Osteopathic Manipulative Therapy Potentiates Motor Cortical Plasticity

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Context: Osteopathic manipulative therapy (OMTh; manipulative care provided by foreign-trained osteopaths) is effective in managing pain caused by a variety of clinical conditions. Nevertheless, the physiologic mechanisms at the basis of the clinical improvement are poorly understood.

Objective: To investigate the effects of OMTh, muscle stretching, and soft touch interventions on motor cortical excitability through a rapid-rate paired associative stimulation (PAS) protocol.

Methods: In this crossover study, participants underwent OMTh, muscle stretching, and soft touch interventions. A rapid-rate PAS transcranial magnetic stimulation protocol was performed immediately after each intervention session, which consisted of 600 pairs of stimuli continuously delivered to the left primary motor cortex and to the right median nerve at a rate of 5 Hz for 2 minutes. The interstimulus intervals between the peripheral stimulus and the transcranial magnetic stimulation was set at 25 milliseconds. Before and after rapid-rate PAS (immediately after and 15 minutes after), changes in the amplitude of the motor evoked potentials were measured in the right abductor pollicis brevis and the right first dorsal interosseous.

Results: Of the potential 15 participants initially recruited, 12 fit the inclusion criteria. Two of the 12 participants were excluded from the final analysis because of excessive artifact movements. Rapid-rate PAS induced a more pronounced, longer-lasting increase in cortical excitability in the abductor pollicis brevis muscle in patients 15 minutes after the OMTh intervention than after the muscle stretching or sham interventions ($P=.016$).

Conclusion: Results of the current study provide support for the effects of OMTh on cortical plasticity.

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Osteopathic manipulative therapy (OMTh; manipulative care provided by foreign-trained osteopaths) is a patient-focused therapy based on manual contact that uses the relationship between structure and function to optimize the body's self-regulation. The main advantages of OMTh for patients are the effective relief of acute pain and clinical management of chronic pain.¹⁻⁴ Although there is evidence for the effectiveness of OMTh, not much is known about the mechanisms involved.^{1,2,5}

Studies^{6,7} have shown a link between various manual therapy techniques and changes in corticospinal excitability. A 2014 neuroimaging study⁸ showed that manual therapies have an immediate effect on the functional connectivity between brain regions involved in processing and modulating the pain experience. Studies^{9,10} have also shown that cranial osteopathic manipulative medicine could have an effect on the reduction of cerebral blood flow. By assessing electrical activity in the brain cortex through electroencephalography, 2 additional studies^{11,12} showed a decrease in sleep latency and an increase in the absolute power of alpha frequency in patients after undergoing cranial manipulation.

Transcranial magnetic stimulation (TMS) is a safe, noninvasive technique that can be used to investigate various aspects of human neurophysiology.¹³ It can be applied as a single pulse, paired pulses, or a train of repetitive stimuli at various frequencies. Trains of stimuli (repetitive TMS) are able to induce plastic changes of excitability in the human motor cortex and characterize different aspects of motor system excitability. Between repetitive protocols, paired associative stimulation (PAS) has been shown to induce long-term potentiation mechanisms in terms of increased motor evoked potential (MEP) amplitude.¹⁴ In the current study, we used a repetitive PAS protocol to investigate potential modulatory changes in the motor system after manual therapy interventions in a group of asymptomatic participants. We hypothesized that OMTh would cause a longer-lasting increase in excitability in participants than would sham interventions.

Methods

This crossover study was approved by the Fondazione Santa Lucia's local ethic committee and was conducted in accordance with the Declaration of Helsinki. All interventions were performed at outpatient clinics and the Non-Invasive Brain Stimulation Laboratory at the Santa Lucia Foundation in Rome, Italy. Participants were recruited via a single email invitation from a data-

base of students at Tor Vergata University from March 2015 to September 2016. The invitation explained that participation was voluntary and dependent on the inclusion and exclusion criteria. Informed consent was provided before participation.

A clinician with 10 years of clinical experience (G.K.), who was not involved in the intervention sessions, assessed the eligibility of participants according to the inclusion and exclusion criteria. Participants were eligible for inclusion if they were aged between 18 and 30 years and were found to have a somatic dysfunction after completing a TMS screening questionnaire¹⁵ and undergoing a physical examination. Only asymptomatic volunteers with somatic dysfunction were included. For each participant, the authors used the outpatient osteopathic SOAP (subjective, objective, assessment, plan) note form. Exclusion criteria included a history of neurologic disease, orthopedic problems, pacemaker implantation, prior intracranial surgical procedures with metal foreign body placement, and use of medications that affect the central nervous system.

Interventions

Participants underwent a different intervention each week in a random order. The interventions were OMTh, muscle stretching, and soft touch. Each session was about 45 minutes. After each intervention, cortical excitability was recorded for each participant.

