CASE STUDY

Improvement in Alpha Brain Waves, Coordination and Emotional Regulation in a Pediatric Patient with Chiropractic Care Using Network Spinal Analysis

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Abstract

Objective: The objective of this report is to describe improvements in Alpha Brain Waves, coordination and emotional regulation experienced by a patient undergoing subluxation-based chiropractic care using Network Spinal Analysis.

Clinical Features: A 7-year-old female presented with slow physical skill acquisition and difficulty with coordination since birth. She had an aversion to using utensils, preferring to use her fingers to self-feed. She also had emotional outbursts and low self-esteem of two years duration.

Intervention & Outcomes: Management of this case is based on Reorganizational Healing (ROH) including chiropractic care through Network Spinal Analysis (NSA) for the reduction of facilitation within the spinal cord. The promotion of structural correction of the misalignment component of the associated vertebral subluxation and Somato Respiratory Integration (SRI) to connect enhanced somatic awareness with respiration were also goals of care. After two months there was improved Alpha Waves, coordination, spontaneous use of silverware for self-feeding and an improvement in emotional regulation.

Conclusion: Further research is warranted to examine the effect of chiropractic on brain waves and the development of coordination and emotional regulation in the pediatric population.

Key Words: *chiropractic, vertebral subluxation, adjustment, coordination, emotional regulation, Network Spinal Analysis (NSA), Alpha Brain Waves*

Introduction

Chiropractic is a health care discipline that serves to optimize health through the principle that the body has an innate intelligence by which it sustains and maintains itself. Chiropractors place particular emphasis on the subluxation, which compromises neural integrity and can cause deleterious effects to health.[1] In recent years, the association between the correction of vertebral subluxation and quality of health has been studied in greater detail with objective measures showing what chiropractors have long been reporting anecdotally.[2-3] Chiropractic care and the correction of vertebral subluxation have been associated with cases relating to improvements in quality of life,[4] structural integrity,[5] attention[6] and development of language,[7] among other aspects of health and wellness.[2-3]

The concept of subluxation is understood through various component models and categorizations of clinical applications as presented by Kent. Tonal approaches tend to view the spine and the nervous system as a functional unit with particular interest on functional outcomes, which are of value in subluxation-centered research.[8] Network Spinal Analysis is

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one such tonal approach, and it is a low-force spinal application within the Reorganizational Healing paradigm that is widely used by chiropractors.

The purpose of Network Spinal Analysis is to improve the cognitive and precognitive awareness of an individual's passive spinal structures, active tension patterns, and development of unique standing waves of skeletal motor activity believed to assist in improved self-organization of the spine and nervous system.[3] Network Spinal Analysis utilizes a system of assessment and intervention for the development of emerging organizational properties in the spine and nervous system to improve spinal and neural integrity, adaptability, and to advance wellness and quality of life.[9] The Network Phasing System is used to identify and prioritize the category of subluxation, and the spinal segment(s) to be adjusted.[10] NSA recognizes two categories of subluxation arising from Panjabi's subsystem model.[11] Structural subluxation is thought to be initiated by physical trauma or mechanical stress, resulting in misalignment and consequent nerve interference. Facilitated subluxation is thought to occur as an effect of spinal cord tension and nerve root pressure, causing osseous misalignment as a result. Facilitation is an aberrant sensory and motor response to the accumulation of sub-threshold stimuli over time, which leads to a loss of spinal integrity.[10]

The application of a low force touch contact following NSA protocol often generates oscillatory movements of the spine synchronized with deep respiration[10] which serve two purposes: to reduce facilitation within the spinal cord while promoting the structural correction of the misalignment component of the associated vertebral subluxation.[10] Clinical outcomes specific to the initial level of NSA care include awareness and entrainment of respiratory motion with spinal motion, reduction of parameters of adverse spinal cord tension, release of tension from spinal stability subsystems, enhancement of spinal and neural integrity, reorganization of spinal structures, development of body's ability to self-regulate tension, and an increase in basic somatic awareness.[9]

It is proposed that a reduction of sympathetic state coupled with an increase in awareness of respiration, energy and movement allows the frontal lobe and vagal centers to more readily assess perception, structure and behavior.[3] One study by Miller found that subjects receiving Network care have a significant decrease in electrodermal activity, an indirect measure of the sympathetic nervous system, compared to control subjects.[12] The biological mechanism by which these changes are promoted is yet to be understood and would benefit from improved outcome measures of cortical activity concomitant with chiropractic care.

The literature describing tonal chiropractic approaches and changes in pediatric behavior is limited. Children most frequently present for wellness care,[13] followed by condition-based care for respiratory, digestive, sleep and musculoskeletal complaints.[13-15] To date, there have been a few studies on chiropractic care in the pediatric population on safety and effectiveness.[13-14] While individuals under Network care tend to report improvements in wellness and positive changes towards health lifestyle practices in adults,[2-3] few studies report the effect on children.

The purpose of this case study is to document the parent-rated improvements in coordination and emotional regulation reported in association with in a 7-year-old female under Network Spinal Analysis care.

Case Report

History

A 7-year-old female presented with her mother for chiropractic care. According to the mother, she had slow physical skill acquisition and difficulty with coordination since birth. She ate with her hands and avoided the use of utensils. She had emotional outbursts and low self-esteem of two years duration. The mother reported that emotional outbursts were drawn out, sometimes lasting from hours to days.

The mother reported that the gestational period was 40 weeks and five days in duration. Ultrasound was utilized at seven weeks for pregnancy confirmation, at 20 weeks to monitor growth, at 23 weeks for gender identification (3D ultrasound) and at 40 weeks prior to birth. A fetal non-stress test was performed at 40 weeks, indicating low activity of the fetus. Labor was induced due to low amniotic fluid and the mother was administered a spinal epidural. The mother had a vaginal (cephalic) birth at a hospital with an obstetrician present. Total duration of labor was 10 hours, including two hours of active labor. Infant was born with no evidence of birth trauma. APGAR score was 9/10 at birth and 10/10 at five minutes. At birth, infant received silver nitrate eye drops, a vitamin K injection, and a Hepatitis B vaccination. The mother experienced post-partum depression with no difficulties breast-feeding or bonding. The child was breastfed for 11 months, after which cow's milk was introduced following the cessation of breast-feeding. At age two, a vaccination series including MMR was administered. The child experienced adverse reactions to vaccinations including fever, malaise, transient hives, irritability, and drowsiness. She developed a respiratory infection shortly post-vaccination for which she received two courses of antibiotics. The child was never introduced to formula and has no known food intolerances or allergies. The child slept well, 8-10 hours a night regularly. The child has no night terrors, sleep-walking or difficulty sleeping.

The mother reported that child's developmental milestones are as follows: responded to sound at one month, followed an object at two months, held head up at four months, sat alone at seven months, crawled at nine months and began walking at one year of age. The mother reports the child as having behavioral problems and emotional outbursts. The child has attended daycare in a home setting since age two. At the time of the writing she is currently 7-years-old and is homeschooled using a computer-based program. She spends over 15 hours a week at the computer, and approximately 24 hours a week at play. Child does not engage in any sports. She does not wear glasses or contact lenses and does not have trouble reading. There is no history of hospitalizations or surgeries. Child eats a healthful diet consisting of organic foods, raw vegetables, beef, poultry, whole grains and fruit supplemented with a daily multi-vitamin. She drinks water regularly.

Chiropractic Assessment

Analysis and adjustment procedures utilized in the management of this case are based on Network Spinal Analysis (NSA), developed by Donald Epstein, DC. An initial examination was performed to assess the presence of Adverse Mechanical Cord Tension (AMCT) including vertebral subluxation and spinal defense patterns using NSA protocol. Spinal and neural integrity was assessed through motion and static palpation, neurological assessment and an evaluation of stress response consisting of electroencephalography, heart rate, skin conductance, temperature, respiratory rate, and surface electromyography.

Motion palpation revealed moderate to severe decrease in intersegmental motion indicating passive subsystem tension at left C1, right C3, T3, T7, T8, right L5 and coccyx spinal segments. Static muscle palpation revealed significantly taut fibers in the cervical spine and at the right sacroiliac area associated with active subsystem tension. On a scale of 1-5, with 5 being the most severe, tension is rated as a 4/5 overall. Tension within the neural control subsystem was present as indicated by heel tension, eversion stress and abduction stress. Significant heel tension, defined as resistance to dorsiflexion from full plantarflexion, was found corresponding to coccyx AMCT and was rated as severe (5/5). Eversion stress, or resistance to eversion from inversion, was moderate to severe (4/5) and is considered demonstrative of lateral cord tension. Abduction stress, as revealed by an increase of resistance to hip abduction, was mild to moderate (2/5). Adduction stress was subclinical (0/5). With patient prone and legs in the extended position, patient has a ½ inch left functional short leg. Head rotation resulted in a fast lengthening of the short leg, characteristic of C1 AMCT associated with a cervical vertebral subluxation.[10]

Examination included a Stress Response Evaluation using electroencephalogram (EEG), heart rate variability, heart rate, skin conductance, temperature, respiration rate and paraspinal surface electromyography (utilizing Neuroinfiniti). The Stress Response Evaluation records two baseline readings with eyes open and eyes closed, three challenges (i.e., cognitive – math/stroop test, emotional – noise stress, and physical – breathing exercise) alternated with three recovery periods. The purpose of this evaluation is to determine the state of activity and engagement at baseline, adaptation under stress, and recovery to baseline when stressors are removed. Setup for the exam includes placement of a respiration belt around the patient's diaphragm, placing temperature, galvanic skin response (GVR) and blood volume pulse (BVP) sensors at the fingertips, sEMG pads at the mastoid, and EEG contacts on ears and scalp.[16] The results are as follows:

- **EEG** is a test of cortical activity using electrodes attached to the ears and scalp to measure brain wave frequencies. Stress events including the math test, noise and breathing exercise typically increase beta activity while increased alpha and theta waves are seen during relaxation and recovery. The stress response test demonstrated good beta engagement indicating good focus, good theta engagement indicating good subconscious relaxation, fair alpha engagement indicating fair conscious relaxation and poor sensorimotor rhythm engagement indicating poor central nervous system reorganization. EEG analysis demonstrated that the alpha wave production was below the ideal 22%, indicating a decreased ability for conscious relaxation. It was noted that the neurological pattern response is under-aroused, indicating a state of too little beta wave activity or too much alpha, theta, or delta.

- **Heart rate variability** is used to measure stress effects, but it was inaccurate in this case due to age and the related increased heart and respiration rates.

- **Heart rate** is a measure of pulse at baseline, under stress, and at recovery using BVP sensors at the fingertips. Heart rate was within normative average for her age at 100-103. Heart rate was increased at baseline reading with eyes closed and there was an inverse response to noise.

- **Skin conductance** is a test of the neurological response to stress and recovery to baseline as measured in the amount of moisture produced by the sweat glands in the hands detected by GSR sensors at the fingertips. It is a measure of a person's ability to reduce the effects of the stressor after the event. The child demonstrated poor recovery after the noise stress challenge and the breathing challenge, high response to the math/stroop challenge and noise challenged, with an increased rate during the breathing challenge.

- **Temperature** was within normal limits at baseline and under stress. The normal response to stress is constriction of blood from the extremities with a reduction of temperature in the extremities.

- **Respiration rate** was measured using a respiration belt around the diaphragm. Child is within normative range for her age at 12-20 respirations per minute. Respiration increased during recovery and decreased during stress events. It is noted that child held her breath during the math test, and had increased rate during the breathing exercise. Breathing rate remained the same at rest and at exercise.

- **Surface EMG** is a test of motor activity in a relaxed state and in active motion, measured with sEMG pads at the mastoid. sEMG analysis demonstrated high muscle tension, high stress response and a high tension response to math test. Child is an upper respiratory breather.

Chiropractic Care

The patient's care plan consisted of two spinal entrainments a week for eight weeks accompanied by weekly Somato Respiratory Integration sessions and a progress examination at the conclusion of eight weeks. At each visit, she was assessed using NSA protocol for indicators of subluxations associated with adverse mechanical spinal cord tension and secondary vertebral subluxations. Specific force applications were utilized based on the above parameters. NSA level of care response was graded according to progression of the Respiratory Wave. Somato Respiratory Integration exercises were facilitated weekly in office for Stages 1 and 2 to increase awareness of the body and of its different rhythms.

Network Spinal Analysis is an application of spinal Reorganizational Healing that is currently practiced by chiropractors. It involves low force contacts to the spine, accessing unique "spinal gateways" in applications termed spinal entrainments to enhance the self-regulation of passive, active, and neural spinal subsystem tension, somatic awareness, and neural coherence. It is accompanied by SRI to create conscious awareness and integration with the body as a tool to "experience life with increasing depths of internal connection and wider ranges of human expression."[9] Network Spinal Analysis and Somato Respiratory Integration (SRI) are elements of Reorganizational Healing (ROH), the overarching paradigm that promotes progressively complex strategies in the baseline function of a system for growth[17] and draws on self-assessment and utilization of resources to promote sustainable change.[9] NSA and SRI are utilized together in this case for the patient's care.

There are five phases in the Network Spinal Analysis protocol, each correlating with specific osseous structures and parameters indicating AMCT. Parameters assessed in NSA include palpation, leg length, heel tension, eversion stress, adduction stress, abduction stress, cervical syndrome and flexion leg check (patient is prone with legs extended, from which knees are passively flexed). These parameters assist the practitioner to determine which phase, and therefore what osseous level to affect.[10] Defense physiology associated with adverse mechanical cord tension is assessed through palpation of the stabilizing spinal subsystems as described by Panjabi.[11] Once the phase is determined, the practitioner then determines the specific location of a "spinal gateway" on the osseous level and a contact is made here with a low force contact to affect an adjustment.[10]

Somato Respiratory Integration utilizes specific exercises that connect enhanced somatic awareness with respiration. These exercises are associated with self-generated dynamic processes to dissipate energy stored as tension, enhance structural flexibility, increase the experience of safety within the body, and demonstrate characteristic shifts in states of consciousness. SRI exercises are facilitated by a practitioner in the office and can be used by the patient at any time as a strategy to focus attention and increase awareness. In this case, Stages 1 and 2 were facilitated to increase somatic awareness and bringing awareness to the body's different rhythms. For the Stage 1 exercise, patient brings awareness to sternum, xiphoid, and umbilical areas and determines the position of most ease and the position with least ease. She then breathes into the area of most ease for 2-3 breathes with a nose-mouth breath and into the area of least ease for 1-2 breaths. This is repeated, alternating with specific statements of acknowledgement relevant to stage 1. In Stage 2, patient breathes into the area of most ease and alternates with the area of least ease until a rhythm is developed. As with stage 1, there are specific statements of acknowledgement relevant to stage 2.[18]

Changes in Behavior and Overall Health

After the first spinal entrainment, the mother reported that the child spontaneously started using silverware, which she previously avoided due to difficulty with coordination. After eight weeks of care, she continues to be able to use silverware during self-feeding. The mother reports that her child is better able to regulate her emotions, specifically when it comes to "changes in plans and doing things she may not want to do." She states that her emotional discharge is complete, instead of being drawn out over days. There also seems to be a deeper understanding in why things need to be done, i.e. homeschool, bathing, etc. She has improved coordination, decreased aversions to tasks requiring coordination (including self-feeding using silverware), and she now is able to play with a soccer ball.

A progress evaluation was performed to assess for progress in the correction and optimization of structural or facilitated spinal subluxation patterns associated with Adverse Mechanical Cord Tension (AMCT). The observed response to care improved from a Level 1AB at the first spinal entrainment to a Level 1C/2A, indicating that a contact made at the sacrum elicited a smooth, muscular movement synchronized with increased respiration at the entire length of the spine. This level of response coupled with a reduction in spinal facilitation suggests progression towards synergy of vertebrae and associated musculature, which is generally accompanied by early signs of improvements in quality of life.[10]

Motion palpation revealed moderate decrease in intersegmental motion indicating passive subsystem (vertebrae, disc, and ligaments) tension at right C1, left C2, left C3, right C6, right T4, T5, T11, right T12, right L4 and left sacrum spinal segments. Static muscle palpation revealed mild hypertonicity in the upper thoracic, left lumbar and right sacroiliac areas. On a scale of 1-5, with 5 being the most severe, tension is rated at a 1/5 overall. Neural control subsystem (spinal cord, nerves and meningeal dura) tension was present as indicated by moderate to severe heel tension (4/5), mild eversion stress (1/5), subclinical adduction stress (0/5), and moderate to severe abduction stress (4/5). With patient prone and legs in extended position, patient has a right functional short leg less than ¼ inch.

