial pressure using ultrasound. 1998 *Acta Neurochir (Wien)* S74: in press.

Hargens AR. Noninvasive intracranial pressure (ICP) measurement. 1999 *Space Physiology Laboratory*.

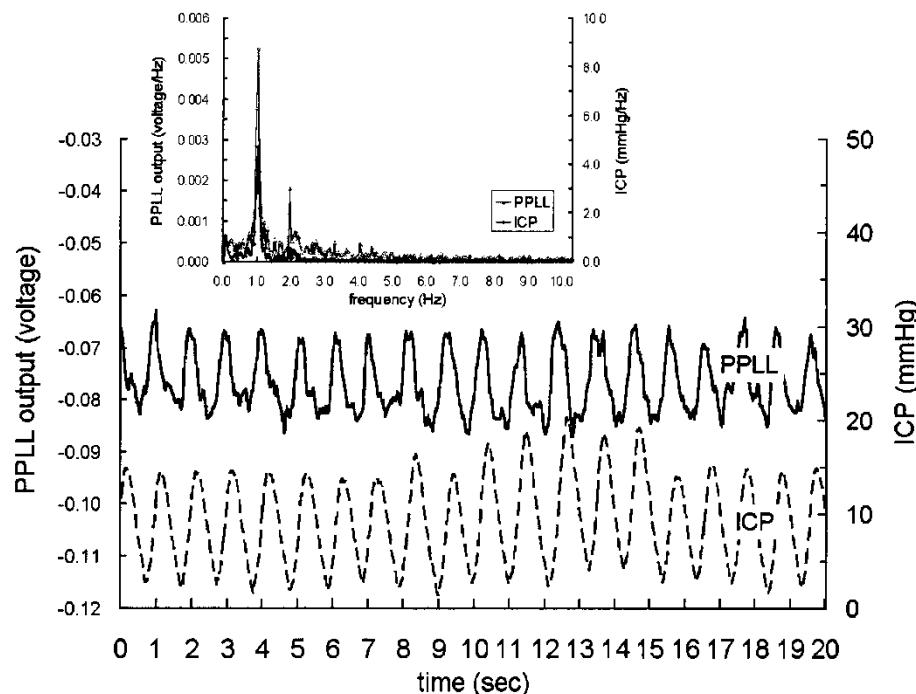
<http://spacephysiology.arc.nasa.gov/projects/icp.html>

- Developed an ultrasound device: (PPLL) sensitivity to **0.1 μm** .
- 3 fresh **cadavers** (ages 85-90).
- Infused saline into 3rd ventricle at a rate of 1 cycle/second (1 hertz). Intracranial diameter (ICD) increased linearly ($\text{ICD} = 0.003(\text{ICP}) - 0.016$, $r=0.91$) with graded elevation of ICP, such that an ICP change of 15 mmHg caused a skull expansion of **0.029mm (29 μm)**

Noninvasive Intracranial Pressure Monitoring



This photograph shows the transducer set upon the subject's temple. The image on the monitor shows reflection patterns within her head.



Ueno T, et al. 1996

6 live humans (ages 18-31)

90° upright, 30°, 0°, -6°, -10°, -6°, 30°, and 90°.

Each angle was maintained for 1 minute. Average path length from forehead to occipital bone increased **1.038 ± 0.207mm** at 10° head-down tilt relative to 90° upright values.

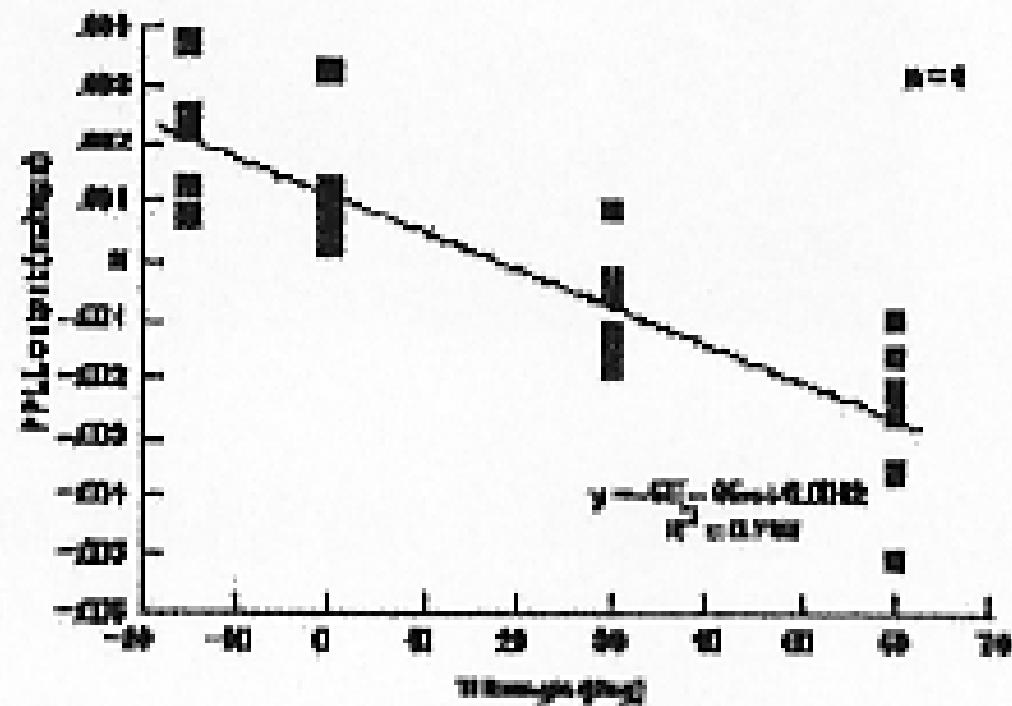


Fig. 2. Results of tilt study ($n = 6$). Amplitudes of pulsatile changes in the PPLL output are shown against the tilt angles. A linear regression line is superimposed.

Cranial Diameter Pulsations Measured by Non-Invasive Ultrasound Decrease with Tilt

TOSHIAKI UENO, RICHARD E. BALLARD, BRANDON R. MACIAS,
WILLIAM T. YOST, AND ALAN R. HARGENS

UENO T, BALLARD RE, MACIAS BR, YOST WT, HARGENS AR. *Cranial diameter pulsations measured by non-invasive ultrasound decrease with tilt*. Aviat Space Environ Med 2003; 74:882–5.

Introduction: Intracranial pressure (ICP) may play a significant role in physiological responses to microgravity by contributing to the nausea associated with microgravity exposure. However, effects of altered gravity on ICP in astronauts have not been investigated, primarily due to the invasiveness of currently available techniques. We have developed an ultrasonic device that monitors changes in cranial diameter pulsation non-invasively so that we can evaluate ICP dynamics in astronauts during spaceflight. This study was designed to demonstrate the feasibility of our ultrasound technique under the physiological condition in which ICP dynamics are changed due to altered gravitational force.

Methods: Six healthy volunteers were placed at 60° head-up, 30° head-up, supine, and 15° head-down positions for 3 min at each angle. We measured arterial blood pressure (ABP) with a finger pressure cuff, and cranial diameter pulsation with a pulsed phase lock loop device (PPLL). **Results:** Analysis of covariance demonstrated that amplitudes of cranial diameter pulsations were significantly altered with the angle of tilt ($p < 0.001$). The 95% confidence interval for linear regression coefficients of the cranial diameter pulsation amplitudes with tilt angle was 0.862 to 0.968. However, ABP amplitudes did not show this relationship. **Discussion:** Our noninvasive ultrasonic technique reveals that the amplitude of cranial diameter pulsation decreases as a function of tilt angle, suggesting that ICP pulsation follows the same relationship. It is demonstrated that the PPLL device has a sufficient sensitivity to detect changes non-invasively in ICP pulsation caused by altered gravity.

Keywords: ultrasound, pulsed phase lock loop, postural change, intracranial pressure.

that we can evaluate ICP dynamics in astronauts during spaceflight. The device was originally developed by Yost and Cantrell at NASA Langley Research Center, and has been refined in collaboration with the Space Physiology Laboratory at NASA Ames Research Center.

The purpose of the present study was to demonstrate the feasibility of our ultrasound technique under the physiological condition in which ICP dynamics are changed due to altered gravitational force. For this purpose, whole body tilting was performed to observe effects of an altered gravity vector on ICP dynamics in normal volunteers. Whole body tilting generates a hydrostatic pressure gradient by altering gravitational force along the body axis. It is reported that postural changes alter the mean value and amplitude of ICP pulsation (2,4,6).

METHODS

Procedure

NASA Ames Human Research Institutional Review Board approved this study. After giving informed written consent, six healthy volunteers including two men and four women, age (mean \pm SD) of 24 \pm 4 yr, height

Ueno T, Ballard RE, Cantrell JH, et al. 1996.

“In other words, when intracranial pressure increase, arterial pulsation produces a higher amplitude ICP pulsation. Increased amplitude of ICP pulsations will be manifested by larger fluctuations in distance across the skull.”

“Although the skull is often assumed to be a rigid container with a constant volume, we and others have demonstrated that the skull moves on the order of a few μm in association with arterial pressure (systolic/diastolic) and changes in ICP pulsations.”

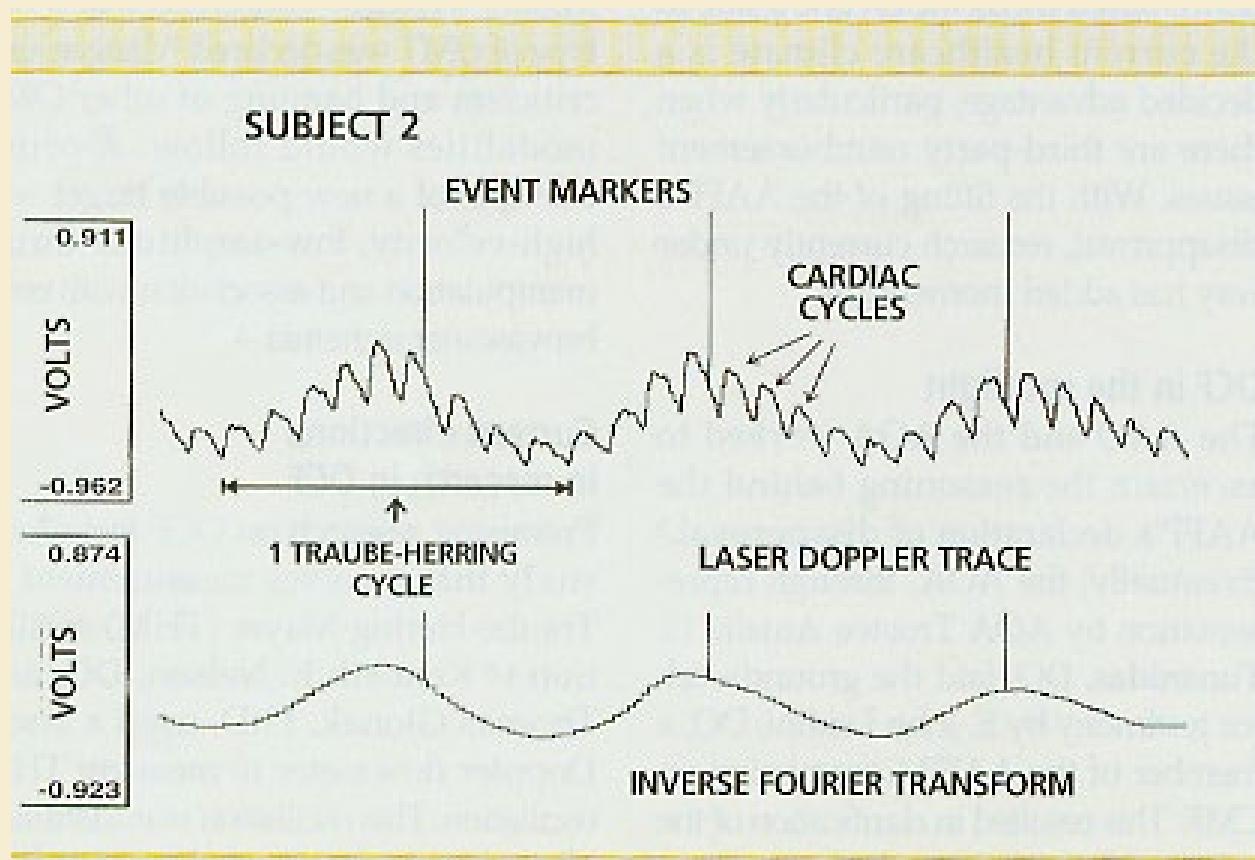
Moskalenko YE, Kravchenko TI, Gaidar BV, et al. Periodic mobility of cranial bones in humans. *Hum Physiol* 1999;25(1):51-58.

(Moskalenko was a former Russian Cosmonaut program researcher)

A series of X-ray pictures taken at rest and during intracarotid injection of 20 ml of radiopaque solution and NMR tomograms with image transformation into the amplitude-time plot were analyzed. It has been shown that the **cranial dimensions in healthy people** undergo continuous changes in the frontal and sagittal sections with a **mean amplitude 0.38 ± 0.21 mm** ($N=18$) and a **maximum deviation of up to 1 mm**... Owing to this the **cranial cavity volume increases by 12-15 mL** under natural elevation of the intracranial. The prevalence of periodic movements with a **frequency of 6-14 cycles/min.**

Nelson KE, Sergueff N, Lipinski CL, Chapman A, Glonek T. The cranial rhythmic impulse related to the **Traube-Hering-Meyer oscillation**: Comparing laser-Doppler flowmetry and palpation. *JAOA* 2001;101(3):163-173.

Sergueef N, Nelson KE, Glonek T. Changes in the **Traube-Hering-Meyer** wave following cranial manipulation. *Amer Acad Osteop J* 2001;11:17.





Left to Right: Viola M. Frymann DO, Yuri Moskalenko PhD, Kenneth Nelson DO,
Tom Glonek PhD, Toshiaki Ueno MD PhD, Frank Willard PhD.

Research

Open Access

Assessment of calvarial structure motion by MRI

William T Crow¹, Hollis H King*², Rita M Patterson^{2,3} and Vincent Giuliano⁴

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* Corresponding author

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Osteopathic Medicine and Primary Care 2009, 3:8 doi:10.1186/1750-4732-3-8

Received: 19 January 2009

Accepted: 4 September 2009



Figure 2
Head mount with human subject in place.

20 healthy subjects

8 MRI images thru
same coronal plane

Analyzed using ImageJ
program from NIH

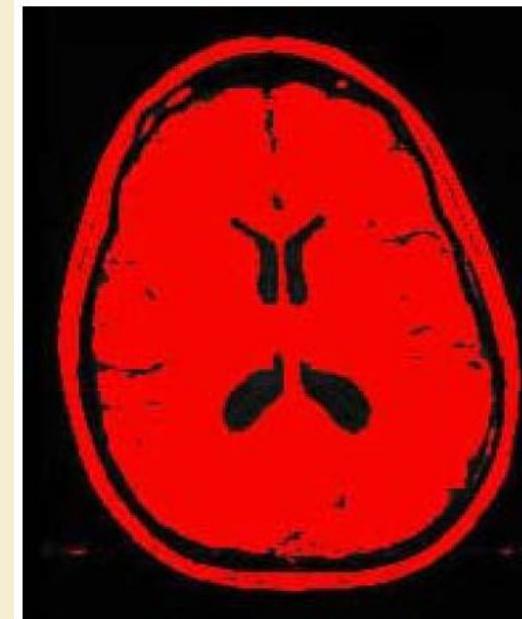


Figure 3
Threshold image.