The OMTh session was performed by an expert osteopath (M.T.) who is a member of the Italian Register of Osteopaths. The OMTh techniques were focused on correcting the dysfunctions found during the initial physical examination and included myofascial techniques, balanced ligamentous tension, and osteopathy in the cranial field.^{14,16,17} Tissue alteration, asymmetry, range of motion, and tenderness parameters were the criteria considered for osteopathic evaluation and intervention.¹⁸

The muscle stretching sessions were performed by a physical therapist with expertise in global postural rehabilitation (A.M.C.) and consisted of specific

exercises that promote proper alignment by increasing the efficiency of dynamic movement and limiting muscle imbalance and overcompensation. Participants were asked to maintain 2 different postures to stretch the anterior and posterior muscle chains. The first posture was an extension of the legs to release the respiratory diaphragm and stretch the anterior muscle chain (diaphragm, pectoralis minor, scalene, sternocleidomastoid, intercostalis, iliopsoas, muscles of the arm and forearm, and hand flexors).¹⁹ For the second posture, participants were asked to lie on their back with their legs flexed to stretch the posterior chain (upper trapezius, levator scapulae, suboccipital, erector spinae, gluteus maximus, ischiotibial, triceps surae, and foot intrinsic muscles). For each posture, the physical therapist used verbal commands and manual contact to maintain alignment and make the necessary postural corrections to optimize the stretching and discourage compensatory movements.²⁰

The soft touch session was performed by another expert osteopath (F.M.). Without inducing any joint mobilization, this session included a sequence of touches in specific anatomical portions of the body in the following order: right ankle, left knee, right hip, diaphragm, right shoulder, neck, cranium. The osteopath mentally counted down from 120 to 0 for each area.

At the end of each session, immediately after the intervention, participants underwent rapid-rate PAS using TMS. The rapid-rate PAS protocol consisted of 600 pairs of stimuli that were continuously delivered to the left primary motor cortex at a rate of 5 Hz for approximately 2 minutes. An initial electrical conditioning stimulus was applied over the right median nerve, and a secondary biphasic TMS was applied over the left primary motor cortex. The interstimulus intervals were set at 25 milliseconds.^{13,21} On the right median nerve, a square wave pulse was applied through a bipolar electrode (Digitimer D-160 stimulator; Digitimer Ltd). The pulse width was 500 microseconds. The cathode was located proximally. The TMS pulse was delivered through a standard figure 8-shaped

coil (70-mm diameter) connected to a Magstim Rapid Stimulator (Magstim Company). The coil was positioned tangentially on the scalp and over the relaxed right abductor pollicis brevis (APB) and first dorsal interosseous muscles, the points in which the largest MEP can be elicited. The intensity of the electrical stimulus was set at 2 times the sensory threshold, and the intensity of TMS was individually adjusted to 90% of the active motor threshold.²²

To investigate the mechanisms of long-lasting facilitation of motor cortical excitability, we recorded MEP amplitude immediately before, immediately after, and 15 minutes after the intervention. The intensity of the motor thresholds was calculated to obtain a motor response of about 1 mV evoked in correspondence with the hotspot over each muscle. Resting motor threshold was defined as the minimum intensity that evoked peak-to-peak MEP of 50 μ V during at least 5 of 10 consecutive trials in the relaxed APB muscle. All MEP measurements were taken by a blinded neurophysiologist (V.P.). Electromyography was recorded with Ag-AgCl surface electrodes positioned over the right APB muscle in a belly-tendon montage. The signal was amplified and band pass filtered (32 Hz to 1 KHz) by a Digitimer D-150 amplifier and stored at sampling rate of 10 kHz on a personal computer for offline analysis (Signal Software; Cambridge Electronic Design). During the interventions, electromyography was continuously monitored with visual feedback to verify that the participant was completely relaxed.

Statistical Analysis

Data were analyzed using Statistica version 8.0 (StatSoft Inc). For each intervention, the mean MEP peak-to-peak amplitudes were calculated. A 1-way analysis of variance was performed to compare the differences between participants' motor threshold values after each intervention (OMTh, muscle stretching, and soft touch). An additional analysis of variance was performed to analyze the relationship between intervention type, motor thresholds of each muscle, and MEP

measurements taken immediately before, immediately after, and 15 minutes after the intervention. When a significant effect was reached, Duncan post-hoc analysis was used to characterize the specific intersymbol interference effect. Statistical significance was defined as $P < .05$.