A Stress Response Evaluation (Neuroinfiniti) was conducted at the conclusion of 8 weeks to include electroencephalogram (EEG), heart rate variability, heart rate, skin conductance, temperature, respiration rate and paraspinal surface electromyography. The stress response analysis demonstrated improved alpha responses at baseline, with noise, and during the breathing exercise as well as improved SMR responses with a shift from an inverse response (engagement during stress) towards a healthy response of engagement during recovery. EEG analysis demonstrated improved SMR responses and improved alpha responses with an increase in alpha power in hindbrain and frontal cortex.

Heart rate variability was not utilized due to inaccuracies relating to age and associated increase of heart rate and respiration rate. Heart rate analysis demonstrated improved heart rate at baseline, indicating decreased anxiety. Skin conductance analysis showed improved skin conductance during recovery from noise and emotional stressors. Temperature analysis indicated a sympathetic response to stress as indicated by coldness of hands. Respiration rate demonstrated an improvement in breathing control and improved respiration responses at baseline. Data from surface EMG analysis was unusable due to poor contact during evaluation.

Discussion

Chiropractic care in this case study was presented from a subluxation-based perspective and a Reorganizational Healing paradigm, which emphasizes the development of strategies for self-sustaining growth towards health and wellness. The outcome measures utilized reflect an enhanced ability of the body to self-regulate tension and the development of improved cognitive and precognitive awareness to more readily assess perception, structure, and behavior.

Central Pattern Generator

The respiratory wave phenomenon, also known as the Network wave, is best described as a Central Pattern Generator, an interconnection of neurons that produces movement of the limbs and trunk that can be sustained in the absence of direct sensory input or higher cerebral involvement. Previous to 2004, Central Pattern Generators have generally been described in its relation to locomotion, including walking, running, swimming, and flying. This was the first time that a CPG has been observed within the spine apart from locomotion or respiration.[19]

The Network wave is a coherent movement elicited by this Central Pattern Generator. A light pressure contact to the spinal gateway is sufficient to elicit an oscillation which rapidly becomes self-sustaining without further sensory input from the practitioner. A contact made at the sacrum elicits an electrophysiological wave that initially dissipates before reaching the cervical spine and after some entrainment eventually reaches the cervical area and triggers oscillation of the neck at a specific vertebral level.[20] The development of the Network wave is believed to be associated with the correction of vertebral subluxation as well as reduction of facilitation within the spine.[10]

Decreased adverse mechanical cord tension is a necessary precursor of the Network wave.[19] sEMG signals recorded at the cervical, thoracic, lumbar and sacral areas demonstrate synchronization of movement and coherence of the wave throughout the spine.[20] Additionally, the respiratory wave exhibits mathematical properties of a central pattern generator. At advanced levels of NSA care, sEMG signals became less random and move towards higher levels of organization with more coherence and predictability. The dynamic movements produced following a contact progress towards increased complexity.[19]

EEG Alpha Activity

EEG is used to measure oscillatory activity of the cortex. Of particular interest is the alpha frequency band (8-12Hz), which has been linked to cognitive performance and creativity.[21] EEG alpha oscillations appear to play a role in cognitive, sensorimotor, psychoemotional and physiological aspects of human life[22] while theta oscillations are intimately related with the cognitive component of the emotional response.[23] Alpha wave activity can also been measured as individual alpha peak frequency, which is the dominant oscillatory frequency in the human EEG during relaxed wakefulness.[24] A variety of EEG rhythmical components are described by the same dominant frequency as the alpha rhythm, with distinct frequency and topographical boundaries.[22]

Individual alpha peak frequency varies intra-individually as a function of age, increasing from childhood until puberty and then decreasing after 40 years.[22] Increases in iAPF are not linear, but occur in several growth spurts.[25] In children, iAPF has been found to have a significant correlation with measures of sensorimotor performance and locomotor skill.[26] This corresponds to a period of increased iAPF between 1 and 3 years of age from 5.5Hz to 8Hz, at which children rapidly develop locomotion and coordination.[25]

Studies have demonstrated an increase in alpha activity during cognitively demanding tasks as well as an increase in frontal activation during creative ideation.[21,27] During a cued-attention tactile detection task, alpha and beta rhythms exhibit phase synchrony from the suppression of stimulus processes and motor response to stimulus.[28] The Neural Efficiency hypothesis is such that these inhibitory processes facilitate cognitive performance while supporting working memory processes.[22] Alpha activity, particularly in the frontal cortex, may reflect high-demand internal processing and top-down inhibitory processes through inhibition of task-irrelevant information.[21]

Children's brain function should shift from theta dominance to alpha dominance by school age, demonstrating an increase in cognitive efficiency and allowing greater capacity to learn, think, and be consciously relaxed. Seeing this increase at CZ (the frontal cortex) is an indicator of this process happening, and correlates with the anecdotal findings reported by the child's mother.

Conclusion

This case reported the improvement in coordination and spontaneous utilization of silverware while self-feeding as well as improvement in emotional regulation following a 2-month period of subluxation-based chiropractic care using Network Spinal Analysis. These changes coincide with an increase in alpha activity as measured in EEG, which suggest an increase in cognitive efficiency allowing greater capacity to learn, think, and be consciously relaxed. These changes are temporally associated to chiropractic care and the correction of vertebral subluxations.

This study provides limited evidence that Network Spinal Analysis care may be safe and effective in improving coordination and emotional regulation. Further research is warranted to determine the effect of chiropractic care on pediatric behavior, wellness and quality of life. Investigations of the physiological mechanisms by which these changes occur are important topics for future study.

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Appendix

	Initial Examination	**Progress Examination** (8 weeks)
Motion Palpation: decrease in intersegmental motion	(4/5) Moderate to severe at left C1, right C3, T3, T7, T8, right L5 and coccyx spinal segments	(3/5) Moderate at right C1, left C2, left C3, right C6, right T4, T5, T11, right T12
Static Palpation: tension in active subsystem	(4/5) Significantly taut fibers in the cervical spine and at the right sacroiliac area	(1/5) Mild hypertonicity in the upper thoracic, left lumbar and right sacroiliac areas
Heel Tension: resistance to dorsiflexion from full plantarflexion	(5/5) Severe, corresponding to coccyx AMCT	(4/5) Moderate to severe
Eversion Stress: resistance to eversion from inversion	(4/5) Moderate to severe	(1/5) Mild
Abduction Stress: resistance to hip abduction	(2/5) Mild to moderate	(4/5) Moderate to severe
Leg Length Inequality	½ inch left	< ¼ inch right

Table 1. Chiropractic Examination Findings
Examination findings, demonstrating increase in intersegmental motion, decrease in hypertonicity, decrease in heel tension, eversion stress, increase in abduction stress and decrease in leg length inequality based on a scale of 1-5, with 5 being severe.

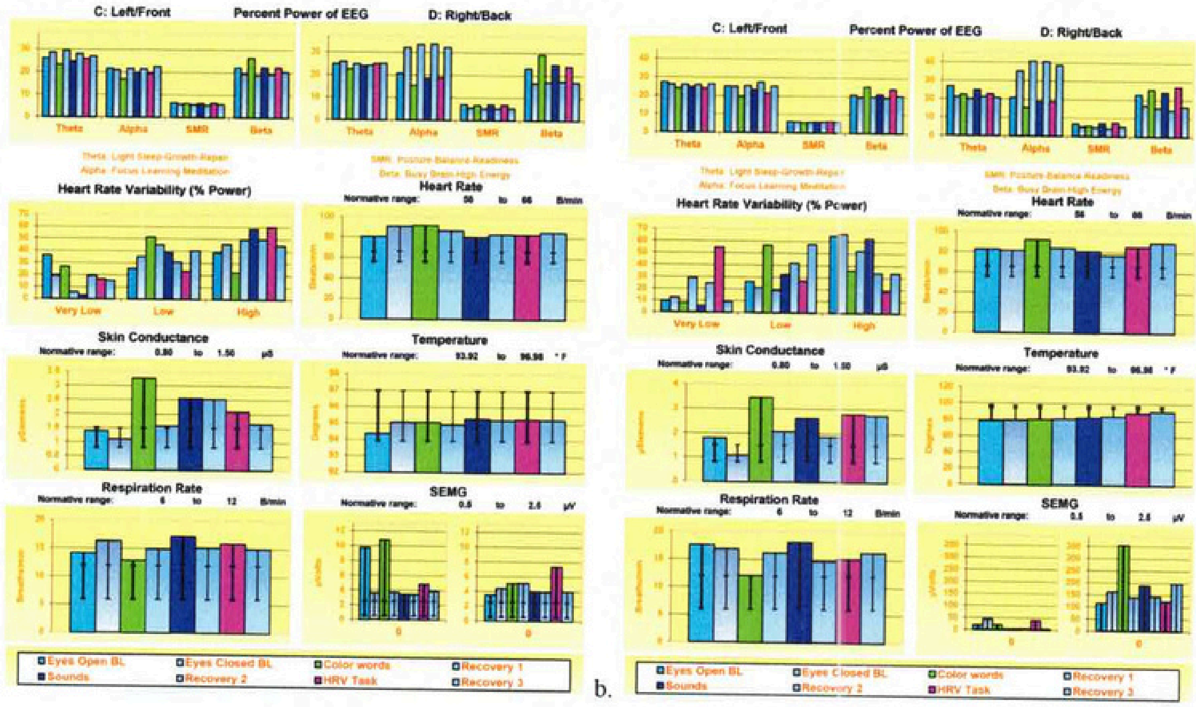

Figure 1. Stress Response Evaluation
Comparison of Electroencephalogram (EEG), Heart Rate Variability (HRV), Skin Conductance, Temperature, Respiration Rate, Surface Electromyography (a) at initial exam and (b) at progress exam.

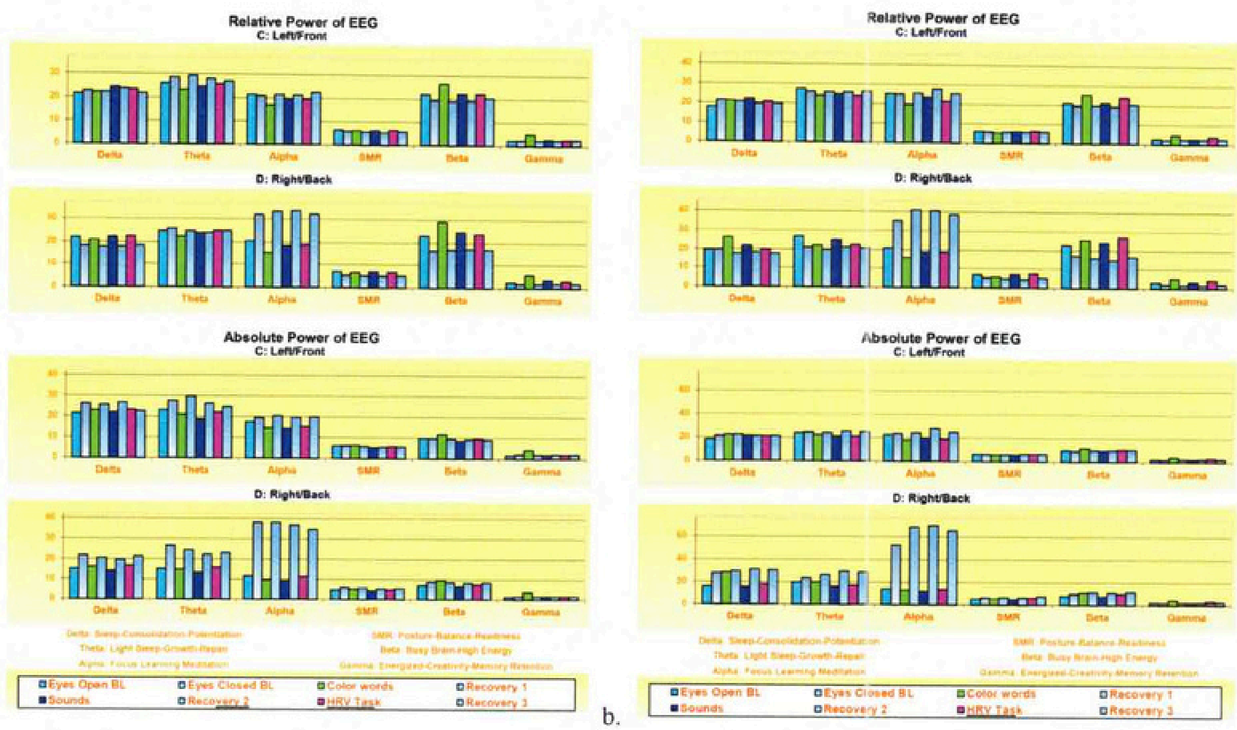

Figure 2. Relative and Absolute Electroencephalogram (EEG)
Comparison of Relative and Absolute Electroencephalogram (EEG) (a) at initial exam and (b) at progress exam.

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A Four Case Study

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The effect of the Chiropractic adjustment on the brain wave pattern as measured by QEEG. Summarizing an additional 100 (approximately) cases over a three year period.

Abstract

An initial study was devised by chiropractors and clinical psychologists to test the hypothesis that chiropractic adjustments affect the central nervous system directly. The method of obtaining data was with a 2-lead QEEG device. The device measures brain wave frequencies. A measurement was taken pre-adjustment and a second QEEG measurement was taken post adjustment. A simple criterion was used to make the determination of the effectiveness of the chiropractic adjustment: First -- the right/left balance; second -- the amount of total activity; third -- primary regions of activity; fourth -- the effect of the adjustment on each of the areas listed above. Data was collected at CEO seminars for approximately 3 years with approximately 100 subjects. These four cases are representative of the effects of the study. It was concluded that the chiropractic adjustment does affect the central nervous system directly.

Introduction

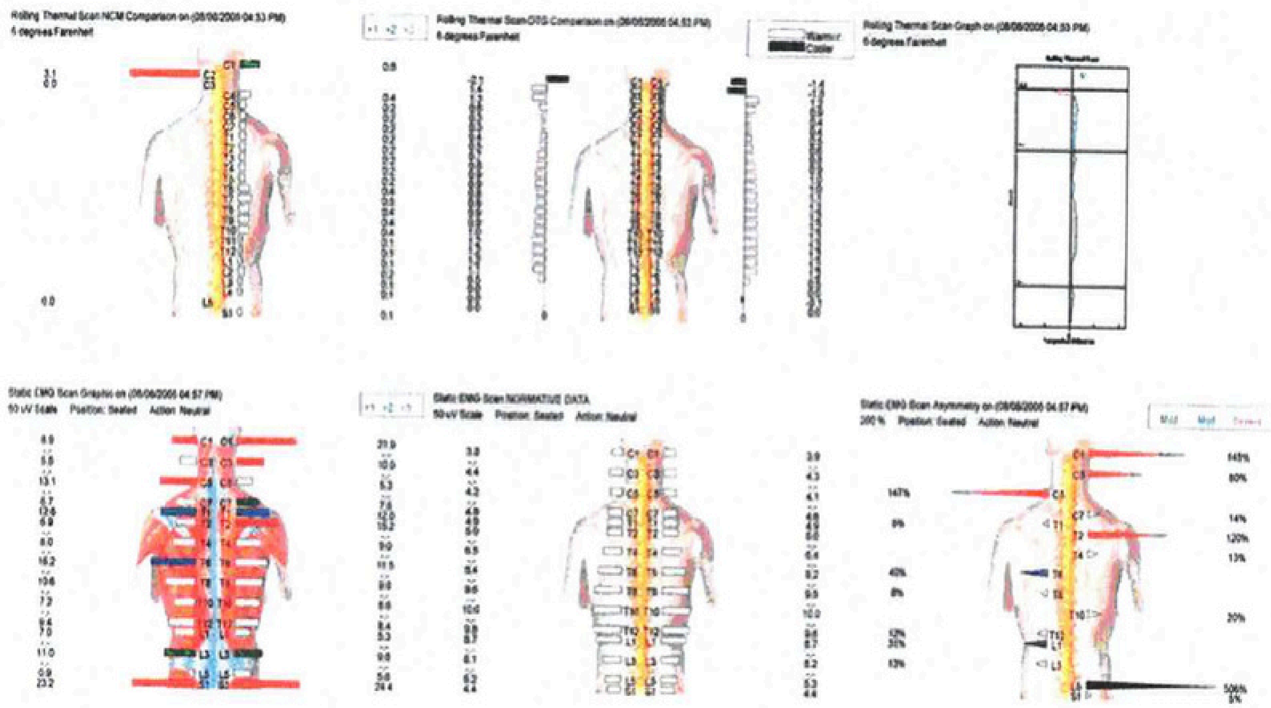
Recent attacks by the medical establishment against the chiropractic profession make it clear that despite volumes of research, chiropractic is still viewed as a limited form of health care. As such, it is still vulnerable to the same threats and misconceptions against which it has been fighting for decades. In the 1960's there was a significant and conscious effort within the chiropractic profession to move away from a focus on the nervous system and concentrate solely on the physical structure, particularly the spine. This was done as a response to relentless and seemingly damaging attacks on chiropractic's efficacy and validity as a health care profession.

