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Immediate Changes After Manual Therapy in Resting-State Functional Connectivity as Measured by Functional Magnetic Resonance Imaging in Participants With Induced Low Back Pain

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Abstract

Objective: The purposes of this study were to use functional magnetic resonance imaging to investigate the immediate changes in functional connectivity (FC) between brain regions that process and modulate the pain experience after 3 different types of manual therapies (MT) and to identify reductions in experimentally induced myalgia and changes in local and remote pressure pain sensitivity.

Methods: Twenty-four participants (17 men; mean age ± SD, 21.6 ± 4.2 years) who completed an exercise-injury protocol to induce low back pain were randomized into 3 groups: chiropractic spinal manipulation (n = 6), spinal mobilization (n = 8), or therapeutic touch (n = 10). The primary outcome was the immediate change in FC as measured on functional magnetic resonance imaging between the following brain regions: somatosensory cortex, secondary somatosensory cortex, thalamus, anterior and posterior cingulate cortices, anterior and poster insula, and periaqueductal gray. Secondary outcomes were immediate changes in pain intensity, measured with a 101-point numeric rating scale, and pain sensitivity, measured with a handheld dynamometer. Repeated-measures analysis of variance models and correlation analyses were conducted to examine treatment effects and the relationship between within-person changes across outcome measures.

Results: Changes in FC were found between several brain regions that were common to all 3 MT interventions. Treatment-dependent changes in FC were also observed between several brain regions. Improvement was seen in pain intensity after all interventions ($P < .05$) with no difference between groups ($P > .05$). There were no observed changes in pain sensitivity, or an association between primary and secondary outcome measures.

Conclusion: These results suggest that MTs (chiropractic spinal manipulation, spinal mobilization, and therapeutic touch) have an immediate effect on the FC between brain regions involved in processing and modulating the pain experience. This suggests that neurophysiologic changes after MT may be an underlying mechanism of pain relief. (J Manipulative Physiol Ther 2014;37:614-627)

Key Indexing Terms: *Magnetic Resonance Imaging; Musculoskeletal Manipulations; Neurophysiology Brain; Chiropractic*

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Improvements in pain intensity and pain sensitivity are often reported after manual therapy (MT).[1–4] Research has demonstrated the following: (1) neurophysiologic changes are observed after MT, and (2) reductions in pain intensity and pain sensitivity are associated with functional changes in central nervous system.[5–8] A current assumption is that neurophysiologic changes after MT may underlie clinical improvement.

Functional magnetic resonance imaging (fMRI) research includes several different approaches to estimate cortical function. Several of these approaches have demonstrated functional changes associated with pain relief. One such measure is functional connectivity (FC). Functional connectivity has been defined as "the temporal correlation of a neurophysiologic index measured in different brain areas" (see Fig 1).[9] Recently, Letzen et al[6] used FC between the default mode network and brain regions associated with pain processing to investigate lidocaine-induced analgesia, whereas Zyloney et al[10] used FC between the Periaqueductal Gray (PAG) and cortical regions to investigate differential effects underlying analgesia from of genuine and sham electro-acupuncture. With the evidence supporting efficacy of MT to reduce pain intensity and pain sensitivity, it is reasonable to assume that the underlying therapeutic effect of MT is likely to include a higher cortical component.[1,4,11,12]

Although models explaining the therapeutic effects of MT on pain and pain sensitivity include the potential for a higher cortical mechanism, the extent that MT exert effects on higher brain centers is not fully understood.[13–16] Thus far, only one study has used fMRI to assess changes in cortical function after MT.[17] Unlike the studies by Letzen et al and Zyloney et al, the study by Sparks et al[17] used a different approach. They used peak blood-oxygen-level–dependent (BOLD) contrast imaging to estimate of cortical function associated with a task. In their study, pain-free volunteers processed thermal stimuli applied to the hand before and after thoracic spinal manipulation (a form of MT). What they found was that after thoracic manipulation, several brain regions demonstrated a reduction in peak BOLD activity. Those regions included the cingulate, insular, motor, amygdala and somatosensory cortices, and the PAG.

The purpose of this study was to investigate the changes in FC between brain regions that process and modulate the pain experience after MT. The primary outcome was to measure the immediate change in FC across brain regions involved in processing and modulating the pain experience and identify if there were reductions in experimentally induced myalgia and changes in local and remote pressure pain sensitivity.

Methods

Study Design

This study is made up of a subset of participants who have completed a larger, ongoing, preclinical trial (NCT01406847). A randomized study design with blinded assessment was implemented with 3 groups, measured at 2 time points. Pain-free volunteers completed an exercise protocol to induce myalgia in the low back. Forty-eight hours after completion of the exercise protocol, participants returned and underwent preintervention assessment. Preintervention assessment included collection of pain intensity, local and remote pressure pain measures, and fMRI data by a blinded assessor. Participants were then randomized to receive 1 of 3 MT interventions. Sealed opaque envelopes were used to inform the treatment provider of assignment. Interventions were performed by either a licensed physical therapist or chiropractor. The randomization sequence was generated by an individual no responsible for determining study eligibility, outcome assessment, or intervention. After the intervention, participants underwent the same assessment (postintervention) performed by the same blinded assessor.

Participants

Seventy-five volunteers read and signed the informed consent form approved by the University of Florida Institutional Review Board. Enrolled participants were recruited from the campuses of the University of Florida and UF Health Hospital and the local surrounding community. Participants were eligible to participate in the study if they were between the ages of 18 and 44 years and currently not experiencing back pain. Participants were excluded from participating in the study if they met any of the following criteria: previous participation in a conditioning program specific to trunk extensors, any current back pain, any chronic medical conditions that may affect pain perception (eg, diabetes, high blood pressure, fibromyalgia, and headaches), kidney dysfunction, muscle damage, or major psychiatric disorder; history of previous injury including surgery to the lumbar spine, renal malfunction, cardiac condition, high blood pressure, osteoporosis, or liver dysfunction; and performance of any intervention for symptoms induced by exercise and before the termination of their participation of the protocol. To be included in these analyses, participants needed to undergone the exercise-injury protocol and have completed resting-state fMRI scans at both time points.

Exercise Injury Model to Induce Low Back Pain

Prior to exercise, all participants completed a 5-minute warm-up consisting of riding a stationary bicycle. After the 5-minute warm-up, participants then performed an isometric test to establish a baseline measure of torque.[18] Participants then performed repetitions of dynamic resisted exercise. Resistance was individualized to each participant using a weight load. Weight loads were equal to 90% of the peak torque measured during the baseline isometric test. Each repetition was performed through the full available range of motion. Participants performed sets of 15 repetitions or until