Table 1: Mean difference between the maximum and minimum values for each of the measures evaluated by ImageJ for each subject (N = 20), using a two tailed paired t-test

Measure	Measure Values (STD, %; CI)	P value
Area (mm) ²	122.69 (75.84, 95%; 81.43 - 163.96)	0.003
Perimeter (mm)	4.00 (6.18, 95%; 0.63 - 7.36)	0.80
Width (mm)	0.49 (0.54, 95%; 0.19 - 0.79)	0.05
Height (mm)	0.63 (0.66, 95%; 0.27 - 0.98)	0.004
Major (mm)	0.67 (0.48, 95%; 0.40 - 0.93)	0.001
Minor (mm)	0.27 (0.19, 95%; 0.16 - 0.36)	0.08
Feret (mm)	0.70 (0.55, 95%; 0.40 - 0.99)	0.001

While statistically different, the measures for width, height, major axis, and feret were below the resolution threshold of 0.898 mm/pixel and could not be used reliably to determine changes in cranial shape due to PRM.

The difference values for **area measure** were both statistically different ($p < 0.003$) and were well above the resolution threshold of 0.898 mm/pixel.

Authors contend that calvarial structures moved in some way.

So.....
if the cranial bones do move 30 to
300+ μm

Can the human sense of touch
perceive it?

Kasparian H, Signoret G, Kasparian J. Quantification of motion palpation capabilities. *J Amer Osteopath Assoc*. 2015;115:604-610.

N = 21 (14 osteopaths, 7 non-osteopaths). Hold the cylinder between their hands and report when feel motion. 6 series of 27 random motions.

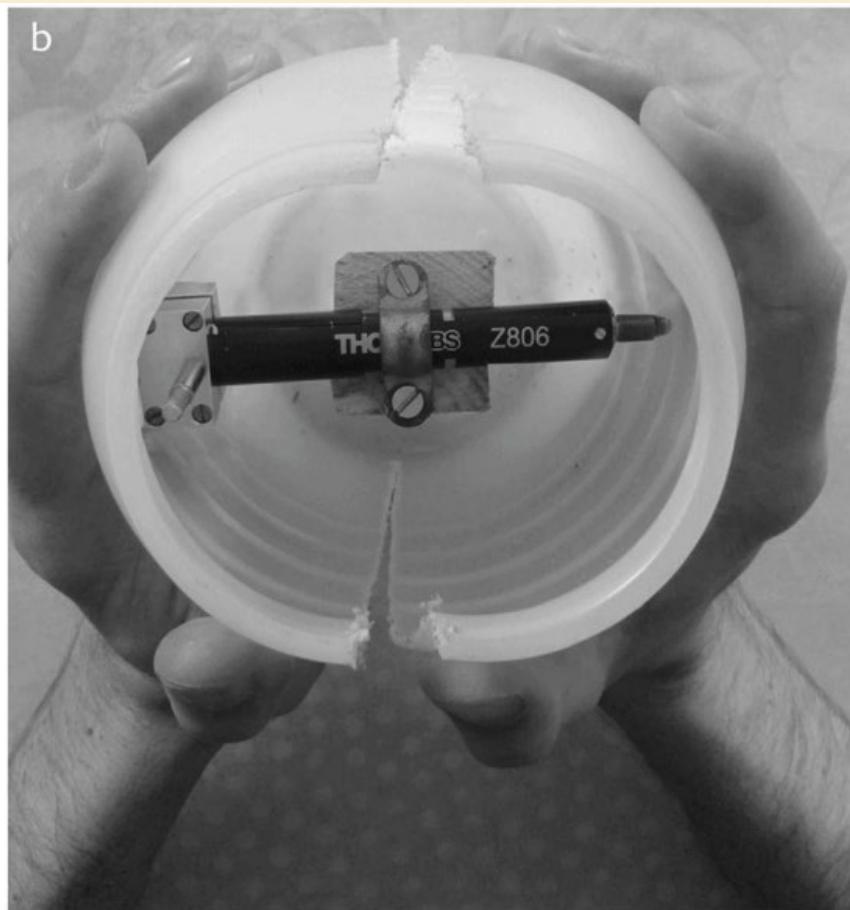
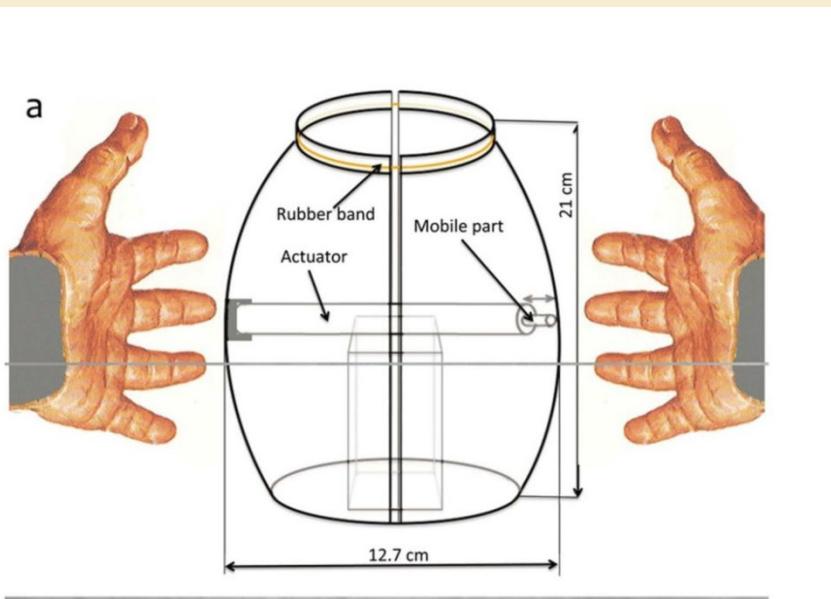
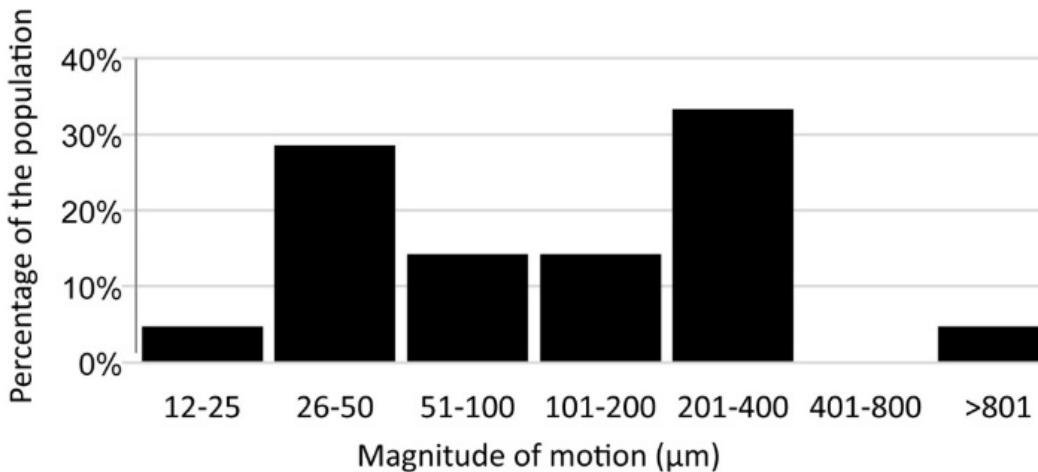


Figure 1. Experimental setup, 1a: schematic (side view), 1b: photo (top view).



Distribution of the smallest detectable motion in our sample
142x69mm (300 x 300 DPI)

	Whole sample	Non-osteopaths	Osteopaths
Best (μm)	15	28	15
Worst (μm)	866	237	866
Mean (μm)	148	123	161
Standard deviation (μm)	127	89	131
Median (μm)	117	100	166
Percentage of the population that can perceive a motion of	50 μm or less	33%	29%
	100 μm or less	48%	57%
	200 μm or less	62%	71%
	300 μm or less	86%	100%

Table 2. Distribution of motion detection capacities in our sample.

Now for the Clinical Research



Most Recent Best and Interesting Clinical Research

Possible Mechanism's of Action

2018-2025

Kashyap S, Brazdzionis J, Savla P, Berry JA, Farr S, Patchana T, Majeed G, Ghanchi H, Bowen I, Wacker MR, Miulli D. Osteopathic manipulative treatment to optimize the glymphatic environment in severe traumatic brain injury measured with optic nerve sheath diameter, intracranial pressure monitoring, and neurological pupil index. *Cureus* 2021;13(3): e13823. DOI 10.7759/cureus.13823

Methodology

This was a **retrospective study** at a level II trauma center that occurred in 2018. The study enrolled **11 patients** with TBI, increased ICP, or brain edema who had an external ventricular drain (EVD) placed. Patients underwent a **51-minute treatment with OMT** with an established protocol. Patients received 51 minutes of OMT to the head, neck, and peripheral lymphatics. The ICP, cerebrospinal fluid (CSF) drainage, optic nerve sheath diameter (ONSD) measured by ultrasonography, and Neurological Pupil Index (NPI) measured by pupillometer were recorded before, during, and after receiving OMT.

OMT Protocol

Patients underwent 51 minutes of OMT divided as follows:
nine minutes for each treatment of:
thoracic inlet opening,
rib raising,
and diaphragmatic release,
followed by six minutes of thoracic or pedal pump
and nine minutes for the ***compression of the fourth ventricle (CV4)***
And nine minutes facial effleurage

Patients were treated 3 times

Results

A total of 11 patients were included in the study, and 21 points of data were collected from the patients meeting inclusion criteria who received OMT.

There was a **mean decrease in the Optical Nerve Sheath Diameter** ONSD of 0.62 mm from 6.24 mm to 5.62 mm ($P = 0.0001$). [inflammation and swelling decreased]

The mean **increase in Neurological Pupil Index** NPI was 0.18 ($P = 0.01$). [The pupil reacted faster to a light stimulus]

Results

A total of 11 patients were included in the study, and 21 points of data were collected from the patients meeting inclusion criteria who received OMT.

The mean **decrease in Intracranial pressure ICP** was 3.33 mmHg ($P = 0.0001$).

There was a significant **decrease in CSF output** after treatment ($P = 0.0001$). [interpreted effect of glymphatic system improvement]

Each measurement of ICP, ONSD, and NPi demonstrated a **decrease in overall CSF volume and pressure after OMT** compared to CSF output and ICP prior to OMT.

Conclusion regarding use of OMT

“As evidenced by our data in patients with severe TBI, OMT can be used to mobilize the glymphatic system and decrease brain edema. Concussion, which by definition meets the criteria as a minor TBI, can similarly be treated using these OMT techniques.”

Conclusion regarding use of OMT

As concussions have been linked to increased brain edema, improving glymphatic function may similarly decrease edema, and promote clearance of toxic metabolites actively being investigated as markers for TBI. Being relatively quick and effective, OMT can supplement the treatment of concussions to great effect. Consideration of implementation of OMT for patients with TBI ranging from mild to severe may be considered based on improvements demonstrated in measures of glymphatic and CSF clearance taken in our patient population within the highest severity category to theoretically promote homeostatic conditions for recovery.

This study is among a growing body of research suggestive of benefits of OMT/OCMM in neurological disorders. (HK)

Roberts B, Makar AE, Canaan R, Pazdernik V, Kondrashova T. Effect of occipito-atlantal decompression on cerebral blood flow dynamics as evaluated by Doppler ultrasonography. *J Osteopath Med.* 2021; 121(2): 171-179.

N = 30 (11 male, 19 female, healthy first year medical students at ATSU-Kirksville)

Crossover design, Ss as own controls. The participants were randomly assigned to 1 of 2 treatment interventions: OAD or sham touch. After one week, participants returned to have the other intervention performed.

OAD: Fingers at cranial base, gentle lateral traction for condylar decompression, held until for 2 minutes.

Sham: Same hand position, but no distraction or lateral traction for 2 minutes

Results

End Diastolic Velocity **EDV increased after OAD in the MCA, ICA, and VA (all $p < 0.001$)**; no change occurred after sham touch (all $p>0.05$).

EDV was greater for all post-treatment timepoints after OAD in the MCA, ICA, and VA than sham touch (all $p<0.001$).

Changes in peak Systolic Velocity (PSV) in the ICA and VA and for HR and BP did not depend on treatment intervention ($p>0.06$).

Cerritelli F, Cardone D, Pirino A, Merla A, Scoppa F. Does osteopathic manipulative treatment induce autonomic changes in healthy participants? A thermal imaging study. *Front. Neurosci.* 2020;14:887. doi: 10.3389/fnins.2020.00887

N = 37 Volunteers, asymptomatic.

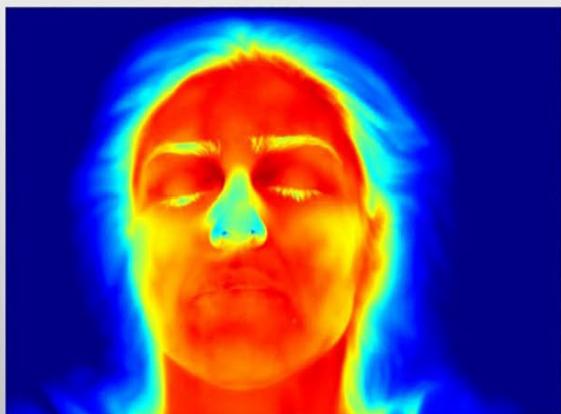
Crossover design, Ss as own control. Two sessions randomized, OMT or Sham for 35 minutes each.

OMT: After assessment of somatic dysfunction, utilized BLT, BMT, OCMM.

Sham: gentle static touching of extremities, pelvis, abdomen, thorax and spine.

No contact with the head as thermography done on the head.
Outcome measures: Head Thermography; HRV; GSR

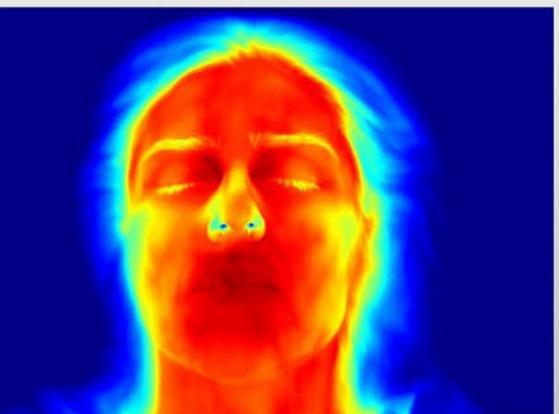
OMT condition



(a)



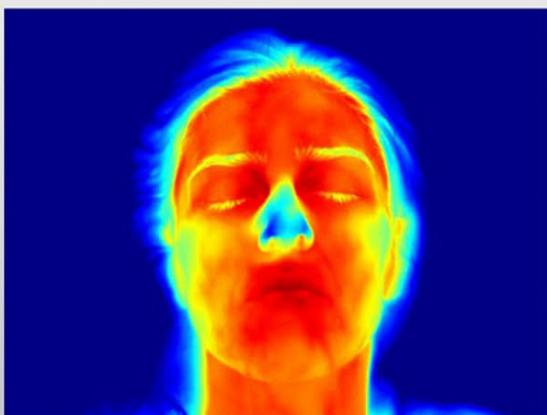
(b)



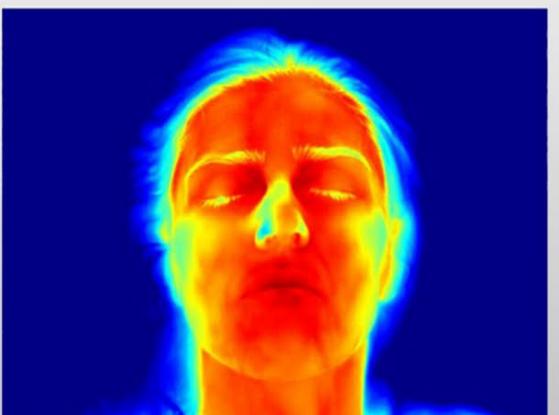
(c)

38,1°C
38
37
36
35
34
33
32
31
30
29
28
27
26,7°C

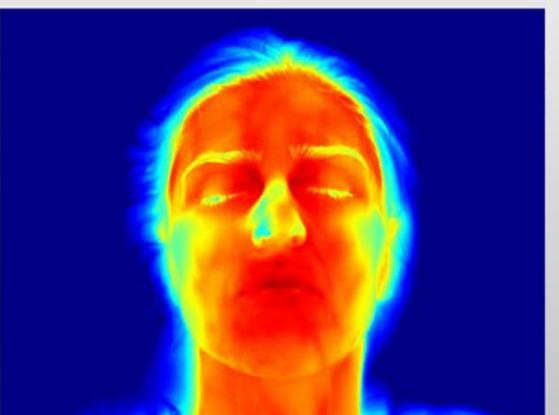
SHAM condition



(d)



(e)



(f)

FIGURE 2 | Facial thermal changes in a representative participant receiving either osteopathic manipulative treatment or sham. Panels **(a,d)** represents baseline period before the touch stimulation. Panels **(b,e)** show touch period. Panels **(c,f)** demonstrate post-touch period. A general temperature increase can be observed over the whole face in the osteopathic group as compared to the sham. In particular, while the chin slightly changes their average temperature values, nose tip, perioral, maxillary, and forehead regions clearly present a temperature increase where red areas can be easily spotted. OMT, osteopathic manipulative treatment.