The profession was at a standstill, as the last major addition to our scientific evidence had been the Neurocalograph and it was in question within the profession, let alone from the medical establishment. In fact, the connection between the autonomic nervous system and the NCM readings was poorly explained, if understood at all. That left the profession with radiograph film studies and structural analysis to define the scientific basis for chiropractic. What resulted was a limiting burden of research relating structural changes relative to back pain.

Today, we live in this chiropractic model. It served its purpose as the attacks on our profession, which were based on not being scientific, stopped. The back pain studies did show the great benefit of chiropractic care and were reproducible. This led us into the medical system and insurance coverage, which was seen as a great victory for Chiropractic and we all believed we had won a great battle. We became even more focused on the physical spinal approach as our identity, and accepted a narrowly defined scope of practice.

New attitudes in chiropractic also appeared: programs to help offices attract patients with physical needs; better insurance billing systems; new methods of how to bill insurance companies for care that augmented chiropractic; and new

Figure 5. Rolling paraspinal thermography & SEMG at the 13th visit



concepts of the chiropractic model that focused on the spine and subluxation.

The Riekeman and Flesia "Renaissance" program was a major influence in the profession and held a combination of the original principles of Chiropractic and the new structure based attitudes. It introduced a 5 component model of spinal dysfunction complete with neurological studies. These studies established the sensitivity of the dorsal nerve root and the effects on the neurological messages. It brought the term "Vertebral Subluxation Complex" into the Chiropractic lexicon. The banner cry went forth in the profession "Find and correct VSC". Now we had our territory, "The 5 component VSC" and we could easily relate VSC and back pain, neck pain, even headaches, sciatica, brachial neuralgia with Chiropractic care benefits. Again we had it made. Workman's compensation and motor vehicle accident claims could be cared for under Chiropractic as they could be linked to the physical spinal subluxation model.

There were, however, limitations with the model. Clinical results that went beyond physical/structural problems and entered the realm of mental/emotional imbalances could not be directly explained or measured. Things like changes in patient's perception and quality of life were beyond billing codes and x-ray findings. Kent's elegant refinement of the 5 component VSC model into the 3 component VSC model helped to clarify the link between the VSC and the interruption of nervous system function. Yet, that too, needs a further refinement.

Chiropractic has to move beyond the limitations of the Vertebral Subluxation Complex. Clearly the VSC exists, but there is value in looking beyond the spinal subluxation to define Chiropractic and the power of the adjustment. Measuring the Central Nervous System and the role it plays as the central organizing authority in body function is paramount to truly understanding how an adjustment effects the body. A hypothesis was formed that directly explains mind-body integrity. Neurologically based chiropractic must take into account a measurement of how the brain is affected by a chiropractic adjustment.

A discussion between Dr. Annette Long and Dr. Alvah Byers, two clinical psychologists with decades of work in bio-feedback [1], and Dr. Richard Barwell, chiropractor and founder of Chiropractic Equity Offices, led to 3 years of research collecting data to determine if the chiropractic adjustment effects brain function. In the initial discussion in Dr. Byers is office in Pueblo, Colorado, Dr. Barwell shared his hypothesis that the Chiropractic adjustment directly affected the CNS. A preliminary experiment was designed using electroencephalogram equipment of Dr. Long and Dr. Byers.

Materials and Methods

Four subjects were chosen and measured with either a 19 lead Lexacore QEEG (EEG) or Dr. Long's 2 lead EEG equipment before getting adjusted. Each person was adjusted by Dr. Barwell using manual adjusting procedures and then after 20 minutes another EEG measurement was taken on the subject. Results of the initial findings were inconclusive. Dr. Byers was reluctant to make any conclusions stating that though all four subjects demonstrated a change in brain wave pattern after the adjustment, it could be normal variation.

The following two years were spent gathering EEG scan information. Pre and post QEEG studies were done on approximately 100 subjects during the Chiropractic Equity Office program seminars. Subjects were volunteers who attended the seminars. Dr. Byers conducted the scans using a 2-point EEG system. Contacts measured were in the CZ locations with an ear ground as specified by the EEG equipment. All contacts were checked initially for impedance to insure proper data transfer. The pre adjustment EEG reading was taken during a period of 5 minutes. The subject was instructed to close his eyes and do relaxation breathing as per Dr. Byers instruction.

The subject was then adjusted using one of the following techniques: Activator, Torque Release, manual adjusting. All adjustments were performed by Dr. R. Barwell, Dr. T. Berry, or Dr. P. Christopher. A period of 20 minutes was observed before taking the post EEG reading.

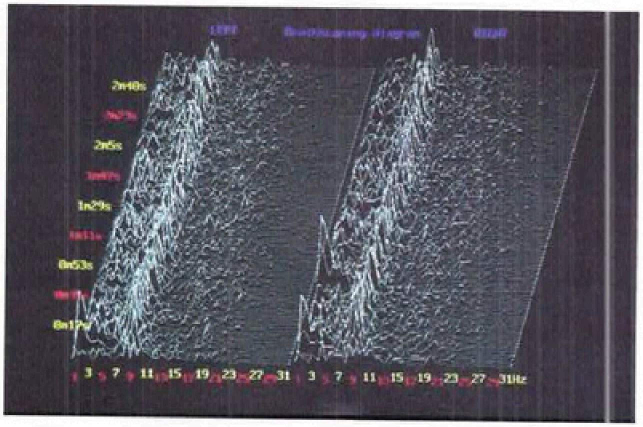
To understand the scans a brief explanation is needed. There are 4 primary frequencies of brain function: Beta, Alpha, Theta and Delta.

Beta -- Highest frequency active brain, busy, high energy consumption 12Hz to 31HZ (20-25 ruminating thoughts; 40 manic) Alpha -- Meditative state, healing mode, earth frequency, learning 7.4Hz low A* - 9-12Hz high A

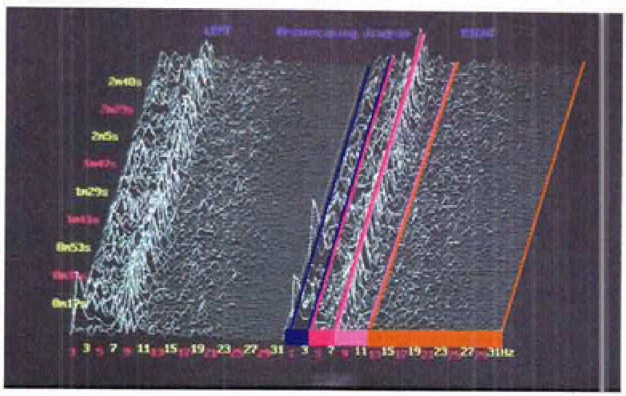
Theta -- Light sleep, deep relaxation, subconscious, conceptual development 3.5Hz -- 7.4Hz

Delta -- deep sleep, energy storage, repair mode, deep subconscious .5Hz - 3.5Hz deep sleep

The graph in Fig. 1 is an EEG scan to demonstrate how the brain frequencies are represented on paper. This graph shows both left and right hemispheres as indicated at the top of the graph. The first important observation is to see if the hemispheres are balanced in activity. The Hertz range (frequency) is located at the bottom, and numbers from 1-31Hz in each hemisphere. The timed recording segments are called epochs, and are noted on the left of the graph.

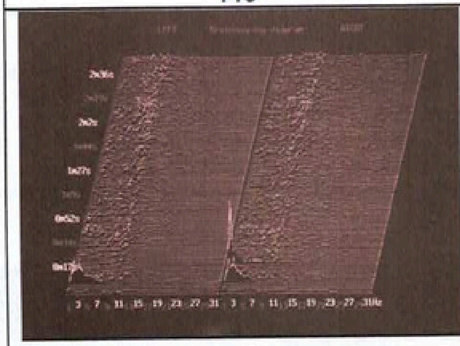
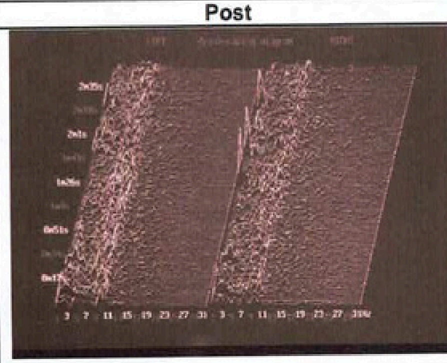
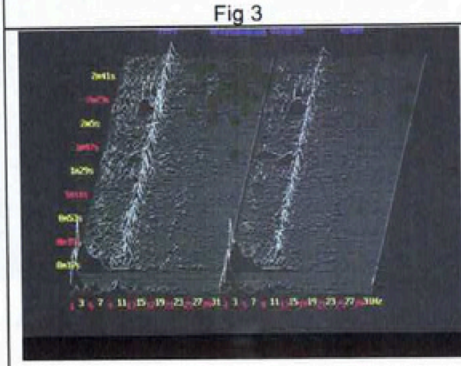
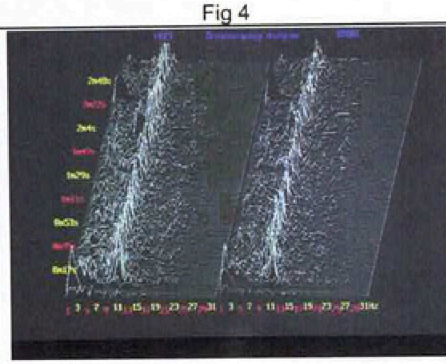
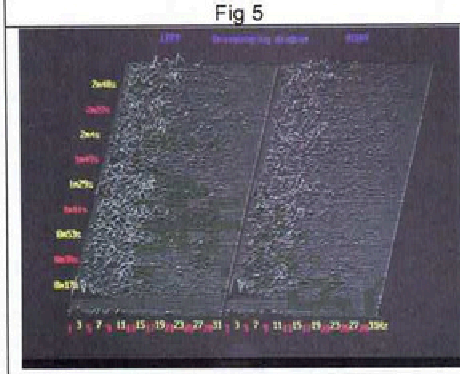
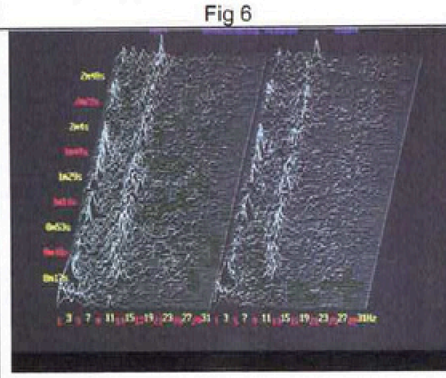
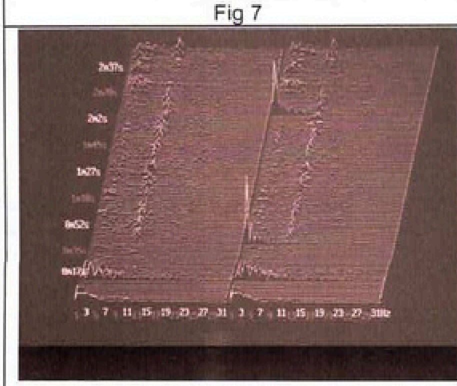
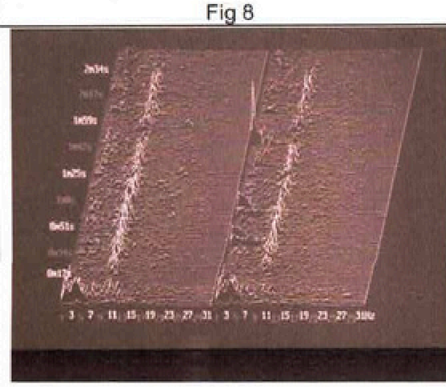


In Fig. 2 you will note the most distinct findings appear at the Alpha level (Area 3) with the mountain range look. The Beta range (Area 4) on the right side of each hemisphere is much broader as the frequency range runs from 12 to 31HZ vs. 7.4 to 12 for Alpha. Theta (area 2) is the light sleep, REM brain frequency while the deeps level of subconscious is the delta (area 1). The large spikes seen to the left of each hemisphere are considered to be artifacts or anomalies.



Results (Based on this four case study)

The first series of scans were done with the approach that we would not note any change in the brain wave patterns when we compared the pre adjustment scan to post adjustment scan. The following scans (Figs. 3-10) are an example of what we found. There are several areas to examine as you look at the scans. First -- the right/left balance; second -- the amount of total activity; third -- primary regions of activity; fourth -- the effect of the adjustment on each of the areas listed above.

Pre	Post
 Fig 3	 Fig 4
 Fig 5	 Fig 6
 Fig 7	 Fig 8
 Fig 9	 Fig 10

In each of the above 4 examples what clearly can be seen is that all of the four areas listed above show improvement.

Discussion

We also found some beautifully balanced and active brains in the pre-scans and the adjustments showed little, if any change, in the post-scans on each of these individuals, such as the one in Figs. 11-12. This seems to suggest that the chiropractic adjustment does not have a deleterious effect on the CNS. The studies have continued and the findings continue to show significant changes in the CNS pattern after a Chiropractic adjustment on those individuals with less than a balanced active brain.

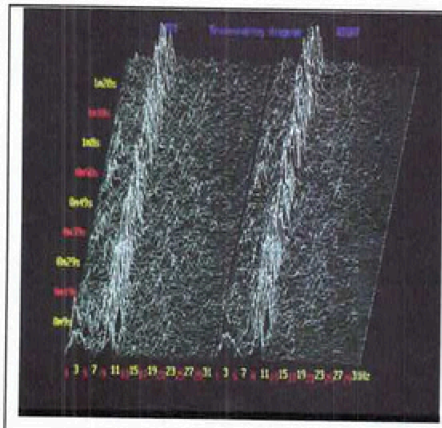


Fig 11

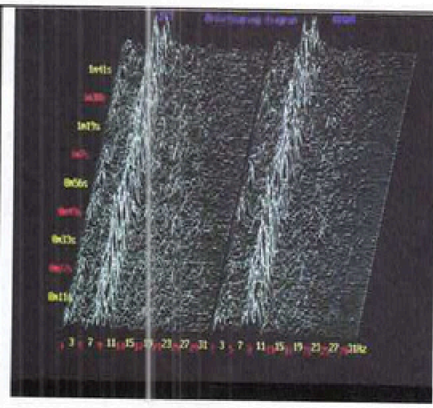


Fig 12

The nature of the study was initially designed to determine solely if the chiropractic adjustment affected the CNS. Collecting and analysis of the data was done with the intention of disproving that the chiropractic adjustment did affect the CNS. During the Toronto CEO seminar on October 23, 2000, Dr. Byers announced to the audience, "I can unequivocally state that the Chiropractic adjustment directly affects the Central Nervous System." Our preliminary studies suggest the adjustment does change the activity level in the CNS.

One of the expected results was that the chiropractic adjustment would place the subjects into a predominantly Alpha brainwave pattern. Alpha is the conscious, meditative state, classically associated with a greater degree of relaxation and health. As that was our intent during the adjustment trials, and that seemed to be the result we got on the scans. We noticed that the alpha activity was also accompanied by an increase in general brain activity.

Obviously, much more research is needed to explore the vast potential of how exactly the chiropractic adjustment affects the CNS. A proper series of studies in a more controlled environment is necessary.

Conclusion

In order to position the chiropractic profession as a legitimately respected health care service, those of us in this profession need to embrace the full extent of what we do. [2] The concept of vertebral subluxation needs to be refined in a broader context: that of neurological based chiropractic care.

An hypothesis was formed that the chiropractic adjustment affected the function of the Central Nervous System. Preliminary research was completed by Chiropractic Equity Offices Inc. showing that the extent of the chiropractic adjustment affects the nervous system beyond the dorsal nerve root and affects the function of the brain itself. The study utilized EEG equipment that showed a definite change in brain wave frequencies following a chiropractic adjustment. Four criterion were looked at: First -- the right/left balance; second -- the amount of total activity; third -- primary regions of activity; fourth -- the effect of the

Original Research

Effects of Manual Approaches with Osteopathic Modality on Brain Correlates of Interoception: An fMRI Study

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Abstract

The present randomised placebo controlled trial explored the extent to which osteopathic manipulative treatment (OMT) affects brain activity, particularly the insula, during both an "interoceptive awareness" and "exteroceptive awareness" task in a sample of 32 right-handed adults with chronic Low Back Pain (CLBP) randomly assigned to either the OMT or sham group. Patients received 4 weekly sessions and fMRI was performed at enrolment (T0), immediately after the first session (T1) and at 1 month (T2). The results revealed that the OMT produced a distinct and specific reduction in BOLD response in specific brain areas related to interoception, i.e., bilateral insula, ACC, left striatum and rMFG. The observed trend across the three time points appears uncharacteristic. At T1, a marginal increase of the BOLD response was observed in all the above-mentioned areas except the rMFG, which showed a decrease in BOLD response. At T2, the response was the opposite: areas related to interoception (bilateral insula and ACC) as well as the rMFG and left striatum demonstrated significant decreased in BOLD response. The findings of this study provide an insight into the effects of manual therapies on brain activity and have implications for future research in the field.