Results

Of the potential 15 participants initially recruited, 12 fit the inclusion criteria. Of the 12 participants, 6 were men (50%) and 6 were women (50%). The mean (SD) age of the participants was 26.4 (2.3) years. Two of the 12 participants were excluded from the final analysis because of excessive artifact movements. No significant differences were found between the mean resting and 1-mV motor thresholds of the 2 muscles (APB and first dorsal interosseous) after OMTh, muscle stretching, and soft touch interventions ($F_{2,18}=0.03$; $P=.96$) (Table). Participants showed a more pronounced, longer-lasting increase in motor cortex excitability after OMTh than muscle stretching and soft touch interventions. Analysis of variance showed an interaction between intervention type, motor thresholds of each muscle, and MEP amplitude taken immediately after and 15 minutes after intervention ($F_{2,16}=3.43$; $P=.05$). Duncan post-hoc analyses, corrected for multiple comparisons, showed that there was a longer-lasting increase in cortical excitability in the APB muscle 15 minutes after the OMTh interven-

tion than after the muscle stretching and soft touch interventions ($P=.016$) (Figure).

Discussion

Results of the current study show that OMTh can modulate motor cortical excitability in a more profound way than other manual interventions. Studies²³⁻²⁵ have suggested that joint and spinal dysfunction may lead to altered afferent input to the central nervous system, which can cause plastic neural changes. We hypothesized that, in the current study, the OMTh intervention targeting somatic dysfunction could have enhanced the corticospinal excitability produced by the PAS protocol in participants and that this increased excitability of the central motor system may result from a summation of sensory afferent inputs evoked from various tissues as a consequence of OMTh. These results affirm the results of previous studies,^{26,27} in which modification of the MEP amplitude clearly indicated a central motor facilitation after manual therapy. These mechanisms are thought to modulate the gain of the motoneuron pool of inhibitory and excitatory postsynaptic potentials from corticospinal pathways.²⁸

Results of the current study could support a theoretical basis for the use of OMTh with regard to the neurologic model of structure-function relationships.¹⁶ This model recognizes the dynamic balance between the parasympathetic and sympathetic nervous system and the potentially disruptive influences of biomechanical

Table.
Motor Threshold of Muscles After Osteopathic Manipulative Therapy,^a Muscle Stretching, and Soft Touch Interventions in Asymptomatic Participants With Somatic Dysfunctions (N=10)

Muscle	Mean (SD) Motor Threshold, 1-mV			P Value
	Osteopathic Manipulative Therapy	Muscle Stretching	Soft Touch	
Abductor pollicis brevis	46.2 (14.9)	43.7 (12.2)	44.9 (11.9)	.89
First dorsal interosseous	45.5 (13.2)	43.6 (11.9)	44.9 (12.5)	.69

^a Manipulative care provided by foreign-trained osteopaths.

Figure.

The mean motor evoked potential amplitude measurement in participants' abductor pollicis brevis (A) and first dorsal interosseus (B) immediately before, immediately after, and 15 minutes after osteopathic manipulative therapy (OMTh; manipulative care provided by foreign-trained osteopaths), muscle stretching, and soft touch intervention in asymptomatic participants with an identified somatic dysfunction.

strain on those systems.²⁹ It is possible that the long-lasting changes in cortical excitability induced by OMTh may have been mediated by the activity of the endocannabinoid system. This finding is consistent with previous research. A 2005 study³⁰ showed that

OMTh was associated with changes in serum levels of anandamide, 2-arachidonoylglycerol, and oleylethanolamide. Another study³¹ showed that cannabinoids have metaplastic effects on the motor cortex, as revealed by repetitive TMS protocols, and

strongly suggested that the endocannabinoid system is involved in the modulation of synaptic plasticity in humans.

The current preliminary study has several limitations. Although participants underwent each intervention in a randomized order in 3 different sessions of the same duration, we could not control for the overall amount of muscular activation induced by each intervention. Moreover, we were not able to report significant clinical improvement because recruited participants were generally healthy and did not have a history of chronic pain. Also, OMTh sessions were not protocol based; rather, they were individually tailored to each participant according to the physical examination findings.

Further studies performed in a symptomatic population on a larger sample are necessary to better understand the clinical importance of these findings in both normal physiologic and pathophysiologic states. For example, it is known that some neurophysiologic mechanisms can be impaired in specific neurologic disorders. It could be interesting to investigate whether the clinical enhancement after OMTh is parallel to an improvement in functioning of the network involved in that disease.

Conclusion

In a group of asymptomatic volunteers who had somatic dysfunction, differences in the increase of motor cortex excitability after OMTh, muscle stretching, and soft touch interventions were observed. Osteopathic manipulative therapy was able to induce relevant neurophysiologic effects in terms of cortical plasticity more effectively than sham interventions. The clinical importance of this finding is still unclear. Therefore, further study of different disease states with larger populations is needed.

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