Cerritelli et al 2020

HRV improved $p < .01$

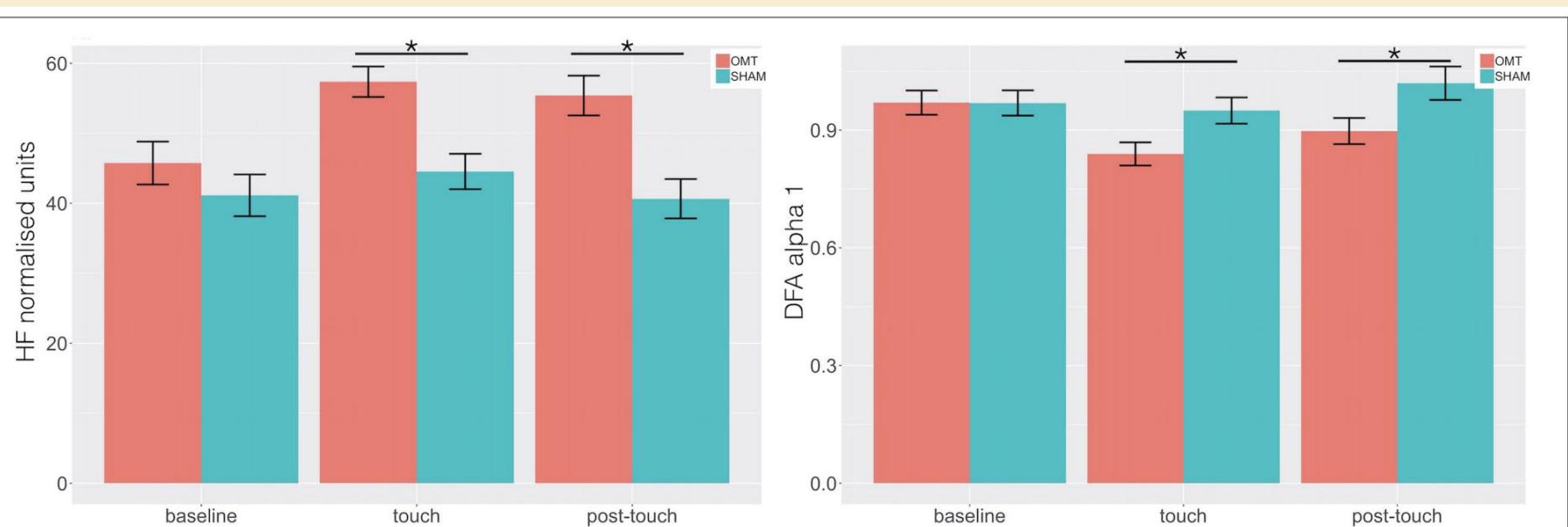
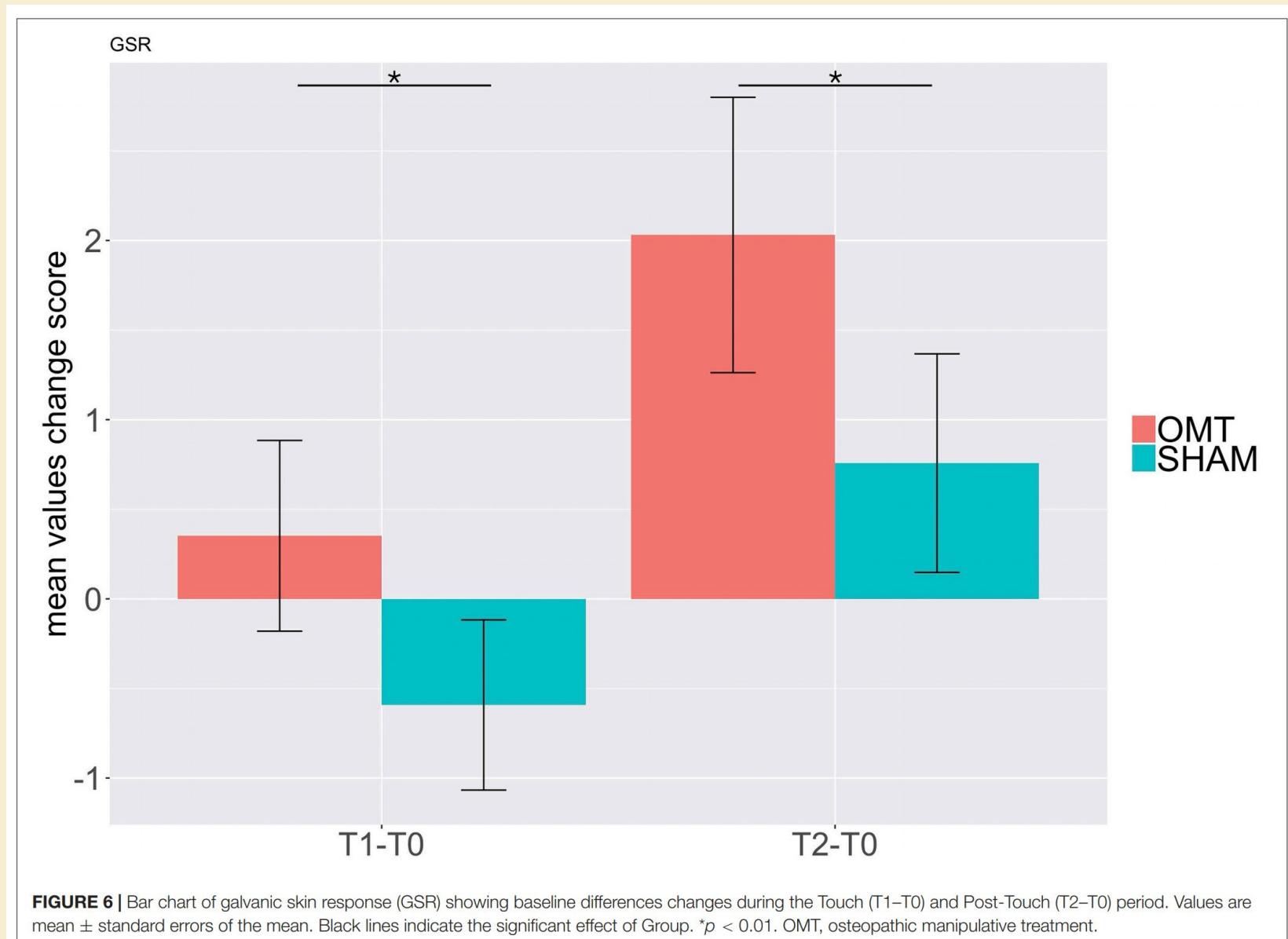


FIGURE 5 | Bar chart displaying the mean heart rate variability (HRV) parameters values recorded in the baseline, Touch and Post-Touch period among the osteopathic and sham group. HF, high frequency in normalized unit; DFA-1, detrended fluctuation scaling exponent. Data presented are means \pm standard errors of the mean. Black lines indicate the significant effect of Group. $*p < 0.01$. OMT, osteopathic manipulative treatment.

Skin conductance increased in OMT/OCMM group



Tamburella F, Piras F, Piras F, Spano B, Tramontano M, Gili T. Cerebral perfusion changes after osteopathic manipulative treatment: a randomized manual placebo-controlled trial. *Front. Physiol.* 2019;10:1-9. doi: 10.3389/fphys.2019.00403

N = 30 OMT = 15 Sham = 15

Asymptomatic volunteers (18-49 years old)

OMT: MFR, BLT, Visceral, OCMM

Sham: Passive touch without joint mobilization in pre-set order. Touched lumbar and dorsal spine in prone position for 20 minutes, supine 20 minutes on shoulders, hips and neck. 5 minutes on sternum and chest.

One session of 45 minutes OMT or Sham. Baseline MRI before and MRI after intervention and 3 days later.

Methods

MRI utilized **Arterial spin Labeling (ASL)**. ASL involves the utilization of an endogenous tracer, thus avoiding the risks associated with exogenous radioactive ones. ASL uses magnetically labeled arterial blood water and changes in decay as a measure of cerebral blood perfusion. ASL is specific to intravascular changes and can provide absolute quantification of perfusion values.

Hypothesis is that OMT could induce cerebral perfusion effects through parasympathetic/sympathetic modulation.

Results

Tamburella et al 2019

Only in the OMT group were there significant changes:
Perfusion decreased in cluster comprising the left cingulate cortex
(PCC) and the superior parietal lobule, while increase in the right
posterior cingulate cortex.

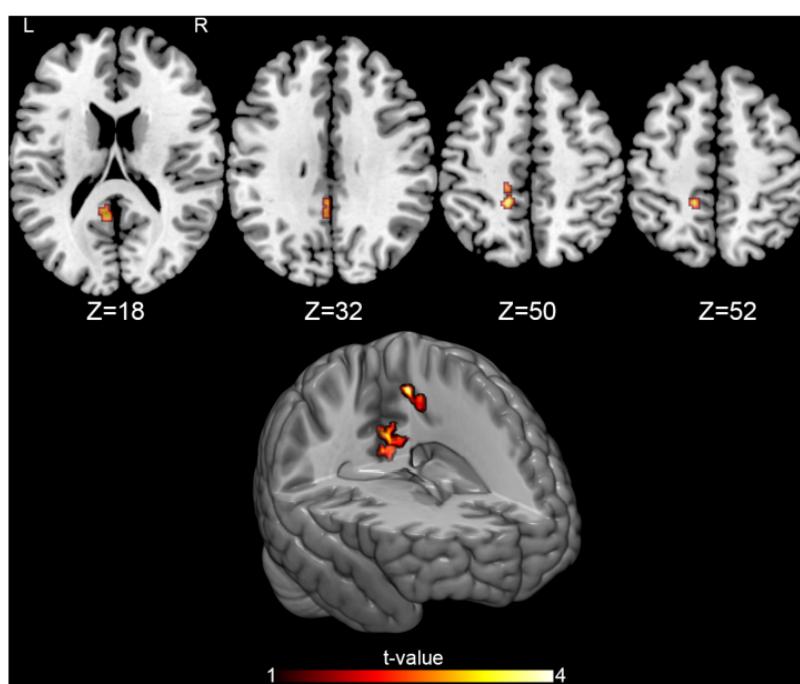


FIGURE 3 | Perfusion changes induced by treatment. The figure shows the baseline-controlled group $[(\text{OMT_T1} - \text{OMT_T0}) - (\text{P_T1} - \text{P_T0})]$ differences between treatment and placebo administration, indicating a significant decrease of the CBF after treatment in two regions: the left posterior cingulate cortex (PCC) $[(-4, -46, 31) \text{ MNI space coordinates}]$ and the left superior parietal lobule $[(-14, 42, 52) \text{ MNI space coordinates}]$. Signal changes were deemed significant at $p < 0.005$ voxel level uncorrected, corresponding to a minimum cluster size of 40.

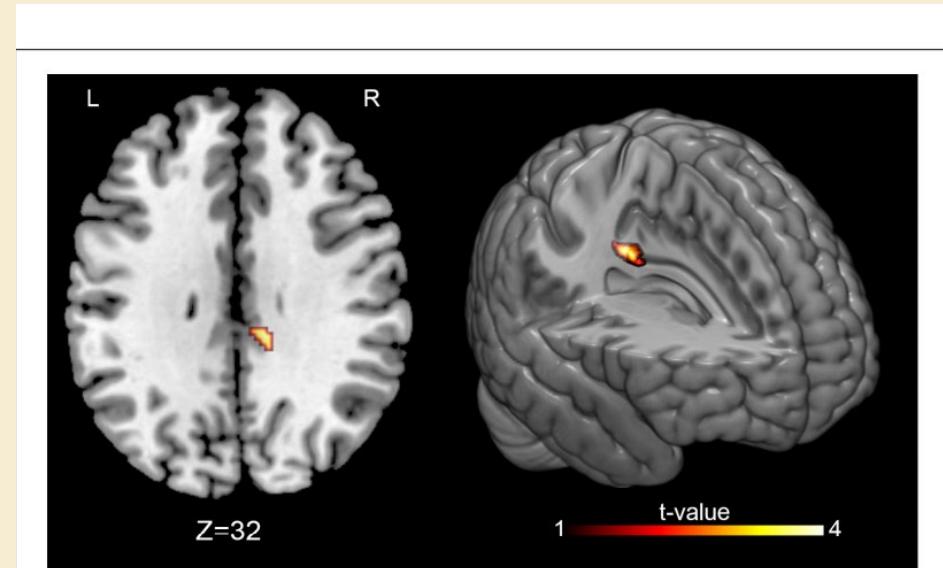


FIGURE 4 | Perfusion changes induced by treatment at follow-up. The figure shows the post-treatment-follow up $[(\text{OMT_T2} - \text{OMT_T1}) - (\text{P_T2} - \text{P_T1})]$ differences between treatment and placebo administration, indicating a significant increase of the CBF at follow-up in the right PCC $[(8, -30, 31) \text{ MNI space}]$. Signal changes were deemed significant at $p < 0.005$ voxel level uncorrected, corresponding to a minimum cluster size of 40.

Cerritelli F, Chiacchiaretta P, Gambi F, et al. Osteopathy modulates brain-heart interaction in chronic pain patients: an ASL study. *Scientific Reports*. 2021;11:4556.

N = 32 OMT = 16 Sham = 16 (Age 42.3 ± 7.3 ; M/F: 20/12)

4 weekly sessions of 30 minutes each of OMT. All subjects had Chronic Low Back Pain (cLBP) duration: 14.6 ± 8.0 months

To assess the effects of OMT on both the autonomic nervous system (ANS) and cerebral blood flow (CBF) the researchers used **Arterial Spin Labeling (ASL)**. ASL allows assessment of regional brain perfusion and simultaneous measurement of cardiac and respiratory activity to derive ANS indexes such as heart rate variability (HRV).

ASL offers the opportunity to obtain a measure of a well-defined physiological variable that can quantify both baseline and task induced (eg. Use of OCMM) variation of brain activity.

Cerritelli F, Chiacchiaretta P, Gambi F, et al. Osteopathy modulates brain-heart interaction in chronic pain patients: an ASL study. *Scientific Reports*. 2021;11:4556.

Hypothesis: that OMT, as compared to the control condition, would induce a decrease in rCBF in a widespread network of brain regions including (but not exclusively) those of the pain matrix and an increase in parasympathetic activity as measured by HRV.

OMT/OCMM

Techniques used in the current study were balanced-ligamentous, balanced-membranous and fluidic techniques to areas of somatic dysfunction in head and body.

These procedures are clearly those typically used in OCMM practice. The authors described specific procedures rather than just say cranial procedures.

Sham: Received osteopathic-like manual contact, without using any type of specific osteopathic technique or procedure. Used a pre-defined set of body areas using static touch.

Results

OMT showed decreased baseline rCBF within several regions considered the **Pain Matrix** (areas reflecting the experience of pain) compared to sham.