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Introduction

The interaction between the sense of touch and the body is a well recognised process that takes place at different neural levels, with different effects and mechanisms of action. In the brain, the effect of this interaction produces different mental representations or experiences - also called feelings - of the body[1]. These include inputs from the physiological milieu of the body in terms of metabolic, structural and functional conditions at any given moment, a concept referred to as interoception[2]. Those feelings can be modulated by different stimuli and sources, including touch, ultimately modifying the perception of the internal and external world[3].

Several neurobiological studies posed that the insula (INS) is a critical hub for multimodal interoceptive integration, involved in interoceptive processes, such as awareness of sensations from the body[4], but also exteroceptive elements, such as perception of pain[5,6], taste[7,8,9,10], smell[11], and touch[12]. In fact, external stimuli, i.e. pain, smell or taste, serve as body-mapped signals of the so-called peripersonal space [that is the space immediately surrounding the body][13,14]. Moreover, in the anterior insula exteroceptive and interoceptive information overlap with emotional domains[11], suggesting an underlying commonality[15]. In fact, the insula has been referred as a meeting point between external and internal milieus[16,17,18,19]. Detailed reviews of the interoceptive evidence are available elsewhere[2,3,20].

Methods to measure interoceptive differences comprise the use of questionnaires and behavioural tests that either exploit natural fluctuations in internal physiological signals or manipulate organ physiology experimentally[21,22]. For practical reasons, heartbeat detection tasks are measures largely utilised to assess differences among individuals regarding interoceptive accuracy and ability[23,24,25]. These tests quantify an individual's ability to distinguish his own heartbeat at rest, by counting, tapping or by judging heartbeat timing relative to an external stimulus. Due to their nature, these tasks can be utilized in the context of an fMRI study with good validity and reliability[26].

Low back pain (LBP) is a widespread health problem and a major cause of disability worldwide[27,28]. Lifetime prevalence estimates of LBP range from 60% to 70%[27]. In Europe, LBP represents the second highest cause of morbidity measured by disability-adjusted life years[28]. Research evidence suggests that several brain areas are modified after exposure to chronic low back pain (CLBP) - typically defined as pain lasting more than 3 months[29]. Indeed, these changes seem to be correlated to changes in the anterior INS and Anterior Cingulate Cortex (ACC)[30]. Other studies highlighted the predominance of the medial prefrontal cortex (mPFC) as a key regulator of pain perception[31]. Apkarian et al. demonstrated that modelling the activity of mPFC and INS it is possible to quantify the magnitude and duration of back pain with an error of 20%[31]. Furthermore, other research showed that subjects with chronic pain are characterised by an abnormal function of the resting state networks with higher firing on the INS and ACC[32,33,34], as well the mPFC[33]. Taken together, these studies seem to indicate a critical role for the INS and ACC in the modulation of pain.

Preliminary research in field of manual therapies such as osteopathy indicates that interoception mediated through the sense of touch may play an important role in their therapeutic effects[35,36,37]. Touch is recognised as both an exteroceptive and interoceptive modality, where the latter seems to be supplied by small-diameter low-conducting unmyelinated C-tactile (CT) fibres, which uses the lamina I spinothalamocortical tract to subserve homeostasis and create the basis for feelings[2]. Researchers have proposed an 'affective' homunculus in the insula that maps the hedonic properties of gentle touch, based on the inferred increase in innervation density of CTs in more proximal body sites[38]. On this point, the CT fibres might be key neurobiological component in the touch-based manual therapies underpinning mechanisms[38].

Although not formally tested, it can be argued that the link between the observed manual therapy effects, specifically osteopathy, and interoception is plausible, particularly in the light of current neuroscience literature. Our hypothesis, therefore, is that touch-based therapy can affect neural activity when perceiving heartbeat. In this study, we investigated the effect of an osteopathic treatment on brain correlates, specifically insula-based networks, on patients with CLBP.

Results

Description of the sample at baseline

Thirty-two right-handed patients were randomised and divided into the study (N = 16) and control groups (N = 16). Three patients (1 in the study group and 2 in the control group) dropped out during the trial, leading to a final sample size of 29 patients. At baseline, there were no statistically significant differences between groups in terms of age, gender, BMI, marital situation, and academic and professional qualifications (Table 1). Considering the pain measurements, groups were comparable for level of pain measured by VAS and McGill score, and disability index measured both by Roland-Morris and Oswestry (Table 1).

Behavioural results

When the mean error for the IA is considered, the results of MVM analysis showed a group × time interaction effect ($F = 6.78$; $p < 0.01$) but not group effect ($F = 4.98$; $p = 0.12$).

Indeed, no statistically differences were observed between groups at both baseline (OMT: 3.5 ± 0.50 vs sham 3.4 ± 1.1; $t = 0.33$, df = 20.95, $P = 0.74$, two-tailed) (Fig. 1). Statistically significant differences were found at T1 (OMT: 2.2 ± 0.7 vs sham 3.2 ± 1.2; $t = -2.88$, df = 24.15, p-value <0.001) and T2 (OMT: 1.94 ± 0.63 vs sham 3.0 ± 0.96; $t = -3.69$, df = 25.90, p-value <0.001). Besides, OMT group showed a significant reduction compared to baseline both at T1 (mean of differences: 1.30; 95% CI: 0.86–1.74; $t = 6.04$; df = 27.15; $p < 0.001$) and T2 (mean of differences: 1.53; 95% CI: 1.15–1.97; $t = 7.76$, df = 28.53, p-value <0.001). Analysis of the EA task did not reveal any differences between groups and time. Amongst 14 patients allocated to the sham group, none of them was able to correctly guess the nature of the treatment.

fMRI results

To study the relationship between IA, OMT and brain activity in the insula and in other correlated interoceptive areas, a well-established fMRI paradigm[39] including IA and EA tasks, was applied. Task difficulty effects between interoceptive and exteroceptive awareness (IA and EA) were excluded by showing no significant differences between the total mean error of IA (mean: 3.43 ± 0.6) and EA (mean: 2.28 ± 0.53) condition ($t = 1.43$, df = 470.63, p-value = 0.15).

Firstly, the group activation maps at T0 showed a significant activation of bilateral insula, bilateral cingulate cortex, bilateral sensory-motor cortex and medial prefrontal cortex for the IA task and bilateral superior temporal gyrus, bilateral sensory-motor cortex for the EA task (Fig. 2). At baseline, there were no differences between OMT and SHAM group in the activation of interoceptive and exteroceptive areas. These results confirm that the two groups were balanced regarding the interoceptive and exteroceptive tasks. Considering ROIs analysis for the IA task, there was a significant effect of group (OMT < SHAM) in the right anterior cingulate cortex (ACC, $F = 10.81$; $p < 0.001$), right insula cortex (rINS, $F = 10.12$; $p < 0.001$), left insula cortex (lINS, $F = 9.96$; $p < 0.001$), left striatum ($F = 11.42$; $p < 0.001$) and right middle frontal gyrus (rMFG, $F = 7.12$; $p < 0.001$) (Fig. 3). Significant effects were found also for time (ACC: $F = 8.67$, $p < 0.001$; rINS: $F = 8.98$, $p < 0.001$; lINS: $F = 9.11$, $p < 0.001$; left striatum: $F = 7.67$, $p < 0.001$; rMFG: $F = 8.42$, $p < 0.001$) as well as group × time interaction (ACC: $F = 10.21$, $p < 0.001$; rINS: $F = 10.43$, $p < 0.001$; lINS: $F = 10.01$, $p < 0.001$; left striatum: $F = 11.67$, $p < 0.001$; rMFG: $F = 10.11$, $p < 0.001$).

Comparing the two groups, OMT showed a significant reduction of beta values in the ACC ($t = -4.07$, $p < 0.001$), rINS ($t = -3.87$, $p < 0.001$), lINS ($t = -3.16$, $p < 0.001$), left striatum ($t = -4.97$, $p < 0.001$) and rMFG ($t = -3.45$, $p < 0.001$) mainly at T2 (Fig. 4). Interestingly, only the rMFG revealed a statistically significant different between the two groups at T1 ($t=-2.65$, $p<0.01$).

The within group timepoints comparison showed statistically significant differences for the OMT group only. In general, there was a significant difference between T2 and T0 beta values for ACC (T2 vs T0: $t=-2.97$, $p<0.01$), lINS (T2 vs T0: $t=-2.47$, $p<0.01$), rINS (T2 vs T0: $t=-2.35$, $p<0.01$), left striatum (T2 vs T0: $t=-3.34$, $p<0.01$) and rMFG (T2 vs T0: $t=-2.54$, $p<0.01$).

In relation to the EA task, the OMT and sham groups were comparable, with no significant difference detected in brain activation.

Discussion

The present study showed that osteopathic manipulative treatment produces a distinct and specific BOLD response in specific areas related to interoception. Compared to the sham group, patients receiving OMT demonstrate these effects specifically in the rINS, lINS, ACC, left striatum and rMFG. The trend across the 3-time points seems to be uncharacteristic. Indeed, immediately after the first OMT session, it was shown a marginal increase in BOLD response in all the above-mentioned areas but not for the rMFG, which showed a decrease. At T2, the response appeared to be opposite: areas related to interoception (bilateral insula and ACC) as well as rMFG and left striatum significantly decreased the BOLD response, i.e. these clusters exhibited a clear modulation after 4 OMT sessions. This is particularly observable in the OMT group when compared to the other time points (T0 and T1) and to the sham group.

Besides, considering the mean errors in the IA task, results showed that at T2 the OMT group reduced the number of errors compared to baseline and compared to the sham group. This might suggest that participants in the OMT group improved their ability in the heartbeat tracking task, a measure of interoceptive accuracy. It is noteworthy to consider that the chance of task habituation and thus predictability of the heartbeat tracking was controlled by the randomisation of the task (both between IA-EA and within the task sequence). In addition, it seems to be unlikely that patients performing the IA task at baseline, that means 4 blocks by 15 sec each (one minute in total), would have been adapted and trained for that task and thus influence the performance one month later. This is confirmed by the fact that mean errors in the sham group were similar between T0 and T2. Considering the above-mentioned points, it might be possible that the use of OMT procedures could improve the perception of heartbeat, enabling patients to detect more accurately their own heartbeat. It is well-established in the literature that to perceive your own heartbeat the salience network needs to be recruited[26,40,41]. It can be argued that a more efficient network means a better ability to perform the IA task and thus feel more accurately one's own heartbeat[42]. Thus, we could speculate that the use of OMT might produce specific effects in interoceptive brain areas, possibly reflecting an increased efficiency to decode bottom-up interoceptive heart-based stimuli.

In addition to the salience areas activated, the rMFG activation seems to show a similar pattern. Interestingly, under the Corbetta's "circuit-breaker" proposal[43], the right MFG would be in charge of the modulation of exogenous and endogenous attention. Japee and colleagues have revealed that the rMFG could play an important role in reorienting attention from exogenous to endogenous attentional control[44]. Considering the findings of the current study, we would argue that the use of OMT can influence activity in the rMFG allowing a more precise attentional control in order to re-orient more efficiently one's own attention towards endogenous stimuli. Although not formally tested yet, we can hypothesise that the use of OMT might act on the rMFG facilitating the switch from external to internal milieu. This would eventually impact on the accuracy of perception from within the body.

This study has some limitations that should be outlined. Although the analysis presented here was robustly driven by a specific rationale, it can be considered a first step that will be complemented by further work based on more complex approaches to assess e.g., functional and effective connectivity during both resting and task paradigms. For example, graph-theory analysis (GTA)[45,46] can yield metrics for both connectivity profiles and network efficiency, enabling researchers to examine the efficiency of individual nodes to integrate signals at global and local levels. Previous research based on GTA has demonstrated that brain network is structured in a 'small-world' topology characterised by dense intra-modular connections and relatively few inter-modular connections[45,46,47]. In the context of the present study, GTA might be useful to test any distinct brain networks during post-osteopathic resting state. This will provide direct evidence that the post-treatment resting state contains osteopathic-related effects that might be due to the specific touch-based nature of osteopathy.

Furthermore, effective functional connectivity (defined as the influence that one area exerts on another) during tasks can be investigated using Dynamic Causal Modeling[48]. This will lead us to investigate interactions among relevant regions involved in the exteroception/proprioception vs interoception by analysing the effective connectivity between brain regions.

The study of manual therapies from a neuroscience point of view might bring new insights within a still unexplored research field. Despite the large use of different manual approaches and touch-based interventions[49], research on brain activity is still lacking. Neuroscience can provide different methodologies allowing researchers to decode unique patterns within- and between-manual treatments. In addition to this, setting up ecologically-relevant studies is essential. On this point, selecting appropriate samples is a prerequisite as well as building up robust rationale is necessary. Too often, studies in the context of manual therapies lack of details, significantly impairing the validity, reliability and clinical applicability of the research.

The present research investigated the effect of OMT on brain correlates, specifically insula-based networks, in patients with CLBP. The findings of the study, particularly the observed changes in the insular cortex and its associated interoceptive role, support the hypothesis previously proposed by D'Alessandro and co-workers that manual therapy might exploit an interoceptive paradigm which may explain some of the clinical effects of manual treatments[35]. Therefore, we would argue that the present research with preliminary clinically-based evidence, can provide an insight into the effects of manual therapies on brain activity and have implications for future research in the field.

Methods

The present randomised placebo-controlled trial was designed to explore the extent to which OMT can change activity in the insula and therefore of its anterior circuit during both an "interoceptive awareness" and "exteroceptive awareness" task in a sample of CLBP patients.

Population

Patients were recruited from the outpatient department at a neurological and orthopaedic rehabilitation centre of the University of Chieti (CUMFER). Interventions, assessments and data collection, and data analysis were conducted at the same study site. Adult patients (≥18 years and ≤60 years old) referred to the trial clinic for Chronic Non-specific Low Back Pain (CLBP) treatment by their general practitioner or specialist were invited to participate in the trial. If no medical referral was given, e.g. as a response to the public invitation in local print media, an independent orthopaedic specialist at the study site examined the patient for eligibility and to confirm diagnosis (CLBP). Symptoms included any chronic (>3 months) pain or discomfort localised below the costal margin and above the inferior gluteal folds, with or without referred leg pain[50]. Written, informed consent was provided prior to the beginning of any of the study procedures.

Meeting any of the following criteria led to exclusion[51]: clinical sign of neurological damage with sensorimotor impairments (i.e., radicular syndrome, paresis or tingling in limbs); suspected or confirmed spinal pathology (e.g., tumour, infection, fracture or inflammatory disease); history of spinal surgery (e.g., decompensation or stiffening); whiplash injury within the last 12 months; cervical pain that reduces active movement to less than 30° rotation to each side; known vestibular pathologies; major surgery scheduled during study period; physiotherapy during the last 12 weeks; inability to follow the procedures of the study - e.g., due to language problems, psychological/psychiatric disorders, dementia and parallel participation in another study. At enrolment, eligible patients were assessed by a senior medical doctor in order to confirm the diagnosis and to exclude psychiatric disease and/or any other exclusion criteria.

The procedures were approved by the local ethics committee (University of Chieti-Pescara number: 7/09-04-15) and conform to the Declaration of Helsinki. The protocol (supplementary materials provide details of the protocol) was registered on clinicaltrial.gov (ID: NCT02464475 on 08/06/2015). No data was recorded before written informed consent to participate and to publish was given by the participant.

Randomization and masking

Eligible patients were randomly divided into two groups using a 1:1 ratio and were assigned to either the OMT group or Sham group. Block randomization was applied according to a computer-generated randomization list using a block size of 10. All patients, allocated using sealed envelopes, were not aware of any step of the study design as well as outcomes or group allocation. The randomization list was stored in a dedicated and protected web-based space and an information technology consultant was in charge for the entire process. Research staff were kept blinded to the randomisation list and to patient allocation throughout the study. Moreover, they were blinded to patients' allocation, since all patients had a touch-based intervention by the practitioner. Only the osteopathic practitioner was aware of the patients' group allocation. Moreover, the practitioner who performed OMT had no role in patient care decisions. The researchers operating the fMRI and dealing with fMRI data were unaware of patients' allocation.