Left posterior insula

Left anterior cingulate cortex

Left thalamus

And in **Sensory regions**

left superior parietal lobe

Middle frontal lobe

Left cuneus

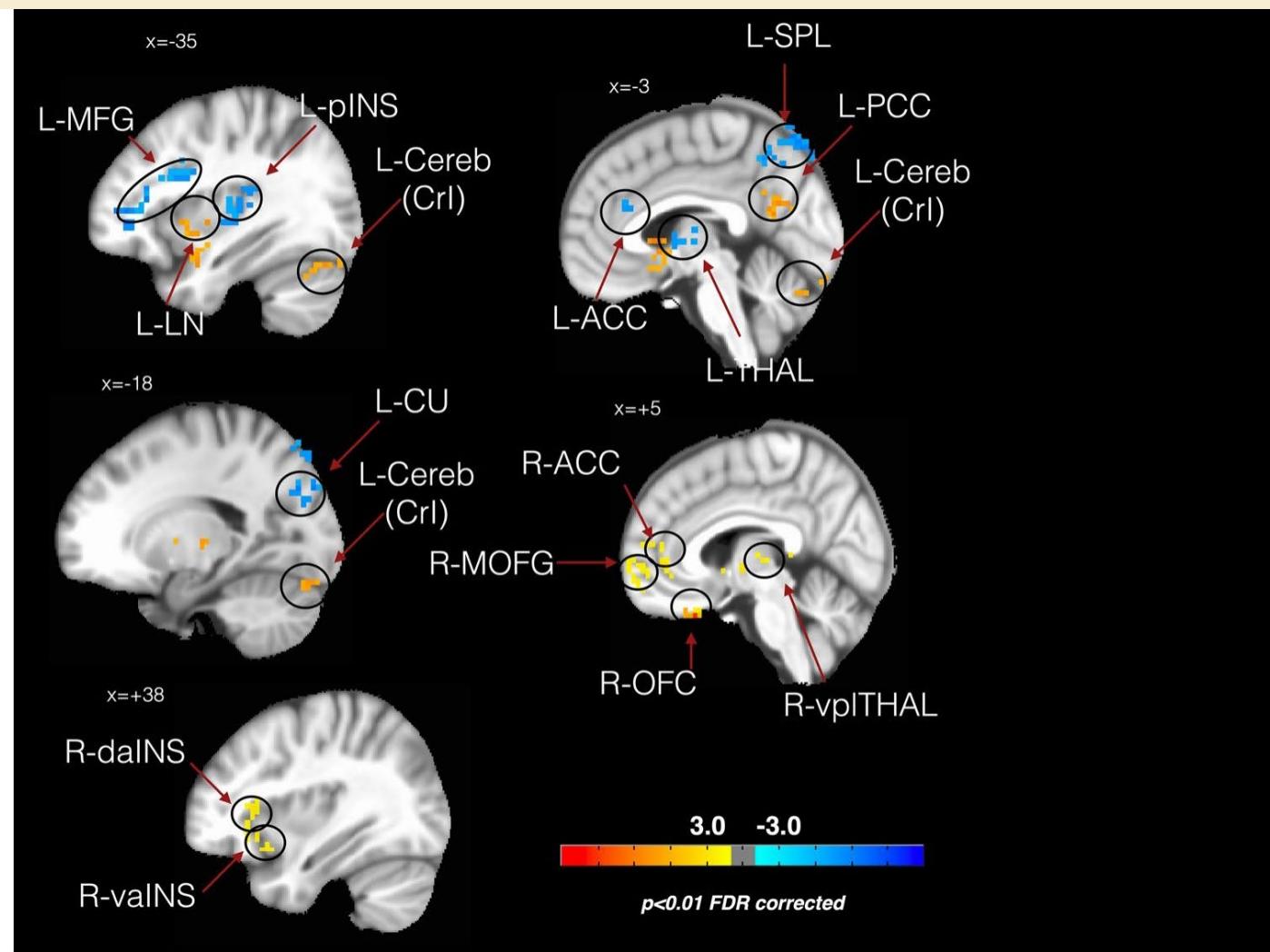
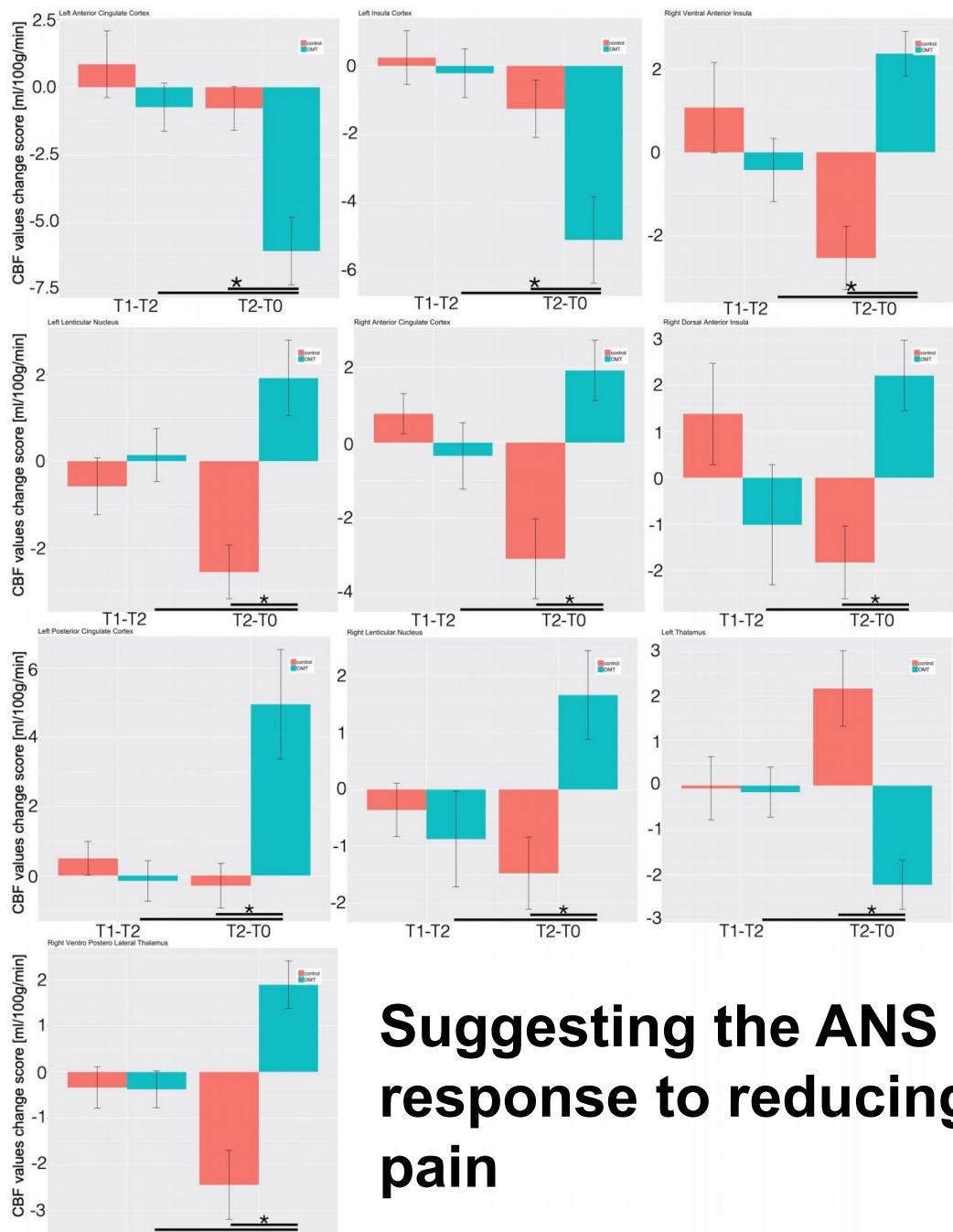


Figure 1. The effects of osteopathic treatment on regional cerebral flow. The figure shows CBF changes baseline-controlled group differences between treatment and sham group at T2 (referring to the contrast described in the text as (T2_OMT-T0_OMT) vs (T2_SHAM-T0_SHAM)— $p < 0.01$, false discovery rate (FDR) corrected). *L-MFG* left middle frontal gyrus, *L-pINS* left posterior insula, *L-LN* left lentiform nucleus, *L-Cereb(CrI)* left cerebellum (Crus I), *L-ACC* left anterior cingulate cortex, *L-SPL* left superior parietal lobe, *L-PCC* left posterior cingulate cortex, *L-THAL* left thalamus, *L-CU* left cuneus, *R-ACC* right anterior cingulate cortex, *R-MOFG* right mid orbitofrontal gyrus, *R-OFC* right orbito frontal cortex, *R-vpITHAL* right ventroposterior lateral thalamus, *R-dalINS* right dorsal anterior insula, *R-valINS* right ventral anterior insula.

Results

Conversely, rCBF was increased in the OMT group compared to the sham group in...

Right anterior insula
Bilateral striatum
Left posterior cingulate cortex
Right prefrontal cortex
Left cerebellum
Right ventroposterior lateral thalamus



Suggesting the ANS response to reducing pain

Figure 2. Longitudinal CBF delta changes. The figure shows the longitudinal CBF mean change within the regions of interest for the two groups. *Statistically significant differences ($p < 0.05$) between groups.

OMT showed a statistically significant negative correlation between baseline High Frequency HRV changes and rCBF at T2 (after last OMT) in left posterior insula and bilateral lentiform nucleus. These findings suggest that OMT can play a significant role in regulating brain-heart interaction mechanisms.

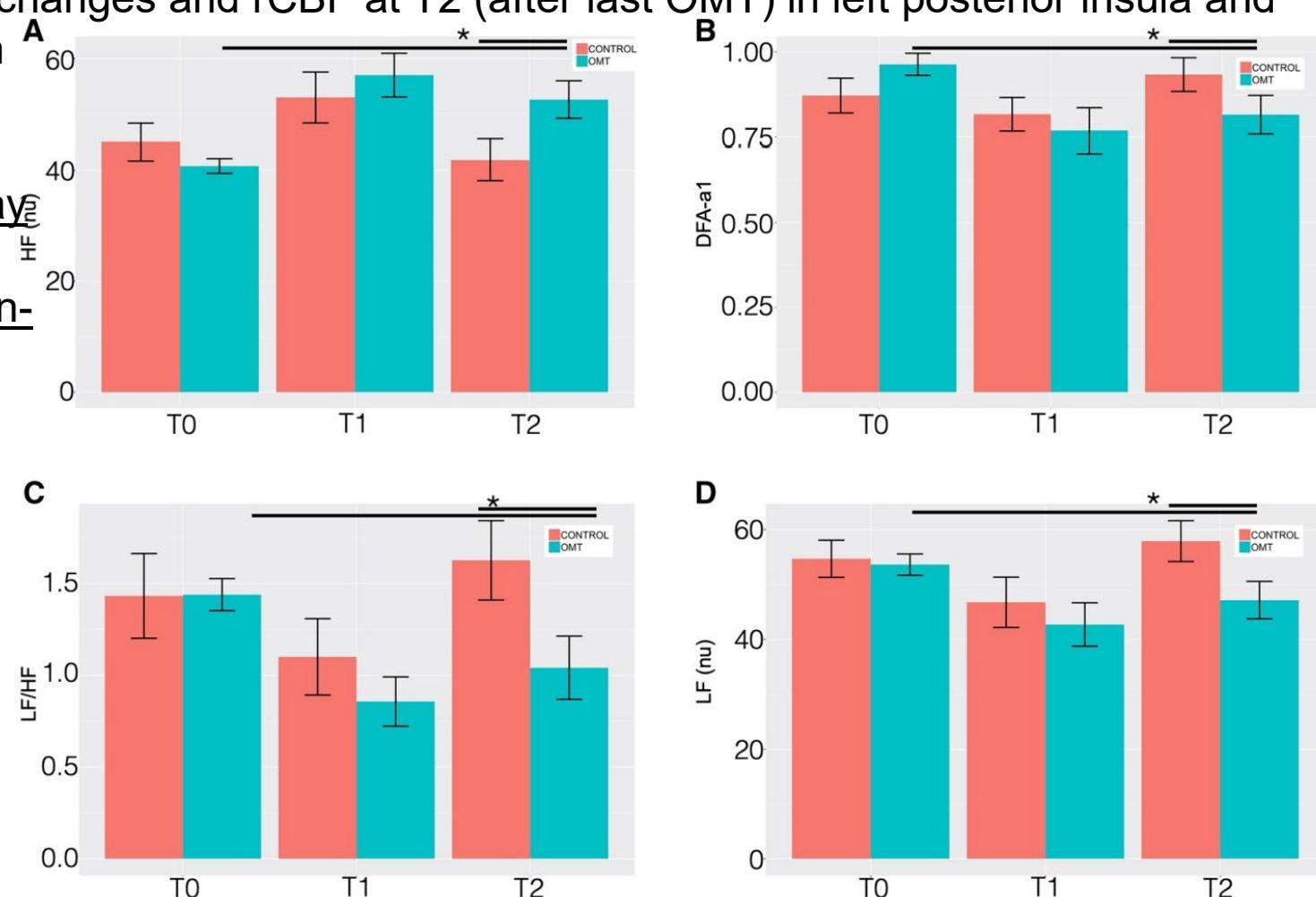


Figure 4. Heart rate variability changes between the study and control group. Heart rate variability (HRV) findings for: (A) high frequency (HF) normalised units (nu); (B) detrended fluctuation scaling exponent (DFA α 1); (C) low frequency/high frequency ratio (LF/HF); (D) low frequency (LF—nu). Data presented are means \pm standard deviation (SD). *Statistically significant differences ($p < 0.05$) in OMT group compared to sham and control groups.

Conclusion

While the previous research (Tamburella et al 2019) has used CBF measurements immediately after a single OMT session and after 3 days, here we report not only that larger CBF flow changes are observed in response to longer osteopathic treatment period (4 sessions over a 1-month treatment period) but that these effects are linked to a change in autonomic response. **We interpret the accompanying decrease in CBF in pain-related areas as reflecting the positive influence of osteopathic treatment on heart rate variability and pain perception on LBP patients' physiological state, hypothesizing a potential OMT effect on central mechanisms of endogenous pain modulation.**

Recent Research on the Application of OCF/OCMM in Clinical Conditions



Pediatrics

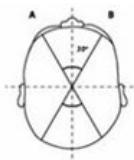
Original Article

Hollis H. King*, PhD, DO, Julie Mai, DO, Mary Anne Morelli Haskell, DO, Kimberly Wolf, DO and Megan Sweeney, MPH

Effects of osteopathic manipulative treatment on children with plagiocephaly in the context of current pediatric practice: a retrospective chart review study



Figure 1: Superior views of pediatric heads. (A) A 4-month-old with a normocephalic head. (B) An 11-month-old patient with asymmetrical deformational plagiocephaly (DP) and occipital flattening.



The cranial vault asymmetry index (CVAI) is the difference between the lengths of two diagonals measured 30 degrees from midline, divided by the larger of the two diagonals. Multiplication by 100 results in a percentage.

$$CVAI = \frac{A - B}{A} \times 100$$

Severity of DP based on CVAI: Grade 1 (Normal) <3.5; Grade 2 (Mild) 3.5 – 6.25; Grade 3 (Moderate) 6.25 – 8.75; Grade 4 (Severe) 8.75 – 11.0; Grade 5 (Very Severe) >11.0.

Figure 2: Diagram of head dimensions utilized in calculating the cranial vault asymmetry index (CVAI).

Characteristic	N=26
	Mean (SD), [range]
Males	19 (73 %)
Age during first treatment, months	4.4 (2.2), [2–10]
Age during last treatment, months	7.0 (3.2), [2.3–13.5]
Treatment duration, months	2.8 (2.6), [0.5–10]

SD, standard deviation.

Table 2: Results.

Variable	Pre-OMM Mean (SD), [range in mm]	Post-OMM Mean (SD), [range in mm]	p-Value
Diagonal A, mm	133.3 (\pm 10.4), [114–156]	139.6 (\pm 10.6), [120–158]	<0.001
Diagonal B, mm	137.7 (\pm 8.6), [125–153]	142.2 (\pm 10.4), [124–159]	<0.001
Circumference, mm	417.0 (\pm 25.7), [365–460]	435.0 (\pm 25.7), [380–470]	<0.001
Cephalic index	0.968 (\pm 0.07), [0.89–1.16]	0.983 (\pm 0.04), [0.93–1.13]	0.088
CVAI	6.809 (\pm 3.335), [1.53–15.6]	3.834 (\pm 2.842), [0.65–12.9]	<0.001
Severity grade	3 [1–5]	2 [1–5]	

CVAI, cranial vault asymmetry index; OMM, osteopathic manipulative medicine; SD, standard deviation.



Hollis H. King*, DO, PhD, Robert N. Weinreb, MD, Evan Walker, MS and Linda M. Zangwill, PhD

Effects of a single osteopathic manipulative treatment on intraocular pressure reduction: a pilot study

N = 16

<https://doi.org/10.1515/jom-2024-0206>

Received September 23, 2024; accepted February 4, 2025;
published online March 4, 2025

Table 2: Comparison between last pretreatment IOP (visit 3 AM) and all posttreatment IOP measurements (visits 3–5) among subjects who received OMT and those that did not. All AM times were approximately 8:00 AM and PM times were 4:00 PM.

Comparison of pretreatment visit 3 (AM) to the following	Treated group (n=9 subjects; 18 eyes)		Untreated group (n=7 subjects; 14 eyes)		Treated vs. untreated
	IOP mean difference, mmHG	p-Value	IOP mean difference, mmHG	p-Value	p-Value
Post-treatment	1.4 (0.2, 2.5)	0.027	0.4 (−0.9, 1.6)	0.578	0.271
Visit 3, PM	0.8 (−0.1, 1.6)	0.098	0.4 (−0.7, 1.5)	0.450	0.626
Visit 4, AM	0.2 (−0.9, 1.3)	0.719	0.8 (−0.4, 1.9)	0.201	0.513
Visit 4, PM	1.6 (0.3, 2.8)	0.016	1.1 (0.2, 2.0)	0.030	0.617
Visit 5, AM	1.2 (−0.1, 2.4)	0.080	1.2 (−0.3, 2.7)	0.139	0.965
Visit 5, PM	1.4 (0.4, 2.4)	0.014	0.9 (−0.7, 2.5)	0.260	0.601

IOP, intraocular pressure; OMT, osteopathic manipulative treatment.

A Biomechanical Approach to Headache Associated with Traumatic Brain Injury Using Osteopathic Manipulation: a Proof-of-Concept Trial

Joshua Alexander, DO, MPH¹ Alice Chen, DO² William Andrew, DO² Megan Sweeney, MS² Meredith Pung, PhD² Hollis King, DO, PhD²

¹ Scripps Clinic Division of Neurology, La Jolla, California; ² University of California, San Diego, La Jolla, California

Background

- Post-traumatic headaches (PTH) are one of the most commonly reported sequelae of traumatic brain injury.
- 58% prevalence at 12 months post injury¹.
- Migraine after head trauma is common (prevalence varies widely by source) and therefore the focus of this study^{2,3,4}.
 - NB at the time of the study PTH had yet to be thoroughly defined
- PTH responds poorly to standard migraine treatment⁵.
- Osteopathic manipulative medicine (OMM) is a non-pharmacologic, noninvasive, and low risk approach that addresses structural (biomechanical) and physiologic dysfunction in the body that may be impacting the body's innate ability to heal and recover.
- OMM involves a structural exam and precise application of manual techniques called osteopathic manipulative treatment (OMT) to address these structural (somatic) dysfunctions.
- Data support exploring OMT as a treatment approach.
 - Reduces headache days per month, medication use, headache impact, & headache associated disability^{6,7,8}
- This is the first study to explore the effect of OMT for PTH with migraine features that incorporates the principles of osteopathic cranial manipulative medicine and balanced ligamentous/membranous tension.

Hypothesis

- Osteopathic manipulation reduces the number of headache days experienced by patients with migraine type post traumatic headaches.

Methods

- UCSD IRB approval (#140773; #160892).
- Recruitment took place over two periods (2014-2016 and 2020-2022). The second phase aimed to add power but was impacted by the COVID-19 pandemic.
- 24-week prospective, single arm study
 - Initially a 30-week double arm but this became moot
- Source population: 2 tertiary care centers and a Traumatic Brain Injury Community Support group
- Inclusion criteria:
 - History of TBI; Headache frequency \geq /equal 4 per month; Post-traumatic headache, migraine type with any MIDAS Grade; Headaches continue to occur 3 months to 2 years after the injury; No history of uncontrolled migraine prior to head injury
 - Participants were asked to continue headache medications and not to seek OMT outside the study.
- Intervention: 12 weekly 60-minute osteopathic treatments (OMT); participants were randomized to 1 of 4 OMM physicians, standarized osteopathic exam, treating physician given flexibility
- Primary Outcome: Headache Days.
- Secondary Outcomes: Headache intensity (Visual Analog Scale 0-10), Migraine Disability Assessment Test (MIDAS)¹⁴; Centers for the Epidemiologic Study of Depression (CES-D),¹⁵ Short Form-36 (SF-36),¹⁶ Number of headache medications use
- Data collected at baseline (before start of OMT), immediately after intervention (12 weeks), and 12-weeks after completion of intervention (24 weeks).
- Intention-to-treat (ITT) and per-protocol (PP) analyses were completed. Missing data was handled using last observation carried forward imputation technique.
- Demographic and baseline characteristics were analyzed using descriptive statistics. Repeated measures ANOVA with a within-subject factor of time (baseline, 12 weeks, 24 weeks) were used for analysis. Pairwise group comparisons were used to compare baseline with 12 weeks and 24 weeks.
- Initially Wilcoxon rank sum was employed but the final exploratory analysis yielded to ANOVA.
- All statistical tests were conducted using SPSS version 29 using two-tailed tests with a p-value of 0.05 or less indicating statistical significance.



References

1. Menconi I, Cibola A, Luca AC, Bakris IW. Post-Traumatic Headache: A Review of Prevalence, Clinical Features, Risk Factors, and Treatment Strategies. *J Clin Med*. 2023 Jan 28;12(13):4231. doi: 10.3390/jcm12134231. PMID: PMC3042482.
2. Erickson L C. Chronic outcome of chronic post-traumatic headaches after mild head trauma in US soldiers: An observational study. *Headache*. 2011;51:932-941.
3. Chen MH, Chang YF, Chen WC, Chang CH, Chen JF. Risk of Migraine after Traumatic Brain Injury and Effects of Injury Management Levels and Treatment Modalities: A Nationwide Population-Based Cohort Study in Taiwan. *J Clin Med*. 2023 Feb 10;12(4):1530. doi: 10.3390/jcm12041530. PMID: 36722000.
4. Barlow KM. Post-traumatic headache: An update. *Medical record (Auckland)*. Nov 2012;15(10):1445-1446. doi:10.31121/med13424241.
5. Bafna D, Patel R, Wright A, Joseph D. Osteopathic Manipulative Treatment Relieves Post-concussion Symptoms in a Case of Polytrauma. *J. Neurosurg. Pediatrics*. March 18 2020;20(3):e301-302. doi:10.3171/2019-07-JNSP-00085.
6. Chappell C DE, Dombrowski GV. Assessing the immediate effect of osteopathic manipulation on sports related concussion symptoms. *Chiropractic & Manual Therapies*. 2012;20(1):1.
7. Dombrowski C, Chappell C, Dombrowski G, and Niles A. Osteopathic manipulative therapy for headache associated with mild traumatic brain injury. *Journal of Osteopathic Medicine*. 2010;110(12):610-615. doi:10.7556/jom.2010.120610.
8. Kovalic D, Eason C, Christensen SR, Smith M, Ellinger H, Hajig and Baker G. Osteopathic Manipulative Treatment for Severe Concussion After Acute Severe Traumatic Brain Injury. *Journal of Osteopathic Medicine*. 2010;110(12):610-615.
9. DeAngelis T, Levin M, Hsu J, and Hsu J. Osteopathic manipulative therapy for headache associated with mild traumatic brain injury. *Journal of Osteopathic Medicine*. 2012;112(1):3-7. doi:10.7556/jom.2012.12010001.
10. Di Palo D, Maffioli T, Buzzi MG. Effects of Osteopathic Manipulative Therapy on Pain and Mood Disorders in Patients With High-Frequency Migraine. *Journal of the American Osteopathic Association*. 2017;117(10):605-609. doi:10.7556/jaoa.2017.0207.
11. Schubert U, Koenig W, Koenig W, Schubert-U, Schubert-Koenig W, Beck M, Vogt K, Bergmann A.. Efficacy of osteopathic manipulative treatment of female patients with migraine: results of a randomized controlled trial. *Journal of Alternative and Complementary Medicine*. 2011;17(1):14-20. doi:10.1089/acm.2010.0673.
12. Schubert U, Koenig W, Koenig W, Schubert-U, Schubert-Koenig W, Beck M, Vogt K, Bergmann A.. Effectiveness of Osteopathic Manipulative Treatment on Headache in Women With Migraine: A Randomized Controlled Trial. *Journal of the American Osteopathic Association*. 2020;120(4):323-329. doi:10.7556/jaoa.2019.03077.
13. Was SC, Zhi A, Lester A, Mancini A.. Effectiveness of Osteopathic Manipulative Treatment in Concussion Education in Training Student Athletes With Acute Concussion Symptoms. *Journal of the American Osteopathic Association*. 2020;120(4):323-329. doi:10.7556/jaoa.2019.03077.
14. Stewart WF, Davies AL, Davies AL, Stewart WF. Development and testing of the Migraine Disability Assessment (MDAS) Questionnaire to assess headache related disability. *Neurology*. 2001;56(3):Suppl 1-2. doi:10.1212/WNL.56.3Suppl_1-2.20.
15. R, The CES-D Scale: A Self-Report Depression Scale for Research in General Population. *Arch Psychol Res*. 1977;10:385-401. doi:10.1177/03600569770100006.
16. Wang SJ, Lu SH, Jiang GD. What it offers among headache diagnostic analysis: an SF-36 survey in 902 headache patients. *Pain*. 2002;90(3):285-292. doi:10.1016/S0304-380X(02)00080-8.
17. Barthol T, Götz G. The trigeminal cervical complex and migraine: current concepts and systems. *Curr Pain Headache Rep*. Oct 2013;17(10):374-380. doi:10.1007/s10637-013-0036-y.
18. Erck DK, Rohr ME. The cervical trigeminal bridge, a review of literature and clinical implications. *J Clin Osteoporos*. Jun 2014;5(2):284-287.

Results

Table 1. Summary of Primary and Secondary Outcomes: Baseline compared to 12 and 24 weeks, Baseline to 12-weeks, and Baseline to 24-weeks

	Intention to treat (n=15)			Per protocol (n=11)		
	Mean	S.D.	p	Mean	S.D.	p
Headache Days						
Baseline-12-24 wks	55.1	37.6	0.02	49.7	37.1	0.03
12wks	35.3	36.1	0.02	29	33	0.08
24wks	32.2	37.8	0.02	24.8	34.7	0.04
Headache Intensity						
Baseline-12-24 wks	6.5	1.8	0.01	6.3	1.7	0.04
12wks	4.7	2.1	0	4.4	2.2	0.01
24wks	4.7	2.4	0.02	4.4	2.7	0.04
MIDAS						
Baseline-12-24 wks	129	127	0.01	117	110	0.03
12wks	67.3	107	0.03	48.8	53.3	0.06
24wks	51.3	104	0.01	27	32.3	0.02
CESD						
Baseline-12-24 wks	24.1	14.8	0.01	23.6	15.6	0.01
12wks	14.3	11.7	0.01	10.9	9.4	0.02
24wks	13.3	12.3	0.01	9.6	10	0.01
SF-36						
Baseline-12-24 wks	43.4	22	0	47.1	20.8	0
12wks	59.2	20.3	0	65.5	19.8	0
24wks	69.2	21.5	0	74.9	22	0
Abortive Medication Use						
Baseline-12-24 wks	6.2	10.3	0.04	4.9	9.1	0.08
12wks	2.5	4.4	0.05	2	4.5	0.08
24wks	1.8	3.3	0.04	1.1	2.7	0.08

Main result: OMT significantly reduced headache days, headache intensity, headache disability scores (MIDAS), depression scores (CESD), and improved sense of wellbeing (SF-36) in ITT and PP analysis

- 16 participants consented for the study
 - 1 had data collection error and data excluded
 - 15 participants included in intent to treat analysis
 - 2 dropped out before the start of the study intervention
 - 2 participants did not complete the 12-week intervention
 - 1 completed the entire protocol through follow-up and were included in the per protocol analysis

Participant Injury history, mental health history, and demographics are reported in tables 2-4.

Table 2. Injury History

	ITT (n=15)		PP (n=11)	
	Mean / n	S.D.	Mean / n	S.D.
Time since Injury (days)	343	269	261	149
Mechanism of Injury	Mean / n	% of total	Mean / n	% of total
Motor Vehicle Collision	7	46.7	5	45.5
Sports Related	6	40	5	45.5
Trauma	2	13.3	1	9.1

Table 3. Mental Health Diagnosis at Baseline

	ITT (n=15)		PP (n=11)	
	n	% of total	n	% of total
Adjustment Disorder	1	6.7	0	0
Bipolar	1	6.7	1	9.1
Multiple Diagnoses	1	6.7	1	9.1
PTSD	4	26.7	3	27.3
None	8	53.3	6	54.5

Table 4. Participant Demographics

	ITT (n=15)		PP (n=11)	
	Mean / n	S.D. / % of total	Mean / n	S.D. / % of total
Age (years)	37.5	14.4	36.5	15
Sex	Male 6	40	5	45.5
	Female 9	60	6	54.5
Race	White 11	73.3	7	63.6
	Asian 2	13.3	2	18.2
	Multi-racial 2	13.3	2	18.2
Marital	Married 1	6.7	0	0
	Divorced 6	40	4	36.4
	Single/Never Married 8	53.3	7	63.6

Table 4 continued

	Education		Employment	
	High school/GED	Some College	College Graduate	Grad School/Prof Degree
	2	13.3	1	9.1
	1	6.7	1	9.1
	10	66.7	8	72.7
	2	13.3	1	9.1
	4	26.7	3	27.3
	2	13.3	2	18.2
	5	33.3	3	27.3
	2	13.3	1	9.1
	1	6.7	1	9.1
	14	93.3	10	90.9
	1	6.7	1	9.1

Discussion & Conclusion

OMT significantly reduced headache burden in TBI patients irrespective of time from injury to intervention. The therapeutic effect continued even after intervention ended, suggesting a lasting effect from OMT. The study supports OMT as a possible therapeutic tool for migraine type PTH.

Biomechanical forces play an important and underrecognized role in the mechanism of headache after mTBI. Injury from linear and rotational acceleration of the head and neck is present in every type of concussion. Using a physical approach to address anatomical changes from trauma may help to correct physiologic disturbances from biomechanical disruption. Therefore, OMT may more effectively target the root cause of the disorder.

Both the trigeminal cervical complex and the myelodural bridge play important roles in headache. The mechanism by which OMT facilitates improvement in headaches could be through direct effects on these structures.