Prescan behavioural assessment

At T0, before the fMRI scan, patients were asked to complete paper-based questionnaires. A socio-demographic questionnaire was administered to collect baseline data in terms of gender, BMI, age, academic degree, civil state, smoking habits and type of work. Besides, the Edinburgh Handedness Inventory was used to investigate the hand dominance (Oldfield, 1971) and the State-Trait Anxiety Inventory (STAI-Y1 and Y2) to test trait anxiety[52].

The Body Awareness Questionnaire (BAQ) is considered a reliable and valid instrument for measuring self-reported attentiveness to bodily processes[53,54]. It is made of 18 statements that measure beliefs about one's sensitivity to normal (i.e., non-emotive and non-pathological) bodily functions and the ability to anticipate bodily reactions. Items are answered on a seven-point Likert scale. Cronbach's alpha coefficient for the BAQ was 0.80 for the Italian sample.

Prescan pain assessment

Several tools were specifically used to assess pain perception in patients. The Roland–Morris Disability Questionnaire is a health status measure to assess physical disability low back pain patient. The questionnaire is composed by 24 yes/no items and has good psychometric properties, evidenced by internal consistency and responsiveness[55]. The Oswestry Low Back Disability Questionnaire (OSW) explores the disability derived from low back pain. The questionnaire consists of 10 items addressing different aspects of functioning (e.g., pain intensity, physical functioning, sleep functioning, social functioning). The reliability, discriminant and construct validities of the OSW are good[56]. The McGill Pain Questionnaire (MPQ) is a widely used tool to assess pain features, with reference to its sensory and affective qualities[57,58]. The MPQ is composed by 15 items describing the pain sensation (11 sensory and 4 affective) which are self-rated by the patient according to their intensity level on a 0–3 Likert scale. The reliability and validity of these measures are good and well-documented[59].

Experimental design and description of the paradigm

All eligible patients were randomised in a study group (OMT) and control group (Sham). The study group underwent four weekly sessions of OMT of 30 minutes each. Osteopathy is a nonpharmacological, non-invasive manual medicine, regarded by some as Complementary and Alternative Medicine (CAM). A series of manual techniques are applied by osteopathic therapists to improve bodily function altered by any somatic (body framework) dysfunction (ICD- 10 code: M99.0–99.9)[60]. In the osteopathic practice two are the essential elements: a structural evaluation for diagnosis and a pool of different manipulative techniques for the treatment. The aim of the structural assessment is to identify specific somatic dysfunctions. Diagnostic criteria for somatic dysfunctions focus on the tone and possible abnormalities of tissue texture. Areas of asymmetry and misalignment of bony landmarks are also evaluated, along with the quality of motion, balance, and organization. The term OMT currently includes>20 types of manual treatments administered by osteopaths[61].

In the current study the treatment was administered by a registered and licensed osteopath. The techniques used for the current study were: balanced-ligamentous tension, balanced-membranous and fluidic techniques, in line with the principles and procedures available in the current osteopathic literature. In brief, these techniques are classified as indirect approaches[62] and use light, gentle touch[38] to correct the somatic dysfunction by applying the Sutherland's point of maximum freedom (balance point) model[62]. All treatment sessions took place in the CUMFER.

The control group received a sham treatment, i.e., sessions without applying any type of osteopathic technique or procedure. Specifically, the operator performed an osteopathic-like manual assessment without paying attention to bodily areas with somatic dysfunctions. After the evaluation, the operator asked the patient to lay down on the plinth and gently placed the hands on a pre-defined number of anatomical areas without applying any type of technique but just using a gentle static or dynamic touch. The parts identified in the protocol were: lumbar spine, sacrum, pelvis, diaphragm, upper thorax, cervical spine and cranium. The sequence to apply during the session was decided by the operator before the session. This was planned to prevent any possible chance from the patient to guess the group allocation. The sessions lasted 30 minutes, as for the OMT, took place in the same location/room and were administered by the same practitioner. This to avoid any possible contamination and allocation bias.

During the study period, all patients were asked to avoid if possible any form of medication.

The study period was organised as follows with fMRI sessions at three major time points (Fig. 5):

1. Baseline (T0): before the treatment.
2. Acute response (T1): Immediately after the first manual session.
3. Chronic response (T2): at the end of the study period (after a month), which included four treatment sessions.

After the clinical evaluation (enrolment) and at T2, patients were asked to fill in the paper-based questionnaires.

Description of the paradigm

The fMRI design used to assess brain correlates of interoceptive and exteroceptive awareness was derived by previous research where it was successfully tested[39,63,64,65]. Specifically, we used a block design with 3 conditions:

- heartbeat tracking for interoceptive awareness (IA).
- auditive tracking for exteroceptive awareness (EA).
- resting period (fixation period) where no structured thinking or action was required to subjects.

In order to limit cognitive processes other than intero- or exteroception, simple visual stimuli were used to indicate the task type. These visual cues were projected via an LCD projector onto a screen visible through a mirror mounted on the headcoil and consisted of symbols described as follows (Fig. 6):

1. Heart, i.e. heartbeat tracking for interoceptive awareness – IA.
2. Treble clef, i.e. auditive tracking for exteroceptive awareness – EA.
3. Dark cross, i.e. resting period (fixation period) where no structured thinking or action was required to subjects.

For task 1, a dark coloured heart on a light background was presented. As long as this cue was visible on the screen, participants were asked to silently count their own heartbeat (a modified version of the Schandry's original heartbeat tracking task[66]). Subjects were instructed to breathe normally and any form of helping strategies (i.e. taking the pulse rate) were not allowed. Furthermore, participants were boosted to consider only heartbeats they were convinced but also advised to recognise weak feelings.

For task 2, the symbol of a dark coloured treble clef with the same size as the heart symbol was presented on the same light background. During this task individuals silently counted the number of tones played through fMRI compatible headphones (NordicNeuroLab audio system).

Each cue was showed on the screen in blocks with a duration of 15 seconds during which the subject had to perform the related task. Four blocks for each task were alternated pseudorandomly with rest periods.

At the end of each task block, the patient had to report the number of heartbeats or tones counted using an fMRI compatible mouse with two buttons. The 2 buttons, left and right, were used to control the units and decimals, allowing the subjects to quickly report their evaluation. Specifically, the left button served to move from decimals to units and back, while the right button was used to select the corresponding quantities. The time for declaring the score was 10 seconds. Fixation periods were indicated by a dark cross (of the same size and colour as the IA and EA symbols) on a light background. Participants were instructed to relax and minimise any cognitive work during these periods. To avoid any habituation effect, the volume of the musical tone was adjusted before the beginning of the fMRI session while the subject was lying down. The total duration of the run was 335 seconds. The run was repeated twice, and the order of the stimuli changed randomly.

The delivery of visual cues was controlled by a software written in Matlab. Visual stimuli were projected via an LCD projector onto a screen visible through a mirror mounted on the headcoil. Immediately before the scan, participants had a practice session and were carefully instructed and familiarized with the task.

fMRI data acquisition

Imaging was performed using a Philips Achieva 3 Tesla scanner (Philips Medical Systems, Best, Netherlands) equipped with an 8-channel phased-array head coil for signal reception and a whole-body radiofrequency coil for signal. First, high resolution structural volume was obtained using a 3D fast field echo T1-weighted sequence (sagittal, matrix 256×256, FOV = 256 mm, slice thickness = 1 mm, no gap, in-plane voxel size = 1×1 mm, flip angle = 12°, TR = 9.7 ms and TE = 4 ms). Then, Blood Oxygen Level Dependent (BOLD) fMRI data were acquired using a gradient-echo T2*-weighted echo-planar (EPI) sequence (matrix 80×80, voxel size 3 mm × 3 mm × 3.5 mm, SENSE 1.8, TE = 30 ms, TR = 1.8 s, 185 volumes per run). During fMRI, physiological signals were recorded at 100 Hz using a pulse oximeter placed on a finger of the left hand and a pneumatic belt strapped around the upper abdomen. All the data were stored and secured at the Department of Neuroscience of University of Chieti-Pescara.

fMRI data pre-processing

Analysis of fMRI data was performed using AFNI. Due to T1 saturation effects, the first five volumes of each run were discarded from the analysis. During preprocessing, transient signal spikes were removed from the EPI time series AFNI's "3dDespike" and slice scan time correction was performed. Motion correction was done by aligning EPI images to the sixth volume of the first run. Then, preprocessed functional scans were coregistered with the corresponding structural data set, normalized to the MNI space, spatial smoothed (6 mm FWHM) and high-pass filtered (cut-off 0.013 Hz).

Statistical analysis

Sample size calculation

The fMRI literature (e.g. comparison of connectivity values between different populations as in Greicius et al.[67]) reported expected effect size estimates to be relatively high (d of Cohen = 1.01). This effect-size, together with an alfa value of 0.05 and a Beta of 0.80 typical in neuroimaging studies[68] have been included in the R statistical program to estimate the sample size, obtaining N = 16 subjects per group, values compatible with those proposed in this study.

Behavioural data

Arithmetic mean and standard deviation as well as median, percentage and range were used to explore the general characteristics of the study population. To compare the OMT and Sham group at enrolment, univariate statistical tests, student t test and chi square test were performed. To study the independent effect of OMT on primary and secondary endpoints, a repeated measure analysis based on linear mixed effect model was applied considering group differences (OMT vs Sham) across time (baseline vs. experimental timepoints) and conditions (Interoceptive vs Exteroceptive). To indicate statistical difference, two-tailed P values of less than 0.05 was considered. The significance threshold was further adjusted for multiple comparisons using Bonferroni's correction. This data analysis was carried out using the R statistical program (v. 3.5.2). No adverse events were reported by any of the included patients.

fMRI data

First, statistical activation maps were obtained for individual subjects using the general linear model (GLM), considering the heart and sound conditions as predictors of interest, whereas, the periods corresponding to the subject's response for both heart and sound were included in the model as predictors of no interest. A two-gamma standard hemodynamic response function was used in order to account for the hemodynamic delay. This analysis was performed in order to identify brain areas of increased/decreased BOLD signal while the subject was performing heart (IA) and sound (EA) tasks. Then, the individual beta values corresponding to the two tasks were used as input in a group analysis based on the multivariate modelling approach (MVM) as implemented in AFNI (program 3dMVM), to assess treatment effects on brain activation. The MVM approach offers increased flexibility with respect to traditional AN(C)OVA and GLM, with voxel level correction schemes when the sphericity assumption is violated[69].

In particular the model included two groups (OMT vs Sham), 3-time points (T0, T1, T2) and 2 conditions (IA vs EA). Thus, it was a $2 \times 3 \times 2$ factorial design where group was considered a between-group variable, whereas time and task were used as within-group factors.

First, the main contrasts T0_IA and T0_EA vs rest (pooling the two groups) were performed to search for areas activated at the group level by IA and EA tasks. The between-groups OMT_T0_IA vs Sham_T0_IA and OMT_T0_EA vs Sham_T0_EA contrasts were also performed, to check that the two groups were balanced regarding the level of activation during the two tasks at T0. Then, the contrasts OMT_(T2-T1-T0)_IA vs Sham_(T2-T1-T0)_IA and OMT_(T2-T1-T0)_EA vs Sham_(T2-T1-T0)_EA were performed to search for areas showing a significant effect.

Statistical maps obtained from these contrasts were thresholded at $p < 0.05$, corrected for multiple comparisons. Correction for multiple comparisons was performed using false discovery rate (FDR). Finally, to quantify activation changes across groups, time and tasks, a region of interest (ROI) analysis was performed. To avoid double dipping problems[70], ROIs were defined using independent coordinates from the literature[71,72,73,74,75,76]. Spherical ROIs with a 9 mm radius were considered for the following areas: left insula

(−36,20,4), right insula (32,18,4), cingulate cortex (8,16,36), striatum (−24,0,8), right middle frontal gyrus (56,8,38).

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Author contributions

F.C., A.F., P.C., F.G. conceptualised the research, F.C., A.F., P.C., F.G., M.G.P., G.B., C.V., R.G.B., R.S. reviewed and approved the protocol. F.C., P.C., A.F. analysed the data. F.C., A.F., P.C., F.G., M.G.P., G.B., C.V., R.G.B., R.S. reviewed and approved the manuscript.

Competing interests

The authors declare no competing interests.

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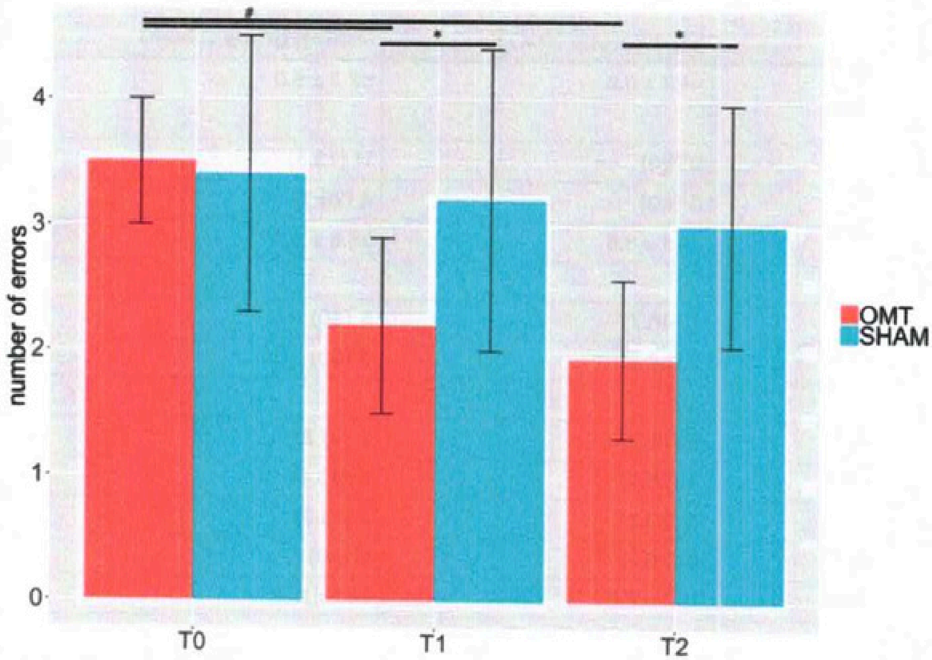
	Study group (OMT)	Control group (Sham)	p < |t|
Age	41.8 ± 6.6	42.7 ± 8.0	0.73
Gender			0.70*
Male	9 (60)	11 (73.3)	
Female	6 (40)	4 (26.7)	
BMI	24.1 ± 3.5	25.5 ± 2.4	0.19
Civil condition			1.00*
Unmarried	7 (46.7)	6 (40)	
Married	8 (53.3)	9 (60)	
Study title			0.62*
Middle school	2 (13.3)	2 (13.3)	
High school	4 (26.7)	5 (33.4)	
Bachelor degree	5 (33.3)	2 (13.3)	
Master degree	4 (26.7)	6 (40)	
Disease duration (m)	15.1 ± 9.2	14.1 ± 6.7	0.72
General scores			
BAQ	68.5 ± 31.4	51.8 ± 30.0	0.15
STAY-Y1	42.4 ± 3.4	42.7 ± 2.9	0.85
STAY-Y2	41.3 ± 3.0	41.1 ± 3.7	0.87
Pain scores			
McGill			
S-PRI	16.5 ± 5.0	16.6 ± 5.9	0.94
A-PRI	6.3 ± 2.7	6.3 ± 2.7	1.00
T-PRI	22.7 ± 6.8	22.9 ± 8.1	0.96
PPI	3.5 ± 0.5	3.5 ± 0.6	1.00
VAS	63.1 ± 21.4	57.5 ± 17.3	0.1
Oswestry	24.9 ± 3.3	26.0 ± 5.2	0.51
Roland-Morris	15.5 ± 4.0	15.3 ± 4.9	0.9

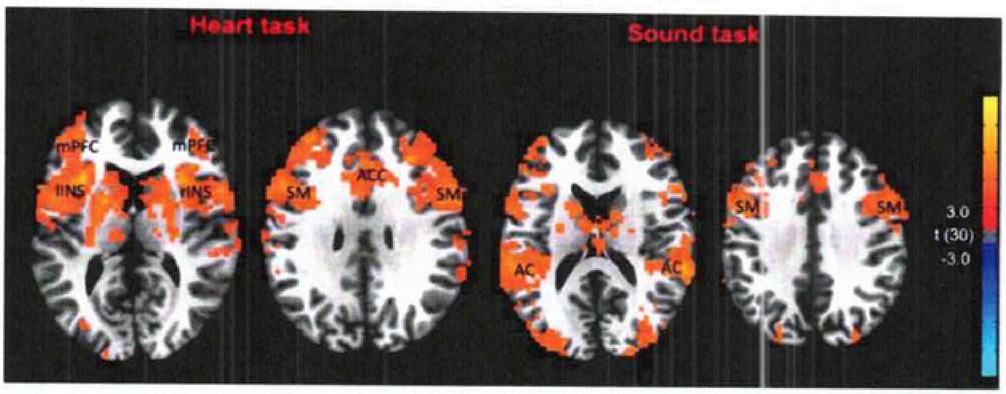
P values from t test. *p values from X^2 BMI = Body Mass Index; BAQ = Body Awareness Questionnaire; S-PRI = Sensory Pain Rating Index; A-PRI = Affective Pain Rating Index; T-PRI = Total Pain Rating Index; PPI = Present Pain Intensity Index; VAS = Visual Analogue Scale.