Acknowledgements and Funding

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References

1. Menconi I, Cibola A, Luca AC, Bakris IW. Post-Traumatic Headache: A Review of Prevalence, Clinical Features, Risk Factors, and Treatment Strategies. *J Clin Med*. 2023 Jan 28;12(13):4231. doi: 10.3390/jcm12134231. PMID: PMC3042482.
2. Erickson L C. Chronic outcome of chronic post-traumatic headaches after mild head trauma in US soldiers: An observational study. *Headache*. 2011;51:932-941.
3. Chen MH, Chang YF, Chen WC, Chang CH, Chen JF. Risk of Migraine after Traumatic Brain Injury and Effects of Injury Management Levels and Treatment Modalities: A Nationwide Population-Based Cohort Study in Taiwan. *J Clin Med*. 2023 Feb 10;12(4):1530. doi: 10.3390/jcm12041530.
4. Barlow KM. Post-traumatic headache: An update. *Medical record (Auckland)*. Nov 2012;15(10):1445-1446. doi:10.31121/med13424241.
5. Bafna D, Patel R, Wright A, Joseph D. Osteopathic Manipulative Treatment Relieves Post-concussion Symptoms in a Case of Polytrauma. *J. Neurosurg. Pediatrics*. March 18 2020;20(3):e301-302. doi:10.3171/2019-07-JNSP-00085.
6. Chappell C DE, Dombrowski GV. Assessing the immediate effect of osteopathic manipulation on sports related concussion symptoms. *Chiropractic & Manual Therapies*. 2012;20(1):1.
7. Dombrowski C, Chappell C, Dombrowski G, and Niles A. Osteopathic Manipulative Treatment for Severe Concussion After Acute Severe Traumatic Brain Injury. *Journal of Osteopathic Medicine*. 2010;110(12):610-615.
8. Kovalic D, Eason C, Christensen SR, Smith M, Ellinger H, Hajig and Baker G. Osteopathic Manipulative Treatment for Severe Concussion After Acute Severe Traumatic Brain Injury. *Journal of Osteopathic Medicine*. 2010;110(12):610-615.
9. DeAngelis T, Levin M, Hsu J, and Hsu J. Osteopathic manipulative therapy for headache associated with mild traumatic brain injury. *Journal of Osteopathic Medicine*. 2012;112(1):3-7. doi:10.7556/jom.2012.010001.
10. Di Palo D, Buzzi MG. Effects of Osteopathic Manipulative Therapy on Pain and Mood Disorders in Patients With High-Frequency Migraine. *Journal of the American Osteopathic Association*. 2017;117(10):605-609. doi:10.7556/jaoa.2017.0207.
11. Schubert U, Koenig W, Koenig W, Schubert-U, Schubert-Koenig W, Beck M, Vogt K, Bergmann A.. Efficacy of osteopathic manipulative treatment of female patients with migraine: results of a randomized controlled trial. *Journal of Alternative and Complementary Medicine*. 2011;17(1):14-20. doi:10.1177/03600569103673.
12. Schubert U, Cokl Impact of osteopathic manipulative treatment on cost of care for patients with migraine headache: a retrospective review of patient records. *Journal of the American Osteopathic Association*. 2020;120(4):301-307. doi:10.7556/jaoa.2019-03077.
13. Was SC, Zhi A, Lester A, Mancini A.. Effectiveness of Osteopathic Manipulative Treatment in Concussion Education in Training Student Athletes With Acute Concussion Symptoms. *Journal of the American Osteopathic Association*. 2020;120(4):323-329. doi:10.7556/jaoa.2019-03077.
14. Stewart WF, Deyo RA, Davies AL, Stewart WF. Development and testing of the Migraine Disability Assessment (MDAS) Questionnaire to assess headache related disability. *Neurology*. 2001;56(3):Suppl 1-2. doi:10.1212/WNL.56.3Suppl_1-2.302.
15. R, The CES-D Scale: A Self-Report Depression Scale for Research in general population. *Arch Psychol Res*. 1977;10:385-401. doi:10.1177/0360056977010003006.
16. Wang SJ, Li SH, Jiang GD. What it offers among headache diagnosis: analysis of SF-36 survey in 902 headache patients. *Pain*. 2002;90(3):285-292. doi:10.1016/S0304-380X(02)00080-8.
17. Bartsch T, Götz G. The trigeminal cervical complex and migraine: current concepts and syntheses. *Curr Pain Headache Rep*. Oct 2013;17(10):374-380. doi:10.1007/s10637-013-0036-y.
18. Erck DK, Rohr ME. The cervical trigeminal bridge, a review of literature and clinical implications. *J Clin Osteoporos*. Jun 2014;5(2):284-287.
19. Menconi I, Cibola A, Luca AC, Bakris IW. Post-Traumatic Headache: A Review of Prevalence, Clinical Features, Risk Factors, and Treatment Strategies. *J Clin Med*. 2023 Jan 28;12(13):4231. doi: 10.3390/jcm12134231. PMID: PMC3042482.
20. Erickson L C. Chronic outcome of chronic post-traumatic headaches after mild head trauma in US soldiers: An observational study. *Headache*. 2011;51:932-941.
21. Chen MH, Chang YF, Chen WC, Chang CH, Chen JF. Risk of Migraine after Traumatic Brain Injury and Effects of Injury Management Levels and Treatment Modalities: A Nationwide Population-Based Cohort Study in Taiwan. *J Clin Med*. 2023 Feb 10;12(4):1530. doi: 10.3390/jcm12041530.
22. Barlow KM. Post-traumatic headache: An update. *Medical record (Auckland)*. Nov 2012;15(10):1445-1446. doi:10.31121/med13424241.
23. Bafna D, Patel R, Wright A, Joseph D. Osteopathic Manipulative Treatment Relieves Post-concussion Symptoms in a Case of Polytrauma. *J. Neurosurg. Pediatrics*. March 18 2020;20(3):e301-302. doi:10.3171/2019-07-JNSP-00085.
24. Chappell C DE, Dombrowski GV. Assessing the immediate effect of osteopathic manipulation on sports related concussion symptoms. *Chiropractic & Manual Therapies*. 2012;20(1):1.
25. Dombrowski C, Chappell C, Dombrowski G, and Niles A. Osteopathic Manipulative Treatment for Severe Concussion After Acute Severe Traumatic Brain Injury. *Journal of Osteopathic Medicine*. 2010;110(12):610-615.
26. Kovalic D, Eason C, Christensen SR, Smith M, Ellinger H, Hajig and Baker G. Osteopathic Manipulative Treatment for Severe Concussion After Acute Severe Traumatic Brain Injury. *Journal of Osteopathic Medicine*. 2010;110(12):610-615.
27. DeAngelis T, Levin M, Hsu J, and Hsu J. Osteopathic manipulative therapy for headache associated with mild traumatic brain injury. *Journal of Osteopathic Medicine*. 2012;112(1):3-7. doi:10.7556/jom.2012.010001.
28. Di Palo D, Buzzi MG. Effects of Osteopathic Manipulative Therapy on Pain and Mood Disorders in Patients With High-Frequency Migraine. *Journal of the American Osteopathic Association*. 2017;117(10):605-609. doi:10.7556/jaoa.2017.0207.
29. Schubert U, Koenig W, Koenig W, Schubert-U, Schubert-Koenig W, Beck M, Vogt K, Bergmann A.. Efficacy of osteopathic manipulative treatment of female patients with migraine: results of a randomized controlled trial. *Journal of Alternative and Complementary Medicine*. 2011

N = 16

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Both the trigeminal cervical complex and the myodural bridge play important roles in headache.^{17,18} The mechanism by which OMT facilitates improvement in headaches could be through direct effects on these structures.

A manuscript is in preparation for submission to a peer-reviewed journal.

King HH, Mills P, Schiesher D, Pung M, Martone J, Wing D. Effects of Osteopathic Manipulative Treatment on the Parkinson's Patient: A Randomized Controlled Trial. In preparation 2025.

OMT for Parkinson's disease – Big Picture
Study funded by AOA , AAO and OPC done at
UCSD subjects treated at OPC.

N = 88

OMT = 30

Light touch (Sham) = 28

Standard Care = 30

OMT protocol emphasized OCMM: VST, CV4

Outcome measures

Cognitive & Psychological tests

Balance tests

Stride analysis

Timed Up and Go

Sit in chair, how fast to get up using
The LEGsys+ body worn sensor system

OMT group Ss were significantly faster than LT and Control,
 $p < 0.05$

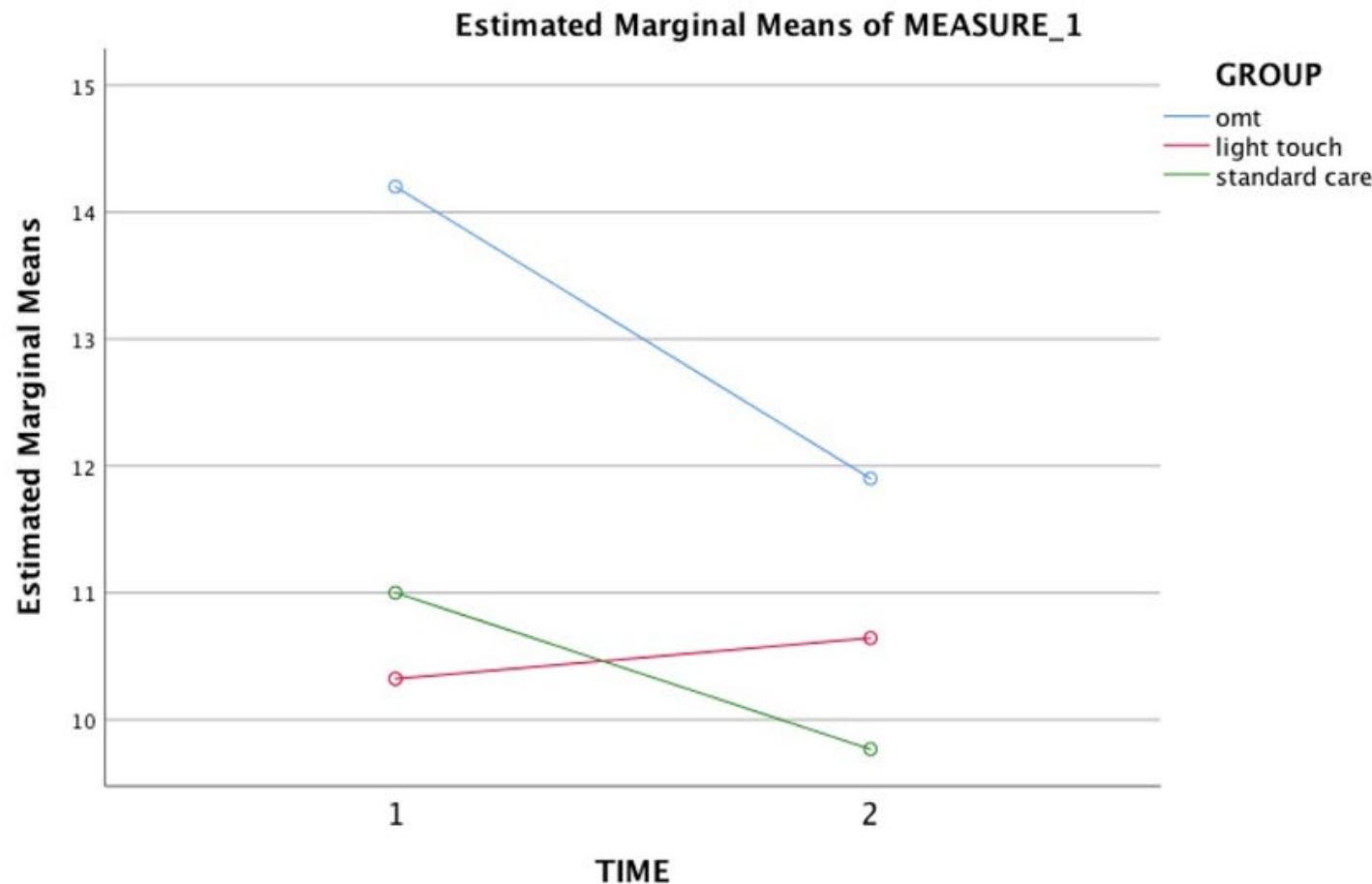
Quality of Sleep

On the Pittsburg Sleep Quality Index (PSQI)
Sleep quality improved for the OMT arm compared to the LT
and SOC groups ($p < 0.001$)

Perceived Stress Scale (PSS)

Significant reduction over time ($p = 0.026$) for OMT

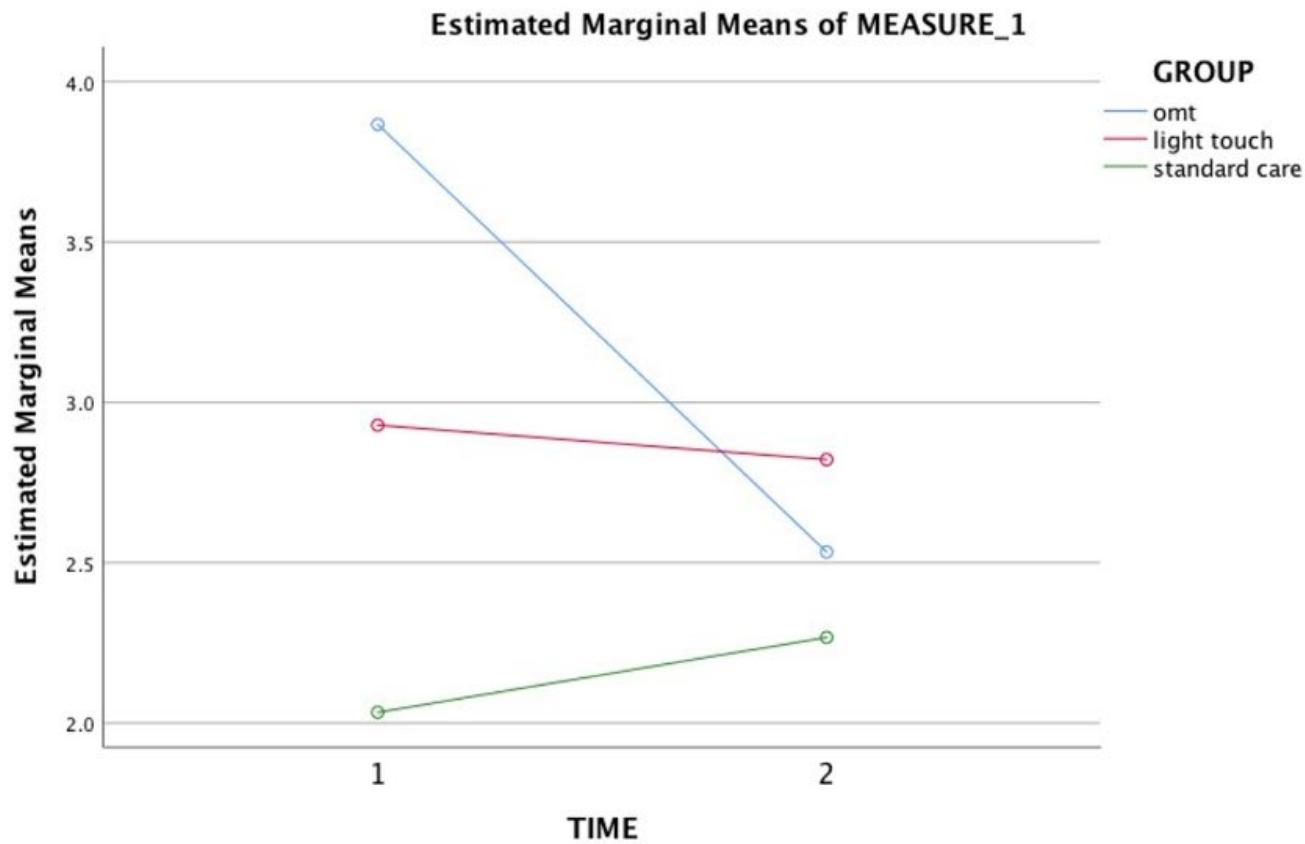
STRESS (PSS)



Geriatric Anxiety Inventory (GAI)

OMT group significant trend ($p = 0.054$) in reduction, while LT and SCO unchanged

ANXIETY (GAI)



The Special Case of the Compression of the 4th Ventricle

CV4

Saturday the CV4 is presented, and there are several CV4 related researches that are interesting and important to know about.

Effects of CV4

1. Sleep Dynamics and Muscle Sympathetic Nerve Activity

Cutler MJ, Holland BS, Stupinski BA et al. Cranial manipulation can alter sleep latency and sympathetic nerve activity in humans. *J Altern Comp Med.* 2005;11(1):183-190.

2. Alzheimer's Disease

Tobey H, Lucas T, Bledsoe D, Mykins M, Campbell C, Berr SS, Sasser T, Helm R, Brolinson PG, Klein BG, Costa BM. Effect of cranial manipulative medicine on an aged rat model of Alzheimer disease. *J Am Osteopath Assoc.* Published online October 15, 2019. Doi:10.7556/jaoa.2019.121

3. Balance and Equilibrium

Lopez D, King HH, Knebl JA, Kosmopolous V, Collins D, Patterson RM. Effect of comprehensive osteopathic manipulation treatment on balance in elderly patients: a pilot study. *J Am Osteopath Assoc.* 2011;111(6): 382–388.

Fraix M, Gordon A, Graham V, et al. Use of the SMART balance master to quantify the effects of osteopathic manipulative treatment in patients with dizziness. *J Am Osteopath Assoc.* 2013;113(5):394–403

Effects of CV4

4. Alpha Rhythm Enhancement

Miana L, Val Bastos VH, Machado S, et al. Changes in alpha band activity associated with application of the compression of the fourth ventricle (CV-4) osteopathic procedure: a qEEG pilot study. *J Bodywork Movement Ther.* 2013;17(3):291-296.

5. Uterine contractions

Gitlin RS, Wolf DL. Uterine contractions following osteopathic cranial manipulation. *J Am Osteopath Assoc.* 1992;92(9):1183 [Abst]

6. Cranial Tissue Oxygenation

Shi X, Rehrer S, Prajapati R, et al. Effect of cranial manipulative medicine on cerebral tissue oxygenation. *J Am Osteopath Assoc.* 2011;111(12):660-667.

7. Dementia

Gerdner LA, Hart LK, Zimmermann MB. Craniosacral still point technique: Exploring its effects in individuals with dementia. *J Gerontological Nursing.* 2008;34(3):37-46

Effects of CV4

8. Safety

Hensel KL, Roane BM. Does compression of the fourth ventricle cause preterm labor? Analysis of data from the PROMOTE study. *J Am Osteopath Assoc.* 2019;119(10):668-672.

9. Multiple Sclerosis

Cordano C, Armezzani A, Veroni J, et al. Osteopathic manipulative therapy and multiple sclerosis: a proof-of-concept study. *J Am Osteopath Assoc.* 2018;118(8):531-536.

8. Autonomic Nervous System and Acupuncture

Hendryx JT, Kannan A, Prashad J, Falk K. Connecting the dots: alterations in bioelectric activity at acupuncture Ting (Jing-Well) points following CV4 cranial manipulation. *J Osteopath Med.* 2023;123(3):151-158.

Tobey H, Lucas T, Bledsoe D, Mykins M, Campbell C, Berr SS, Sasser T, Helm R, Brolinson PG, Klein BG, Costa BM. Effect of cranial manipulative medicine on an aged rat model of Alzheimer disease. *J Am Osteopath Assoc*. Published online October 15, 2019. Doi:10.7556/jaoa.2019.121

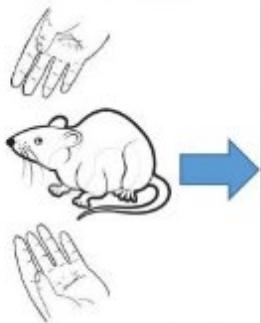
Cranial Osteopathic Manipulation (COM) on Animal Models of AD



Hope Tobey, DO



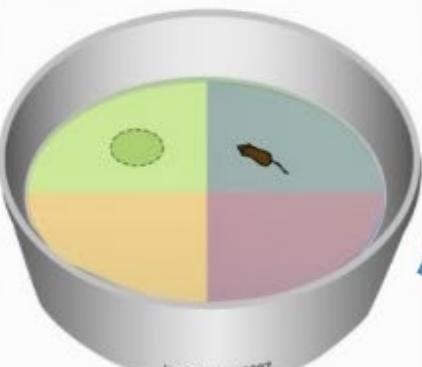
Per Gunnar Brolinson, DO



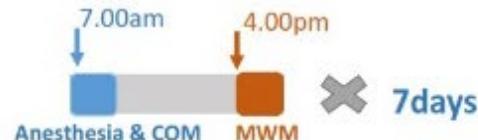
Cranial osteopathic manipulation (COM)
on TgF344 or Aged rat
model of AD.

18months old rats
treated for 7days

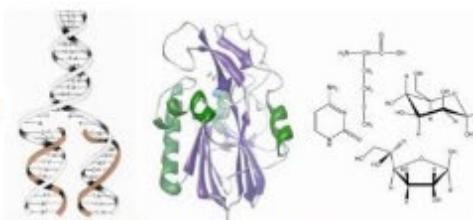
Aim.1



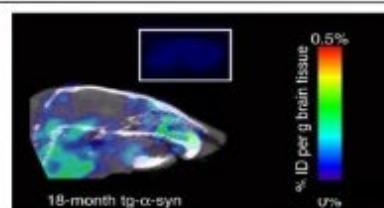
Lynn Talton ©2007
Assessment of Spatial Learning & Memory by Morris water Maze



Experimental Design



Identify changes in brain gene, protein and metabolite levels



Demonstration of Ab^β clearance in live animals by PET imaging



Bradley Klein, PhD

A

Dickerson et al. 2023

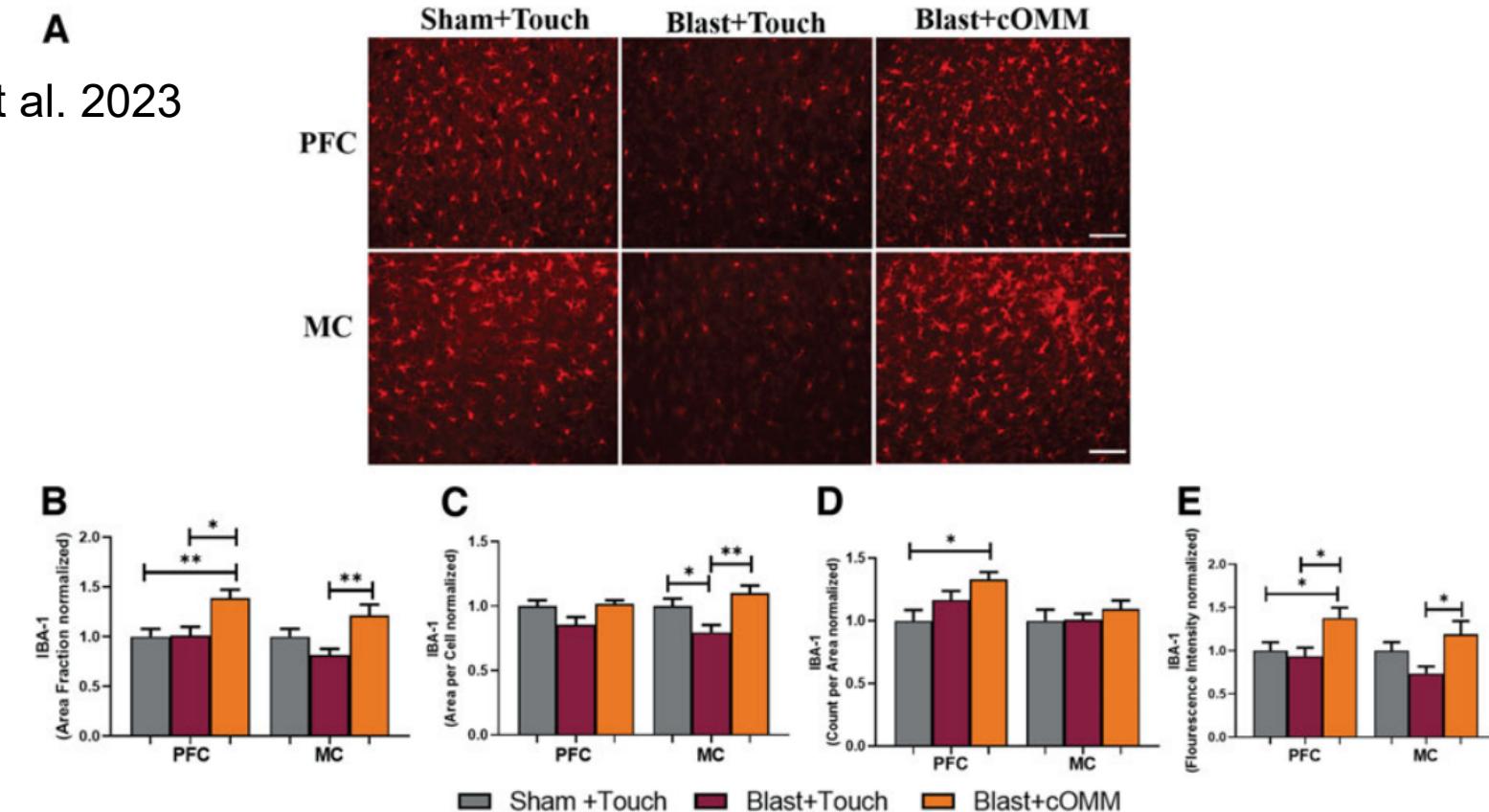


FIG. 5. (A) Representative images of IBA-1 expression within the PFC and MC regions of the brain. Magnification is at $20\times$ and scale bar = 100 um. **(B)** Area fraction was significantly higher within the PFC of the blast + cOMM-treated animals compared to the sham + touch and blast + touch groups. Area fraction of IBA-1 was significantly higher in the MC region of the blast + cOMM group in comparison to the blast + touch group. **(C)** Mean area per cell indicated a significant decrease in microglia cell soma size in the MC of the blast + touch group compared to both the sham + touch and blast + cOMM groups. **(D)** Increased amounts of microglia were observed in the PFC of blast + cOMM animals compared to the sham + touch group. **(E)** IBA-1 expression was significantly increased in the PFC of blast + cOMM animals compared to both the blast + touch and sham + touch groups. Increases in IBA-1 expression were also observed in the MC of the blast + cOMM group compared to the blast + touch group. $*p < 0.05$, $**p < 0.01$. Data are represented as mean \pm SEM. cOMM, cranial osteopathic manipulative medicine; IBA-1, ionized calcium-binding adaptor molecule 1; MC, motor cortex; PFC, pre-frontal cortex; SEM, standard error of the mean.

Treated N = 6 Untreated N = 6

A

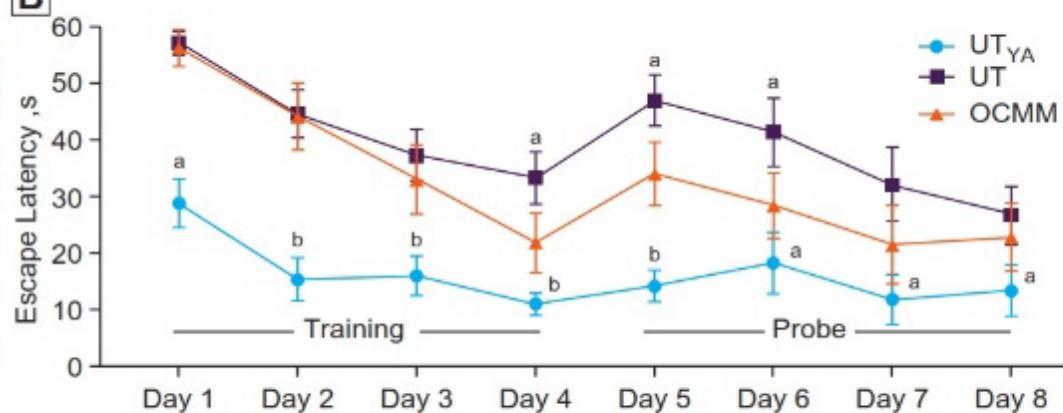


OCMM (CV4) improved spatial learning and memory

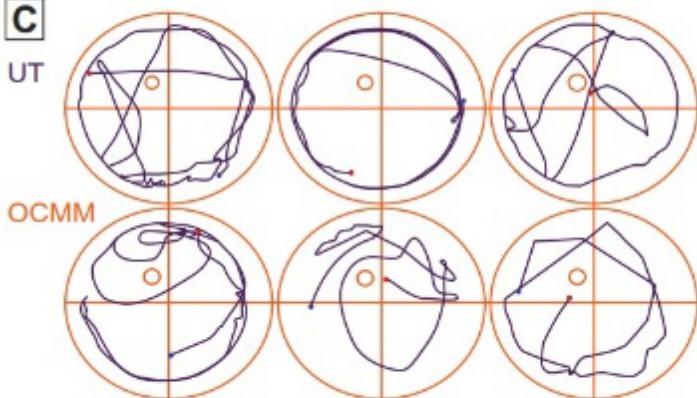
A



B



C



D

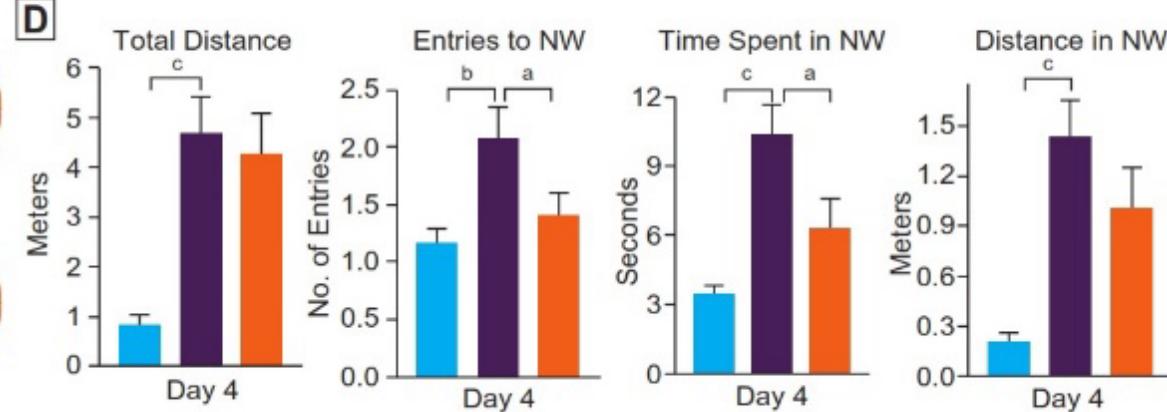


Figure 1.

(A) Position of the anesthetized animal when performing osteopathic cranial manipulative medicine (OCMM) and a closer view of OCMM performance. (B) Time taken to reach platform on each experiment day. Rats received 4 days (days 1-4, platform visible) of training before probe trials (days 5-8, platform invisible). Sixteen-week-old untreated young adult (UT_{YA}) male rats exhibited significantly shorter escape latency on day 1-8 compared with untreated (UT) aged rats. During training day 4 and probe days 5 and 6, OCMM-treated rats reached the platform sooner than the UT rats. (C) Representative plots show the trajectory of UT and OCMM-treated animal movement. Four quadrants, platform location (circle at northwest quadrant), starting (blue dot), and end (red dot) points are marked. (D) Histograms show the distance travelled, number of entries to the northwest quadrant (NW), time spent in NW, and distance travelled in NW on the last day (day 4) of the training trial period. $n=6$; unpaired, 2-tailed, t test, $^aP<.05$, $^bP<.01$, and $^cP<.001$.