Table 1 Description of the sample at the baseline.



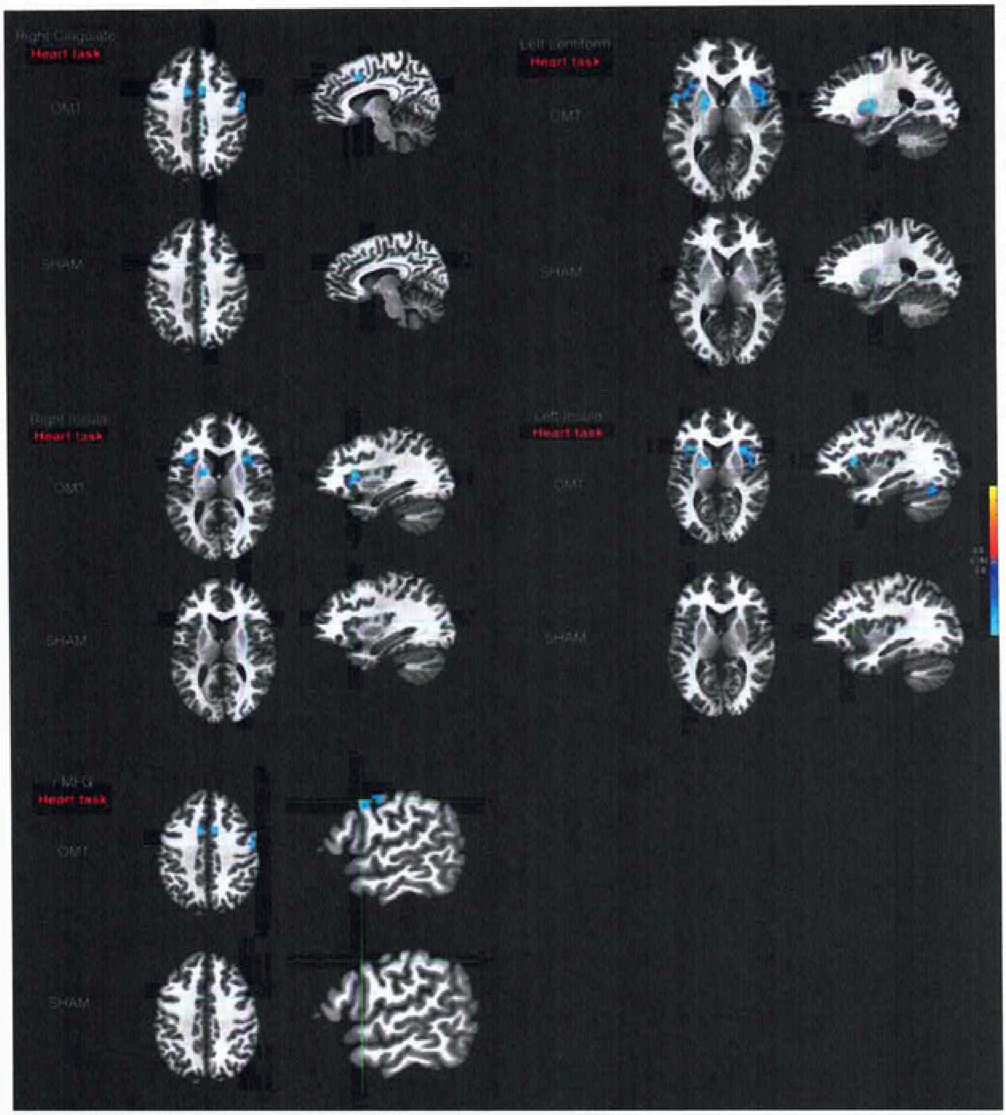
Bar chart of behavioural data. Data show the mean errors in the Interoceptive Attentive task (Mean ± SD). *Statistically significant values between groups. #Paired t test statistically significant values within OMT group.

Figure 1



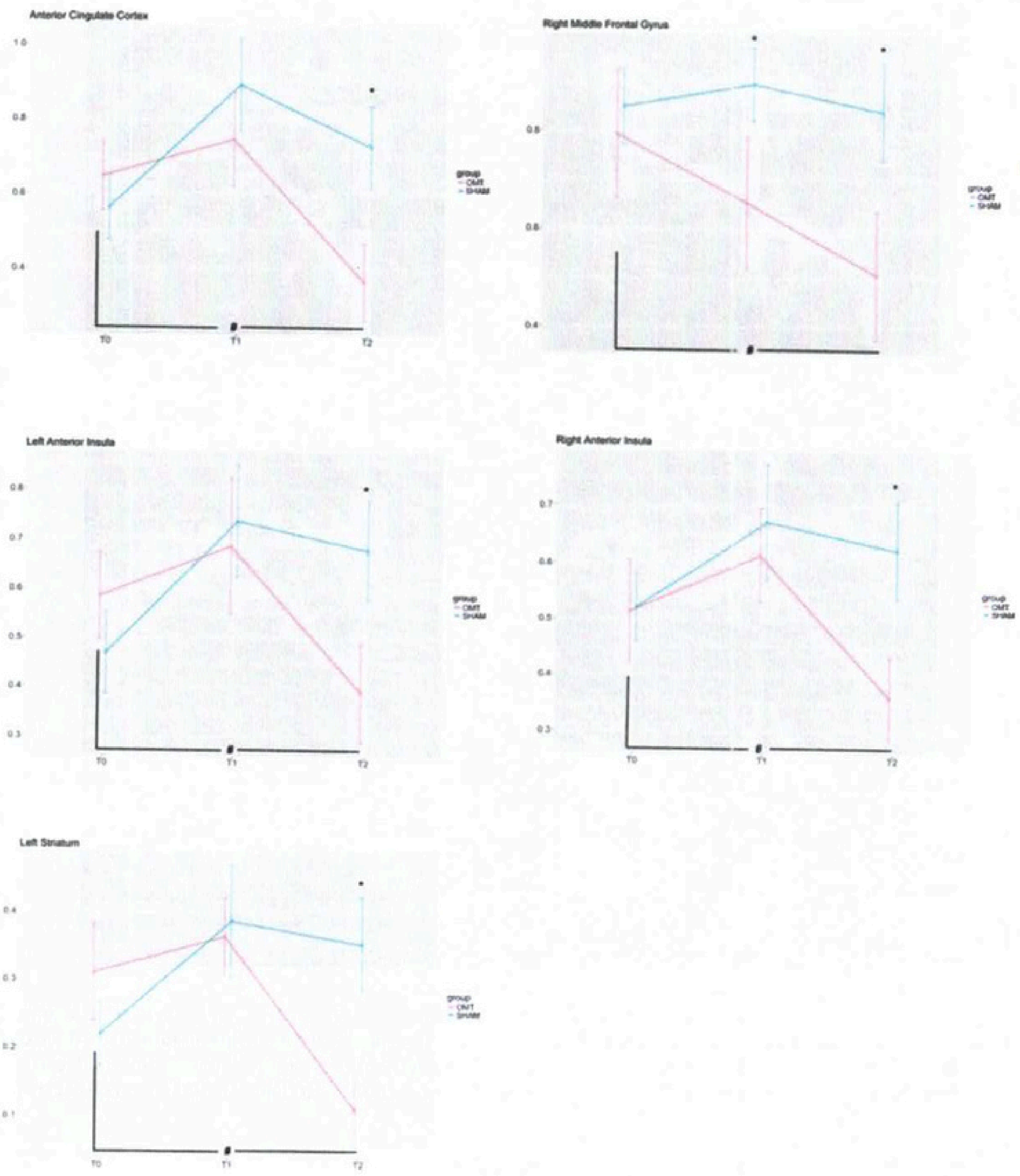
Task specific brain activations at T0 pooling the two groups. The group statistical maps were thresholded at $p < 0.05$. mPFC: medial prefrontal cortex; lINS: left insula; rINS: right insula; SM: somatomotor cortex; ACC: anterior cingulate cortex; AC: acoustic cortex.

Figure 2



Results of the group analysis revealing areas for OMT and Sham group by the contrast T2-T1-T0 in the heart task (interoceptive awareness task) and sound task (exteroceptive awareness task). The group statistical maps were thresholded at $p < 0.05$, corrected for multiple comparisons using FDR, and superimposed on the Talairach transformed structural scan of one of the subjects. Activation was observed in Right Cingulate Cortex, Right and Left Insula, Left Lentiform and right Middle Frontal Gyrus (rMFG).

Figure 3



Activation (GLM beta values ± SEM) over time for the two groups and the different regions of interest. ∗Statistically significant values between groups after Bonferroni-Holm correction. #Paired t test statistically significant values within OMT group.

Figure 4

Hindawi

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Glucose Metabolic Changes in the Brain and Muscles of Patients with Nonspecific Neck Pain Treated by Spinal Manipulation Therapy: A [^{18}F]FDG PET Study

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Abstract

Objective. The aim of this study was tc Feedback nges in brain and muscle glucose metabolism that are not yet known, using ɔn tomography with [^{18}F]fluorodeoxyglucose ([^{18}F]FDG PET). *Methods*. Twenty-one male volunteers were recruited for the present study. [^{18}F]FDG PET scanning was performed twice on each subject: once after the spinal manipulation therapy (SMT) intervention (treatment condition) and once after resting (control condition). We performed the SMT intervention using an adjustment device. Glucose metabolism of the brain and skeletal muscles was measured and compared between the two conditions. In addition, we measured salivary amylase level as an index of autonomic nervous system (ANS) activity, as well as muscle tension and subjective pain intensity in each subject. *Results*. Changes in brain activity after SMT included activation of the dorsal anterior cingulate cortex, cerebellar vermis, and somatosensory association cortex and deactivation of the prefrontal cortex and temporal sites. Glucose uptake in skeletal muscles showed a trend toward decreased metabolism after SMT, although the difference was not significant. Other measurements indicated relaxation of cervical muscle tension, decrease in salivary amylase level (suppression of sympathetic nerve activity), and pain relief after SMT. *Conclusion.* Brain processing after SMT may lead to physiological relaxation via a decrease in sympathetic nerve activity.

1. Introduction

Spinal manipulation therapy (SMT), which is performed by healthcare practitioners such as chiropractors, osteopathic physicians, and physiotherapists, has been applied mainly to musculoskeletal problems such as neck pain or low back pain. Many investigators have performed various experiments to elucidate the mechanism underlying the clinical effects of SMT. The earliest studies analyzed the magnitude of the force applied to the vertebrae and the movement of vertebrae during SMT, with the forces exerted by the practitioner quantified using a flexible pressure mat [1, 2]. The rotation and relative movement of vertebrae after treatment using a mechanical adjusting device (activator adjusting instrument, AAI) [3] have also been reported [4–8]. Previous studies have suggested that SMT has beneficial clinical effects, including pain relief [9] and reduction of blood pressure [10, 11]. It is thought that biomechanical input by SMT could generate a physical response or reflex [12]; however, the mechanism of these clinical effects induced by SMT is still unknown.

In recent years, the findings of brain activation studies using imaging modalities such as functional magnetic resonance imaging, near-infrared spectroscopy, and positron emission tomography (PET) have contributed to advances in brain science [13]. Such studies are able to enhance our understanding of the neurophysiological effects of specific physical/psychological tasks by detecting associated activation and deactivation of brain regions. PET has also been used to elucidate the metabolic changes that alternative therapies induce in living tissues; for example, an ^{18}F-labeled glucose analog has been used to study cerebral metabolic changes after acupuncture [14] and aromatherapy [15], and [^{15}O]H_2O has been used to assess changes in cerebral blood flow during massage [16]. Lystad and Pollard have noted the usefulness of neuroimaging techniques for gaining a better understanding of the neurophysiological effects of SMT [17].

The [^{18}F]-labeled glucose analog, fluorodeoxyglucose ([^{18}F]FDG), is thought to be able to visualize the energy metabolism of various tissues such as brain and muscles in vivo. One of important advantages of [^{18}F]FDG PET is that we can simultaneously measure the energy metabolism of brain and muscles. We have hypothesized that clinical effects such as muscle tension relaxation and pain relief are mediated by the regional brain activity induced by SMT. We have also expected any changes in muscular energy consumption in treatment condition. In addition, we have also expected significant correlation between the regional brain activity and the muscular energy consumption.

Previously, we reported preliminary results of our study to examine our initial hypothesis that a [^{18}F]FDG PET can visualize brain metabolic changes induced by SMT [18]. In this paper, we report our conclusive results on this issue. In addition, the present work tries to examine our additional hypothesis that the [^{18}F]FDG PET can visualize muscular metabolic changes induced by SMT, as well as their association with the regional brain metabolism.

2. Subjects and Methods

We recruited 21 male subjects (mean age ± SD: 26.4 ± 5.9 years) with cervical pain and shoulder stiffness but without abnormalities in neck-to-shoulder MR images and without history of any treatments prior to the present study. We performed MRI examination of the neck to the shoulder area on all participants; the resulting MR images were used as a reference for the anatomical locations of cervical muscles in PET images. Female subjects were not included in this study because of physiological fluctuations due to the menstrual cycle [19–23].

SMT was applied using an AAI, Activator II (Activator Methods International, Ltd., Phoenix, USA), in accordance with the Activator Methods (AM) basic scan protocol [24, 25]. We utilized the AAI to apply impulses to specific vertebrae or joints (Figure 1). SMT was performed on the subject in a prone position without movements such as cervical rotation, lateral flexion, and extension, in order to prevent the muscular [^{18}F]FDG uptake due to muscle contractions during the therapeutic procedure. SMT was carried out on the whole spine, the scapulae, the ilium, and the sacrum, as necessary for each subject. The mean number of SMT-adjusted sites was 8 per subject.

Figure 1

The location of cervical adjustment by the activator adjusting instrument (AAI) in the treatment condition. Spinal manipulation therapy (SMT) by AAI was performed by contact on the joints and did not include muscle massage. SMT on all subjects was performed by the same chiropractor, who was an advanced practitioner of Activator Methods.

PET scanning was performed twice on each subject according to the protocol given in Figure 2 . The interval between the two scans ranged from 7 to 70 days (mean interval ± SD: 23 ± 15 days). The subjects received SMT intervention which lasted for approximately 20 minutes including a diagnostic procedure. Soon after the treatment, [^{18}F]FDG-containing saline solution was injected to the subject through the left cubital vein (mean ± SD: 47.0 ± 8.9 MBq) in quiet room with a dim light next door to the treatment room in the same building. On the other scan day, [^{18}F]FDG was injected to the subject after a 20-minute-long resting phase instead of SMT intervention. The subjects in both conditions were asked to sit in a relaxed position with their eyes closed for 30 minutes before PET scanning. The brain scan and the scan on the neck to the shoulder area of the subject were initiated after 30 minutes of [^{18}F]FDG injection, utilizing a PET scanner, SET2400W (Shimadzu, Inc., Kyoto, Japan). The PET scanning covered the entire brain in one scan, taking 10 minutes for the emission scan and another 5 minutes for the transmission scan for tissue attenuation correction. Scanning from the neck to the shoulder area in one scan took 5 minutes for the emission scan and another 5 minutes for the transmission scan for tissue attenuation correction. Images were acquired with a 128 × 128 matrix and reconstructed using Fourier rebinning and Ordered Subset Expectation Maximization Algorithm [18]. The intensity of subjective pain was evaluated using a 0–10 visual analog scale (VAS) before and after SMT in the treatment condition. VAS evaluation was not done in the resting condition except for in 9 subjects. Cervical muscle tension was measured bilaterally at the superior part of the trapezius muscle using a tissue hardness meter (Muscle Meter PEK-1, Imoto Inc., Kyoto, Japan); the mean value of three measurements was recorded. Additionally, salivary amylase levels were measured for each subject using an amylase monitor (Nipro Inc., Osaka, Japan) to evaluate changes in autonomic nervous system (ANS) function. Figure 2 shows the measurement points. Further details of the study protocol are described in our previous report [18]. The whole protocol was approved by the Ethics Committee of Tohoku University Graduate School of Medicine, Sendai, Japan (number 2008-115).