OCMM (CV4) reduces A β protein

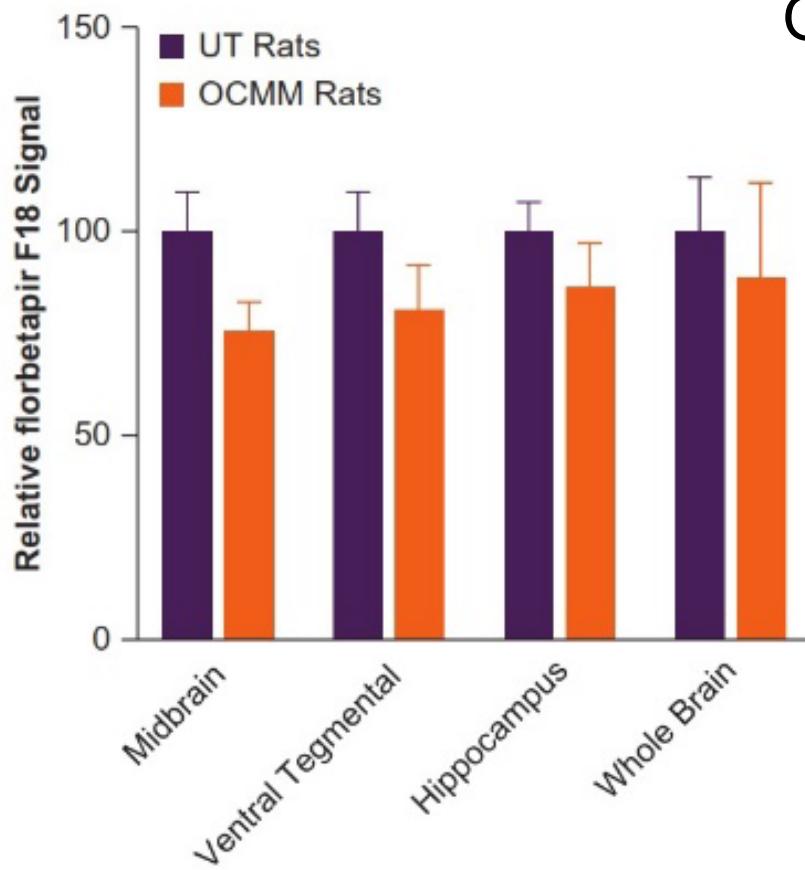
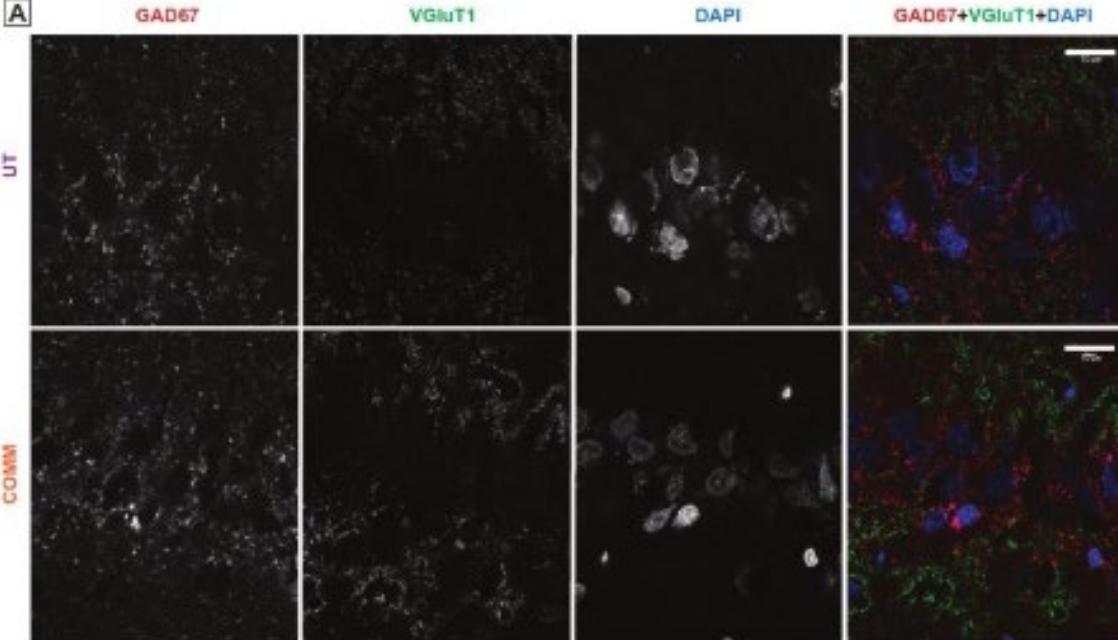
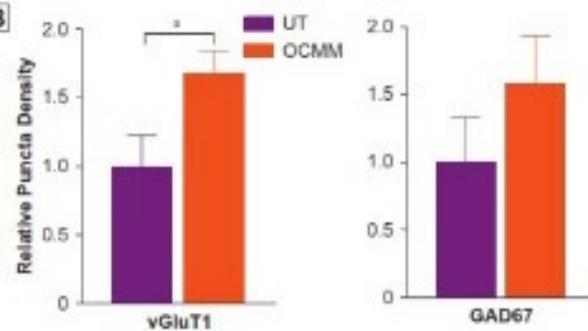
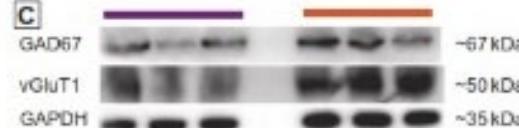
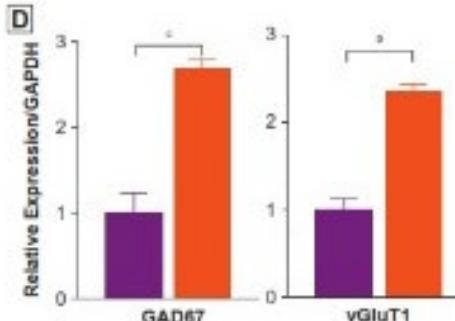


Figure 2.

Histograms show the relative florbetapir F18 signal in untreated (UT; n=3) and osteopathic cranial manipulative medicine (OCMM)-treated (n=3) aged rats. Normalized and averaged (mean [SE]) signals revealed a numerical reduction in amyloid β (A β) levels at midbrain (24.5% [2.4%]), ventral tegmental area (19.1% [2.6%]), hippocampus (13.4% [1.6%]), and whole brain (11.2% [2.9%]) of OCMM-treated UT rats.

A**B****C****D****Figure 4.**

(A) Representative immunohistochemical Images of the hippocampal CA1 region in untreated (UT; n=3) and osteopathic cranial manipulative medicine (OCMM)-treated (n=3) rat brain sagittal sections immunostained for glutamic acid decarboxylase (GAD67), vesicular glutamate transporter 1 (VGluT1), and 4,6-diamidino-2-phenylindole (DAPI). (B) Puncta density analysis reveals significantly increased expression of VGluT1 but not GAD67 in the CA1 region (mean [SEM] puncta density in UT, 1.0 [0.33] vs OCMM, 1.57 [0.34]; $P<.05$). (C) Western blots show the increased expression of GAD67. GAD67 (UT relative density, 1.00 [0.29] vs OCMM, 2.68 [0.11]; $P<.001$) and (D) VGluT1 (UT relative density, 1.00 [0.12] vs OCMM, 2.35 [0.07]; $P<.01$). Histograms represent the normalized averages. Unpaired 2-tailed t test. ^a $P<.05$, ^b $P<.01$, ^c $P<.001$. Scale bar, 10 μ M.

OCMM (CV4)
modulates
synaptic
transmission

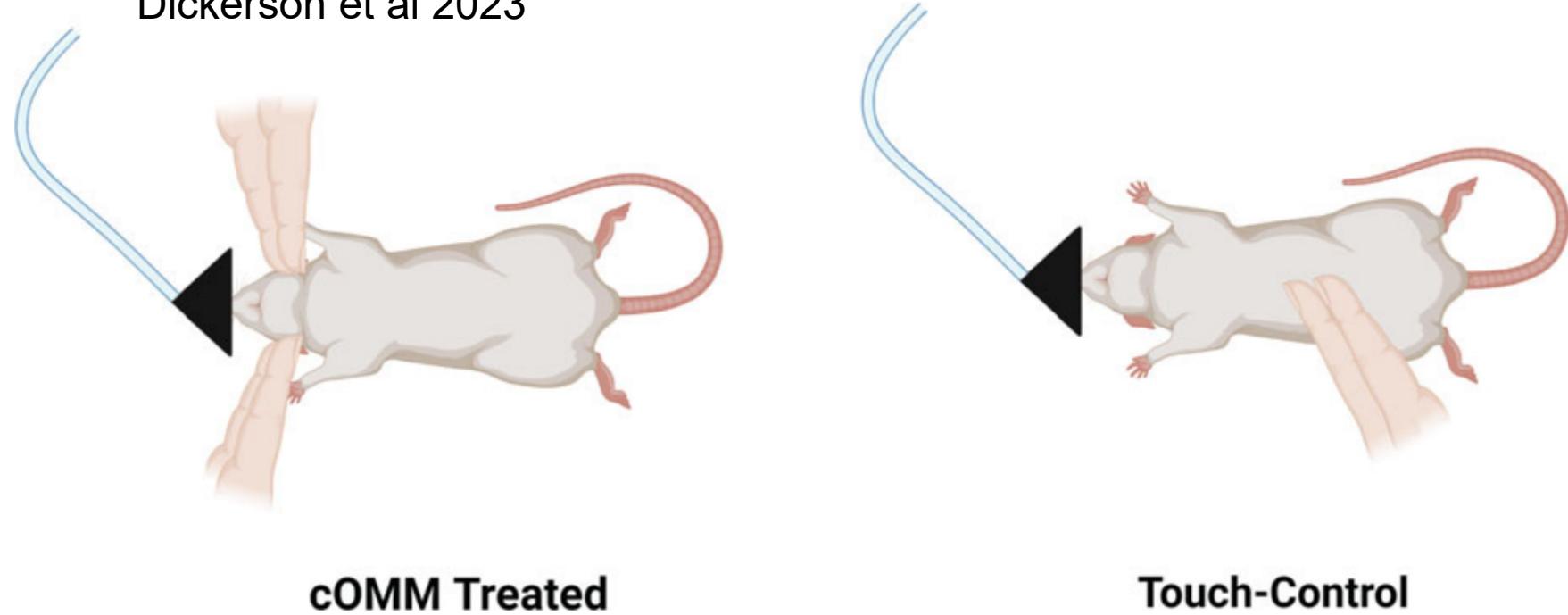
Increased total
amount of
neurotransmitter
molecules in brain

Dickerson M, Murphy S, Hyppolite N, et al. Osteopathy in the cranial field as a method to enhance brain injury recovery: a preliminary study.
Neurotrauma Reports. 2022;3.1. <https://doi.org/10.1089/neur.2022.0039>

Animals were separated into three groups: blast + cOMM treatment ($n = 8$); blast + touch ($n = 8$); and sham + touch ($n = 8$)

Blast Wave Characteristics: Group 3 x 1h; Peak pressure (psi) 16.52 ± 2.12 ; Positive duration (ms) 2.13 ± 0.22 ; Positive impulse (psi*ms) 13.34 ± 1.70 ; Rise time (ms) 0.022 – 0.002.

Ten-week-old Sprague-Dawley rats were anesthetized and exposed to three blast insults separated by 1 h each. Sham animals underwent all procedures with the exception of the blast exposure.



cOMM Treated

Touch-Control

FIG. 1. Position of the anesthetized animal while the clinician is performing the CV4 technique as a part of the cOMM treatment (left). Control animals were touched with the index and middle fingers by a non-clinician for the same amount of time as the treatment group (right). Created with BioRender.com. cOMM, cranial osteopathic manipulative medicine; CV4, compression of the fourth ventricle.



Immediately after CV4, the LPT was performed. To perform the LPT, the operator pressed the abdomen of the anesthetized animal with the thumb on one side and the index and middle fingers on the other side of the medial sagittal plane. The fingers were placed bilaterally, caudal to the ribs. Sufficient pressure was exerted medially and cranially to compress the lower ribs until substantial resistance was produced against the diaphragm, then the pressure was released. Compressions were administered at a rate of approximately one per second for the duration of 45 sec of treatment.



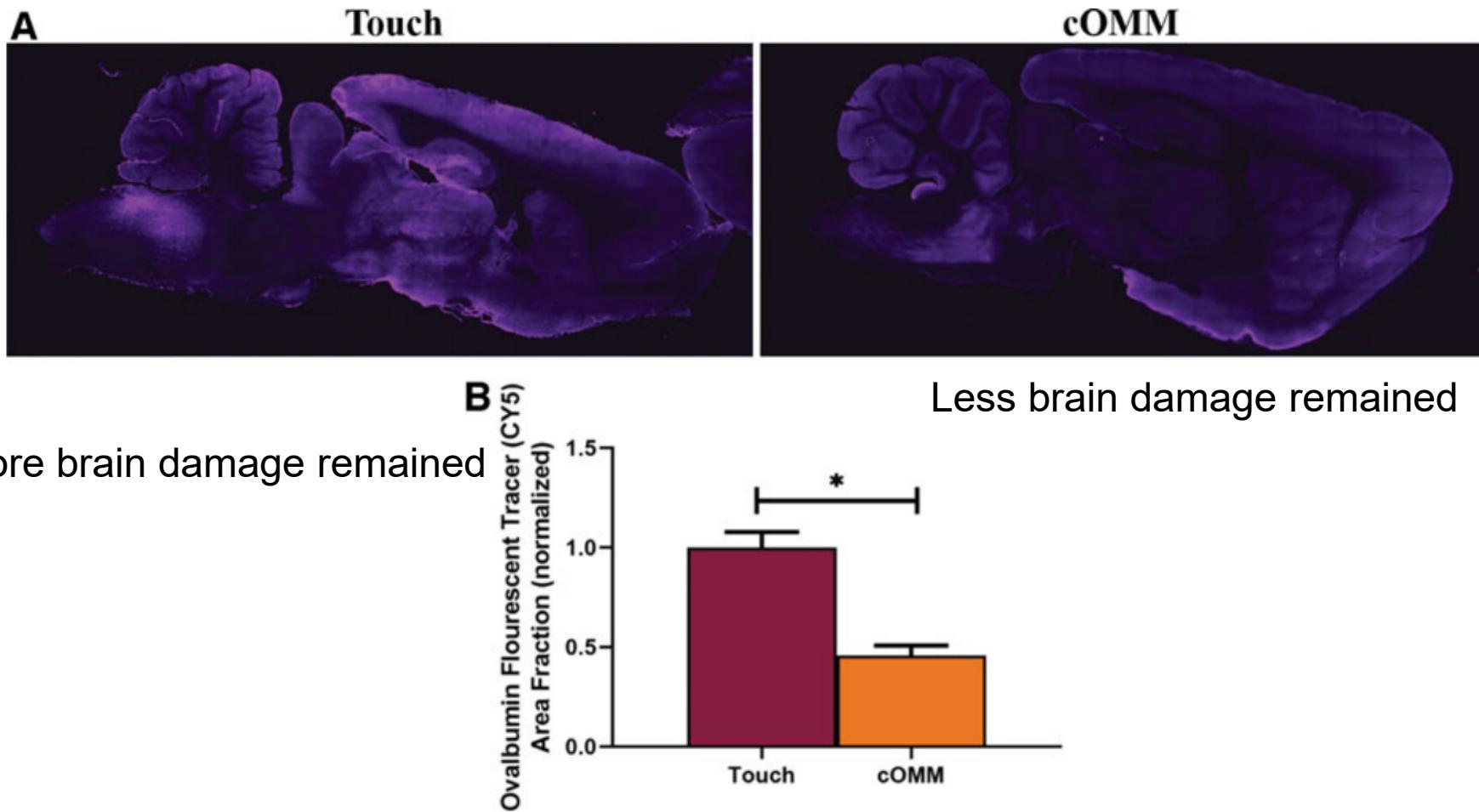


FIG. 2. cOMM enhanced fluid flow within the brain. **(A)** Representative images show that the sham + touch group had higher levels of fluorescent tracers within the brain parenchyma compared to the cOMM group. **(B)** Quantifying tracer levels within brain tissue indicated that the area fraction of tracers in animals exposed to the sham + touch was significantly higher compared to the cOMM group. $*p < 0.05$. Data are represented as mean \pm SEM. cOMM, cranial osteopathic manipulative medicine; SEM, standard error of the mean.

Results of this study indicated that removal of astrocytic APOE4 mitigated tau-mediated neurodegeneration through decreases in tau-induced synaptic loss and microglial phagocytosis. Upregulation of proteins such as APOE4 and Tau are also prevalent in pathological conditions post-TBI, which can lead to a long-term deficit.²⁷ These studies suggest that a therapeutic strategy addressing the rapid clearance of intra- and extracellular proteins could reduce astrocyte reactivity and microglia activation, thus promoting recovery of the injured brain.

Thank You
Any Questions

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