Figure 2

Diagram of the study protocol. Half of the subjects were randomly assigned to be scanned first in the resting condition and then in the treatment condition; the other half were scanned in the reverse order. The intensity of subjective pain was evaluated before and after spinal manipulation therapy only in the treatment condition. Muscle stiffness and salivary amylase were measured before and after the treatment or resting period. MT = muscle tension, VAS = visual analog scale.

For data analysis, differences in values before and after treatment and between the control and treatment conditions were compared using paired *t*-tests for all measurements except for PET data. Brain PET images were analyzed using the voxel-wise statistical analysis software package Statistical Parametric Mapping 8 (SPM8; Functional Imaging Laboratory, London, UK) in order to identify regional glucose metabolic changes [26, 27]. An FDG brain template distributed by Montreal Neurological Institute (McGill University, Montreal, Canada) [28] was used for anatomical standardization (spatial normalization) of the PET images. Each voxel had dimensions of $2 \times 2 \times 2$ mm in the normalized image. The normalized data were smoothed using an isotropic Gaussian kernel of 12 mm (for the *x*-, *y*-, and *z*-axes) to increase the signal-to-noise ratio by suppressing high-frequency noise. The threshold for the statistical significance of the voxel value height in the present study was set at $p < 0.05$ with correction for multiple comparisons (family-wise error correction), while our previous study applied the compromised threshold of $p < 0.001$ without correction. Voxel values of the PET images were compared between the resting and treatment conditions using a paired *t*-test.

PET images of the neck and shoulder regions were coregistered to the MR images of the same subject; regions of interest (ROIs) for cervical muscles were then manually drawn on the PET images using Dr. View software (Version 2.0, AJS, Tokyo, Japan), using the MR images as references. ROIs were drawn on the trapezius muscle at C7-T1 levels bilaterally, the splenius muscles, the semispinalis muscles, the elevator scapular muscles, and the trapezius muscles at C6-C7 levels bilaterally. The standardized uptake value (SUV) for each muscle was calculated using the following formula:

$$\text{SUV} = \text{tissue radioactivity concentration} \ (\text{Bq/g}) \times \frac{\text{body weight(g)}}{\text{injected activity(Bq)}}. \tag{1}$$

SUVs were statistically examined using a paired *t*-test to compare muscle metabolism after SMT and after resting. In addition, the authors searched for specific brain regions associated with muscular energy consumption by applying linear correlation analysis using SUV of each muscle studied here as a parameter in SPM8.

3. Results

The SMT-associated regional brain metabolic changes (activation and deactivation) detected by the SPM8 analysis are shown in Table 1. Statistically significant areas were overlaid on the standard MRI brain template images (Figure 3). PET analysis of the cervical muscles showed a trend toward reduced metabolism (SUV) after SMT compared with the control condition; however, these changes were not statistically significant (Figure 4). In addition, no meaningful correlation was detected between muscular SUV and regional brain activity.

Figure 3

Regional activation (left) and deactivation (right) after spinal manipulation therapy (SMT) using an activator adjusting instrument. Glucose metabolism is increased in regions including the anterior cingulate cortex and cerebellar vermis but is relatively reduced in many sites, including the prefrontal cortex, after SMT. The voxel height threshold is $p < 0.05$, corrected for multiple comparisons; the extent threshold is 10 voxels minimum.

Figure 4

Results of positron emission tomography analysis of cervical muscles (paired *t*-test). The error bars represent standard deviations. The results indicate a trend toward reduction of mean standardized uptake value (SUV) after SMT; however, the difference is not statistically significant. Trap., trapezius muscle; Splenius, splenius muscles; Lev. Scap., levator scapulae; Semispinalis, semispinalis muscles; C7-T1, between the seventh cervical spine and the first thoracic spine; C6-C7, between the sixth cervical spine and the seventh cervical spine.

Table 1

Brain metabolic changes associated with the spinal manipulation therapy intervention.

Anatomical region	Coordinates x, y, and z (mm)	Brodmann area	Cluster equiv.	Voxel Z score
Activation				
Broca's area	−34, 6, 28	44	110	5.84
ACC	2, 8, 40	32	228	5.72
SSAC	16, −26, 48	5	114	5.65
Wernicke's area	46, −48, 20	22	30	5.52
VAC	−6, −88, 38	19	31	5.32
CV	6, −62, −4	—	14	5.28
VC (V2)	24, −80, 6	18	17	5.24
Deactivation				
IPL	−40, −40, 34	39/40	286	6.74
FP	−2, 68, −8	10	160	6.66
IFG PT	40, 28, 16	45	117	6.53
PSMA	30, 14, 44	6	348	6.34
PMC (M1)	−28, −18, 56	4	45	6.12
FEF/dl-PFC	−30, 12, 44	8/9	157	5.93
dl-PFC	−38, 26, 24	46	309	5.70
AG/FG	−40, −60, 8	39/37	177	5.58
ITG	−70, −22, −20	20	20	5.66
TP	40, 22, −44	38	12	5.64
CV (V1)	−14, −66, 24	17	46	5.29

Brain metabolic changes detected by SPM8 are presented (voxel height threshold $p < 0.05$ with corrections for multiple comparisons, extent threshold 10 voxels minimum). The statistical significance of regional metabolic changes is given as Z scores $[(\text{Mean}_{\text{treatment}} - \text{Mean}_{\text{control}})/\text{SD}_{\text{control}}]$.

ACC, anterior cingulate cortex; SSAC, somatosensory association cortex; VAC, visual association cortex; CV, cerebellar vermis; VC, visual cortex; IPL, inferior parietal lobule; FP, frontal pole; IFG, inferior frontal gyrus; PT, pars triangularis; PSMA, premotor area/supplementary motor area; PMC, primary motor cortex; FEF, frontal eye field; dl-PFC, dorsolateral prefrontal cortex; AG, angular gyrus; FC, fusiform gyrus; ITG, inferior temporal gyrus; TP, temporal pole.

In contrast, cervical muscle tension was significantly reduced bilaterally after SMT ($p < 0.0001$ for both sides, Figure 5). Salivary amylase level decreased significantly after SMT ($p = 0.022$) but increased significantly in the control condition ($p = 0.011$, Figure 6). Comparisons of VAS pain scores in the treatment condition revealed a significant decrease after SMT ($p < 0.0001$, Figure 7), while the comparison in the control condition showed nonsignificant difference ($n = 9$).

Figure 5

Muscle tension is significantly reduced after spinal manipulation therapy. $^{*}p < 0.0001$.

Figure 6

Changes in salivary amylase level. Salivary amylase level is reduced after spinal manipulation therapy but increased in the control condition. $^{**}p < 0.05$.

Figure 7

Changes in subjective pain in the treatment condition. The pain scale score is significantly decreased after spinal manipulation therapy. $^{*}p < 0.0001$.

4. Discussion

The findings of the present study demonstrate how stimuli to the mechanoreceptors of the joints and skin during SMT are processed in the brain. Injected [^{18}F]FDG was absorbed into activated brain regions and visualized by PET. We observed multiple changes in brain activity after SMT.

SPM8 analyzes approximately half a million voxels of brain volume data simultaneously. Correction for multiple comparisons is therefore indispensable, making the statistical threshold extremely high. Since many studies have failed to detect significant differences in voxels after correction for multiple comparisons, the SPM8 development team proposed the use of a compromised threshold for voxel height ($p < 0.001$) combined with a voxel extent threshold for the size of each voxel cluster (e.g., 10 voxels minimum), as used in our previous report [26, 27]. This technique has been useful for practical purposes but is prone to Type-1 errors. The significant voxel clusters that survived correction for multiple comparisons in the present work may therefore indicate more robust and reliable findings than those in our preliminary report [18]; we believe these results are worthy of reporting as conclusive findings, despite the fact that the intensity of the observed brain responses to SMT intervention was initially estimated to be much weaker.

As for regional brain metabolic changes after the SMT intervention, activation (increased metabolism) was detected in the dACC (Brodmann area [BA] 32), cerebellar vermis (CV), and somatosensory association cortex, and regional deactivation (decreased metabolism) was detected in regions including the prefrontal cortex (PFC) and temporal sites. Involvement of the ACC in cognitive and emotional processes has been recognized since Papez mentioned the idea in 1937 [29–31], and this area is also involved in placebo and opioid analgesia [32]. Some brain activation studies have also demonstrated activation of the ACC in response to pleasant or unpleasant stimuli such as massages or the olfactory stimulus of isovaleric acid, respectively [33–35]. The ACC is part of network that carries out cognitive processing based on individual factors such as experiences or emotions while making contact with the other regions in the network, such as the limbic system and cortex [32, 36]. Recently, specific features of the dACC functions and their connectivity to other brain regions are not fully elucidated yet, though they have been revealed little by little. For example, dACC is involved in cognitive functions, motivation, and reward-based decision-making as a part of the network including the CV and prefrontal cortex [37]. The neuronal activity changes in dACC and CV were detected in the present study.

The CV receives somatic sensory information from the spinal cord and via the vestibulospinal tract or reticular nuclei of the brainstem through the spinal cord, connecting indirectly or directly with motor cells on the ventral horn. These systems control involuntary muscular tension and reflexes. Our results suggest that stimulation of joints during SMT induced relaxation of reflexive muscle tension. The cerebellum is also thought to have a functional role as an integrator of multiple effector systems, including affective processing, pain modulation, and sensorimotor processing [38]. Recently, many studies have reported roles for the cerebellum in non-motor functions [39, 40]. A study by Sacchetti et al. showed that the CV is activated during mental recall of emotional personal episodes in humans [39]. Lou et al. also reported that the CV, ACC, and some regions of the PFC are activated during relaxation mediation in yoga [41]. However, it is important to note that the PFC was deactivated after SMT in our study. Interestingly, Critchley et al. found that the ACC/dACC (BA24/32) and CV are specifically activated during biofeedback therapy [42], a technique for controlling one's tension to generate a state of relaxation. The activated areas in the present study are similar to those activated during biofeedback relaxation, indicating that the state of the brain after SMT may be similar to that induced by biofeedback therapy. Furthermore, our assessment of body responses in this study showed relaxation of muscle tension and decreased salivary amylase levels—phenomena that are associated with reduced sympathetic nerve activity. Salivary α-amylase levels correspond to plasma norepinephrine levels and are utilized as an accessible measure of sympathetic nervous reactivity in stress research, with lower levels indicating lower activity [43–45].

Ouchi et al. suggested that the comfortable sensation generated by back massage may be related to increased regional cerebral blood flow in the posterior brain—specifically, in the precuneus [16]. SMT stimuli to the joints may be processed differently from those of muscle massage, resulting in decreased sympathetic nerve activity. On the other hand, certain cervical muscles showed a tendency toward decreased glucose metabolism after SMT, although the difference was not statistically significant (Figure 4). Increasing the number of study subjects may increase the significance of this finding. The underlying mechanism of reduced muscular glucose uptake is not yet understood; however, an animal study suggests the involvement of sympathetic nerve activity [46]. Glucose uptake in skeletal muscles may thus be influenced directly or indirectly by the ANS.

Although the mechanism of muscle relaxation is still unknown, we hypothesize the involvement of (a) autonomic nervous activity and (b) improvement of the range of joint movement [47]. In the present study, we observed that SMT stimulus induced physical responses such as muscle tension relaxation, pain relief, and reduced amylase secretion. These changes may be associated with neural processing in the dACC and CV. Neural inputs evoked by SMT stimuli via various receptors in muscles, tendons, and joints may ascend to the somatosensory areas of the brain through the medial lemniscal system. The response signal descending from the brain may then adjust the postural muscles accordingly.

Muscular SUV, an index of energy consumption of skeletal muscles, did not show significant difference between the control and treatment conditions, while muscle tension did show significant difference. In addition, we could not detect meaningful correlation between the SUV of muscular glucose consumption and the regional brain glucose consumption.

As is the case with every study, our methodology is not without limitations. Ideally, the present subjects would have undergone PET scanning before and after the SMT intervention in both the control and treatment conditions. However, this protocol would have assigned 4 PET scans to each subject, resulting in unreasonably high radiation exposure for this kind of study. Furthermore, it is hard to perform serial PET scans within 1 or 2 hours of each other because of the relatively long physical half-life of the [^{18}F] nuclide (110 minutes). In addition, the number of subjects ($n = 21$) was still relatively small for a clinical study; however, we define the present results as conclusive ones in order to minimize radiation exposure of the subjects, who were healthy other than their neck and shoulder symptoms and who are considered to be part of the general public. Previously, we reported preliminary findings with a sample size of 12; however, the study results were only at threshold level [18], and these results seemed to be prone to Type-1 errors because they were based on a compromised statistical examination without correction for multiple comparisons. On the other hand, no voxels survived with a standard statistical examination including correction for multiple comparisons, suggesting that these negative results may be prone to Type-2 errors. By raising the sample size to 21, now we are able to obtain robust results that survived even after correction for multiple comparisons. Thus, the authors believe the present results are more reliable as an evidence for further discussion on clinical effects of SMT interventions while our preliminary report was useful as a "proof of concept" study.

5. Conclusion

In summary, we observed metabolic changes in the brain and skeletal muscles, as well as reductions in subjective pain, muscle tension, and salivary amylase, after SMT intervention. These results may be associated with reduced sympathetic nerve activity, suggesting that SMT induces a kind of relaxation similar to that achieved by biofeedback. The brain response to SMT may reflect the psychophysiological relaxation that accompanies reduced sympathetic nerve activity.

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Competing Interests

The authors declare that they have no competing interests.

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Case Study

Increased Telomere Length & Improvements in Dysautonomia, Quality of Life, Neck & Back Pain Following Correction of Sagittal Cervical Alignment Using Chiropractic BioPhysics® Technique: a Case Study

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Abstract

Objective: To present a prospective case study on the increase of telomere length, improvement in nocturnal polyuria, neck and mid-back pain, autonomic nervous system adaptability, and health-related quality of life following correction of the sagittal cervico-thoracic spinal alignment and posture using chiropractic biophysics® (CBP®) technique.

Clinical features: A 35-year-old white female elementary school teacher presented with chronic neck and mid- back pain for 5 years following a motor vehicle collision as well as nocturnal polyuria. Examination and radiography revealed forward head posture and loss of cervical lordosis consistent with vertebral subluxation. Patient telomere length was derived from nucleated white blood cells obtained from a blood test. Quality of life measures were determined by the Short-Form 36 health survey and heart rate variability was measured.

Intervention and outcome: The patient received CBP® spinal care including Mirror Image® corrective spinal exercises, adjustments, and traction. Full spine and drop table adjustments were administered. After 36 visits, she reported improvement in her nocturnal polyuria, neck and mid-back pain, and quality of life. Cervical x-rays showed correction of cervical lordosis and forward head posture. A blood test showed significant improvement in patient telomere length and heart rate variability improved from a health risk to within normal limits.

Conclusion: Our case suggests that correction of cervical lordosis and forward head postures by CBP® Mirror Image® methods improved the sagittal spinal alignment and posture and was temporally associated with lengthened telomeres, improved nocturnal polyuria, neck and mid-back pain, quality of life, and autonomic nervous system adaptability.

Key Indexing Terms: *Chiropractic BioPhysics®; CBP®; Adjustments; Traction; Cervical spine posture; Lordosis; Telomere length; Quality of life; Nocturnal polyuria; Vertebral subluxation*

Introduction

Human telomere length (TL) is affected by genetic and environmental factors.[1] TL is longest at birth and decreases with advancing age.[2] As such, telomere length is considered a biomarker of biological aging.[2,3] As telomeres shorten, cells can lose their ability to undergo cellular sequencing (replication and division) and may undergo apoptosis (cell death).[4] In various cross-sectional studies, observations of shortened TL are associated with metabolic and inflammatory diseases,[3,5] pulmonary diseases,[3,6] cardiovascular events and diseases,[3,7-10] psychological and stress disorders,[3] neurodegenerative diseases,[3] cancer,[3,11] chronic and serious illnesses,[3] and mortality.[3,10] Additionally, TL is associated with lifestyle choices such as diet, tobacco and alcohol use,[12] physical activity, and sleep.[3] Fewer studies have focused on the dynamic change and regulation of TL by implementing exercise programs,[13,14] vitamin supplements,[15] diet[16] meditation[17] and genetic engineering.[18] Interest in telomere lengthening or length maintenance is due to the notion that this will serve to slow down or cease a person's biological clock providing youthfulness and health longevity.[10] It seems that implementation of healthy interventions or reduction of unhealthy stressors will have a beneficial effect on TL. The effects of chiropractic care on TL have not been studied.

Neck pain (NP) and back pain are common presentations in chiropractic practices and chiropractic management thereof varies between practitioners.[19] Cervical spine misalignment resulting in vertebral subluxation remains an under-diagnosed cause of neck and back pain.[20] Common to all concepts or definitions of vertebral subluxation are some form of biomechanical dysfunction and the neurological implications of the biomechanical dysfunction.[21,22] This includes spinal and postural structural displacements as rotations or translations away from normal spinal alignment in any of the three anatomical planes accompanied by pain or neurologic dysfunction. Correction of vertebral subluxations toward a healthy spinal alignment can alleviate the associated pain or neurologic dysfunction.[23-26] Many chiropractic techniques claim to produce structural correction of the spine. However, very few support their claims with clinical scientific evidence in the form of randomized and non-randomized clinical control trials with proper follow-ups. Chiropractic BioPhysics® (CBP®) technique is a full-spine and posture rehabilitation approach to correcting poor posture, deviation of normal spinal alignment and subluxation through incorporating mirror image® exercise, adjustments, and traction procedures.[27-31] CBP® has an extensive amount of quality scientific evidence supporting reliable correction of spinal and postural misalignment yielding improvements in concomitant neurological, musculoskeletal symptoms, spine movement, and patient disability levels.[20,23-26,32,33] It seems logical to propose that improvements in spinal and neurological health may have a beneficial impact on TL.

Case Report

Clinical features

A 35-year-old white female elementary school teacher presented to the office with the primary complaint of neck and mid-back pain for five years following a head-on motor vehicle collision (MVC) as well as nocturnal polyuria whereas she would need to wake up to urinate four times per night. The patient reported that she took generic, regular strength ibuprofen at bottle-recommended dosages 2 to 3 times per day for the 2 weeks immediately following the MVC. The patient reported that she had not and did not take any other medication. The patient had also sustained three prior MVCs MVCs in which she was rear-ended. The patient reported drinking three to five mountain dew soda drinks per day.

The patient weighed 120 pounds and measured 66 inches tall. She rated her NP and mid-back pain as a 5/10 on the numeric rating scale (NRS: 0=no pain; 10=maximum pain). Heart rate variability (HRV) was performed using the CLA Insight™ Pulse Wave Profiler HRV Monitor (Chiropractic Leadership Alliance, Bethany Beach, DE, USA) and the patient scored 75.35 on the autonomic activity index (AAI) (normal is 80.00 to 100.00) and 55.20(S) on the autonomic balance index (ABI) with increased sympathetic nervous system (S) activity (normal is 80.00(S) to 80.00(P) where P stands for parasympathetic nervous system activity) (Figure 1). Using Health and Wellness Score (FLDC LLC, Cumming, GA, USA) to administer, score, and analyze the Short Form 36-Question (SF-36) health survey, the patient scored a 50/100 in physical function (PF), 20/100 in physical role limitations (PRL), 33.33/100 in emotional role limitations (ERL), 35/100 in vitality (V), 76/100 in emotional well-being (EWB), 62.5/100 in social functioning (SF), 55/100 in pain (P!), 45/100 general health (GH), and 50/100 in change in health status (ΔHS) (Table 1). The scoring of the SF-36 indicates that 0/100 in a quality of life (QoL) domain represents the poorest possible result and 100/100 indicates the best possible result. Taking this into account, higher scores indicate better QoL. For comparison, a score of 50 is considered average based on a large United States nationwide population of healthy individuals. The patient had her blood drawn and analyzed for TL. The patient's telomere value was 73 and is a calculation of the patient's TL derived from nucleated white blood cells obtained from whole blood.

Postural and radiographic analysis

Posture analysis[27] revealed a forward head translation (+TzH). Anterior-to-posterior (AP) and neutral lateral cervical (NLC) radiographs were taken and analyzed using PostureRay® Electronic Medical Records (EMR) Software (PostureCo, Inc., Trinity, FL, USA) according to the Harrison Posterior Tangent method for sagittal spine views[34-36] and analyses for frontal spine views (Figure 2).[37] These examination and analysis methods are valid,[38-42] reliable, and repeatable,[34-38] as is posture.[38]

The AP cervico-thoracic view revealed a spinal alignment within normal limits (WNL). The NLC view (Figure 2) revealed forward head posture (Tz C2-C7) of 24.0 mm (ideal is 0.0 mm and average is 15 mm), an atlas plane line (APL) of-20.2° (ideal is-29.0° and average is 23°), and an absolute rotational angle from C2 to C7 (ARA C2-C7) of-18.8° (normal is-42.0° and average is 34°) (Table 2).

Intervention

The patient was seen for 36 visits over 5 months per CBP® technique protocols incorporating Mirror Image® exercises, adjustments, and traction to correct the cervical hypolordosis and +TzH. Chiropractic care consisted of full-spine chiropractic adjustments and CBP® Mirror Image® drop table adjustments, exercises, and traction at each visit. Mirror Image® refers to the patient being placed into an opposite, over- corrected posture prior to adjustment, as a sustained hold for traction, and as an exercise to facilitate spinal alignment and posture correction. Paraspinal stimulation was administered via the hand-held Impulse® adjusting instrument (Neuromechanical Innovations, Chandler, AZ, USA). The Impulse® adjusting instrument delivers a consistent programmed thrust to stimulate the most mechanoreceptors and proprioceptors possible to relay the position of the body to the brain to retrain the patient's central nervous system (CNS) to adapt to normal posture according to the Harrison Spinal Model. Twenty repetitions of Mirror Image® cervical extension correction exercises were performed 3 times per week. Mirror Image® exercises "attempt to re-train the physiologic adaptations of the soft tissues of the spine by frequently stressing these tissues favoring the optimum loading position balance".[43] The Cervical Denneroll™ Spinal Orthotic (Denneroll Pty Ltd, New South Wales, Australia) was used for Mirror Image® cervical extension traction at 15 minutes per session per visit. A long-duration of deformation forces counter those that are habituated to a patient's abnormal posture.[23-26] The Denneroll is placed in the upper (C2- C4), middle (C4-C6), or lower (C6-T1) cervical region depending on the patient's cervical alignment.

Results

The patient stated that she maintained her lifestyle throughout chiropractic care. After the 36 visits, the patient was re-assessed. The patient reported that her neck and mid-back pain were reduced from NRS 5/10 to <1/10. HRV was performed again and the patient improved to 80.38 on AAI (normal is 80.00 to 100.00) and 88.51(S) on ABI (normal is 80.00(S) to 80.00(P)) (Figure 1). On the SF-36, the patient improved in all QoL domains to 95/100 in PF, 100/100 in PRL, 100/100 in ERL, 75/100 in V, 88/100 in EWB, 100/100 in SF, 90/100 in P!, 70/100 in GH, and 100/100 in ΔHS (Table 1). Higher scores indicate better QoL. The patient had blood drawn again to assess her TL. Her telomere value increased 8.23% from 73 to 79. NLC x-ray (Figure 2) analysis (Table 2) after 36 visits revealed improvements in Tz C2-C7 from 24.0 mm to 17.7 mm, in APL from-20.2° to-25.0°, and an ARA C2-C7 from-18.8° to-27.0° (Figure 2 and Table 2). The patient reported to be virtually pain-free and had been able to sleep through the night without having to go to the bathroom to urinate.

Discussion

This report documents the successful outcome in a 35-year-old patient with neck and mid-back pain and nocturnal polyuria as well as unhealthy spinal alignment and posture and autonomic dysfunction. Near complete resolution of symptoms was achieved following the correction of spinal alignment and posture using CBP® technique and the application of Mirror Image® chiropractic adjustments, spinal exercises, and spinal traction using the cervical denneroll spinal orthotic.

Certain circumstances and concurrences need to be highlighted within this report. First, the patient did not alter her lifestyle throughout her care. Most notable is that she continued to drink three to five Mountain Dew sodas per day and still yielded the extraordinary health improvements documented. The patient stated that chiropractic care was the only change in her everyday routine. Following correction of the cervical spinal alignment and posture, the patient's HRV improved considerably from a health risk to WNL (Figure 1). "Several cardinal features of chronic critical illness — regardless of the etiology — support the assertion that autonomic dysfunction is a core mechanism underlying the development and perpetuation of multiorgan failure".[44] This also helps to understand why TL and HRV may be directly related to each other and inversely related to organ failure (i.e., nocturnal polyuria) and why these variables might be related for this current patient. Woody, et al reported "greater reductions in HRV in response to a stressor are associated with shorter relative TL (i.e., greater cellular aging)".[45] Additionally, improvements in objective health measures (spinal alignment and posture, HRV, nocturnal polyuria, and TL) are directly related to the subjective improvements in the patient's health (pain NRS and QoL).

Chiropractic care is popularly known as care for neck and back pain. However, this does not explain the neurological and visceral implications within this report. Conduction of an action potential along the spinal cord and nerve fibers is accompanied by shortening and swelling of the nerve.[46] Sagittal cervical deformities and vertebral subluxations are orthopedic abnormalities that apply abnormal tensile forces in the brain stem, cranial nerves 5-12, spinal cord, and nerve roots. This increased tension provides resistance against the necessary shortening and swelling of nerve fibers that accompany an action potential. This tension can give rise to local and distant signs and symptoms including neuralgias, spasticity, dizziness, bladder dysfunction, cervical and lumbar spondylosis, disk hernias, trauma to the spinal cord, and autoimmune disorders.[23-26,32,33,47] This serves as a proposed mechanism for the source of this patient's health conditions due to their resolution following sagittal cervical spinal correction. According to Uchida et al, "adequate correction of local sagittal (cervical) alignment may help to maximize the chance of neurological improvement".[48] Additionally, patients under long-term chiropractic care demonstrate higher serum thiol antioxidant levels responsible for reducing oxidative stress on the body, facilitating DNA repair enzyme activity which is directly related to health longevity.[49]

One limitation to report is that this is a case study (n=1) and no long-term follow-up is presented; as such it does not allow correlation or causation. This is a prospective case study and as such does not lend itself to selection bias. Another limitation is that multiple interventions were applied to the patient. As such, it is unclear which intervention or combination thereof had the positive impact on the patient's health measures. And, while spinal manipulation and exercise have not been shown to reliably correct spinal alignment,[31,50-52] there may lie a reliable combination of therapies within permutations of Mirror Image® exercises, adjustments, and traction.[23-26]

Conclusion

Our case suggests, for the first time, that cervical spinal alignment and posture may be directly related to TL (health longevity) and that correction thereof may have a directly related effect on health longevity as represented by TL. This case adds more evidence to claims that cervical spinal alignment may also improve autonomic function (HRV and bladder function), QoL, and neck and back pain. As cervical spinal alignment and posture improved, so did the listed health measures. Randomized clinical controlled trials involving measuring TL of a large population of chiropractic patients should be conducted. Hopefully this case report will serve as a motivation for higher levels of evidence from which correlations and causations regarding the effects that chiropractic spinal corrective care might have on health longevity can be made.

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Abbreviations

Abbreviations: CBP®: Chiropractic BioPhysics®; TL: Telomere Length; NP: Neck Pain; MVC: Motor Vehicle Collision; NRS: Numeric Rating Scale; HRV: Heart Rate Variability; AAI: Autonomic Activity Index; ABI: Autonomic Balance Index; S: Sympathetic Nervous System; P: Parasympathetic Nervous System; SF-36: Short Form 36-Question Health Survey; QOL: Quality of Life; +TzH: Positive Translation of the Head in The Z-Axis; AP: Anterior-to-Posterior; NLC: Neutral Lateral Cervical; EMR: Electronic Medical Record; WNL: Within Normal Limits; Tz C2-C7: Translation of the posterior superior body corner of C2 with respect to a vertical line originating at the posterior inferior body corner of C7 in the z-axis as seen in the sagittal view of the cervical spine; APL: Atlas Plane Line; ARA C2-C7: Absolute rotational angle of the cervical region measuring the angle between the lines tangent to the posterior vertebral body margins of the C2 and C7 vertebrae in the sagittal view; CNS: Central Nervous System; n: Number of participants; RRA: Relative Rotational Angle; ARA: Absolute Rotational Angle; Tz: Translation in the z axis; PF: Physical Functioning; PRL: Physical Role Limitations; ERL: Emotional Role Limitations; EWB: Emotional Well- Being; V: Vitality; SF: Social Functioning; P!: Pain; GH: General Health; ΔHS: Change in Health Status.

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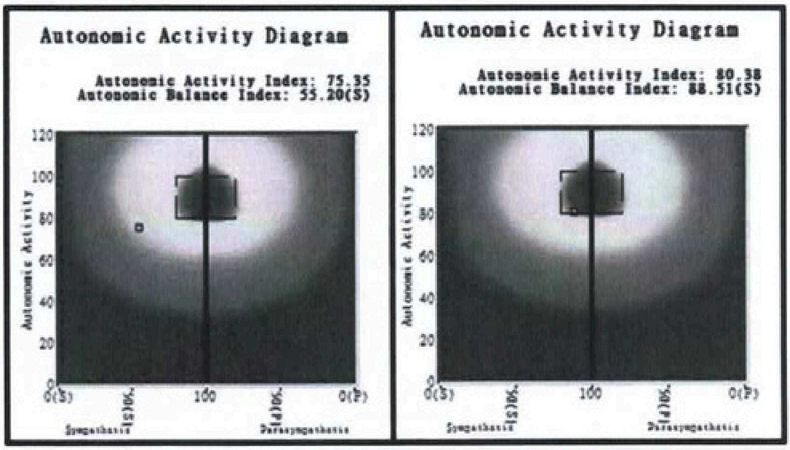
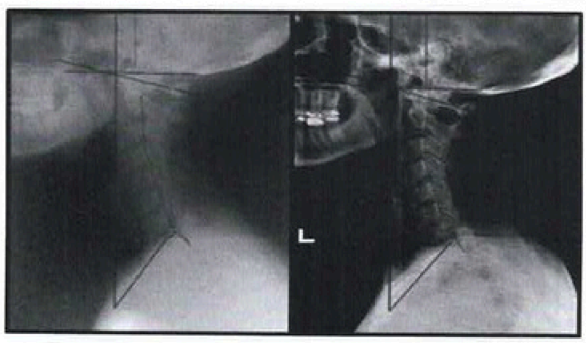


Figure 1: HRV at initial visit and after 36 visits.
Autonomic Activity Index: Percent of Autonomic Activity and measured according to the y-axis; normal is 80-100; Autonomic Balance Index: Percent of Sympathetic or Parasympathetic Activity and measured according to the x-axis; normal is 80(S)-80(P); Patient heart rate variability reading.

#	PF	PRL	ERL	V	EWB	SF	PI	GH	ΔHS
1	50	20	33.33	35	76	62.5	55	45	50
2	95	100	100	75	88	100	90	70	100

PF: Physical Functioning; PRL: Physical Role Limitations; ERL: Emotional Role Limitations; EWB: Emotional Well-Being; V: Vitality; SF: Social Functioning; PI: Pain; GH: General Health; ΔHS: Change in Health Status

Table 1: Health and wellness score initial visit versus after 36 visits sf-36 health survey analysis.



______ The green line represents the normal spinal position and expected path of the posterior longitudinal ligament.
______ The red line represents the patient's position known as George's Line. This is the path of the posterior longitudinal ligament.
______ The blue line represents radiographic lines of mensuration. Atlas Plane Line, Chamberlain's Line, vertical axes, and thoracic morphology.

Figure 2: NLC at initial visit and after 36 visits.

Measurement	Normal values	Xray 1 values	Xray 2 values
C1 to Horizontal	-29.0°	-20.2°	-25.0°
RRA C2-C3	-10.0°	-2.2°	-6.1°
RRA C3-C4	-8.0°	-9.9°	-9.6°
RRA C4-C5	-8.0°	-0.3°	-6.9°
RRA C5-C6	-8.0°	-1.5°	-1.0°
RRA C6-C7	-8.0°	-4.9°	-3.4°
RRA C7-T1	-8.0°	-11.9°	-8.0°
ARA C2-C7	-42.0°	-18.8°	-27.0°
Tz C2-C7	0.0 mm	24.0 mm	17.7 mm

RRA: Relative rotational angle; the angle between the lines tangent to the posterior vertebral body margins of adjacent vertebrae in the sagittal view; ARA: Absolute rotational angle; the angle between the lines tangent to the posterior vertebral body margins of the limits of a spinal region (cervical, thoracic, or lumbar) in the sagittal view; Tz: Translation in the z axis; the distance of translation of one vertebra with respect to another in the sagittal view

Table 2: Posture ray® emr initial visit versus after 36 visits radiographic analysis.