ORIGINAL RESEARCH

Functional Magnetic Resonance Imaging of Cerebral Hemodynamic Responses to Pain Following Thoracic Thrust Manipulation in Individuals With Neck Pain: A Randomized Trial

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ABSTRACT

Objective: The purpose of this study was to examine whether cerebral activation in response to noxious mechanical stimuli varies with thrust manipulation (TM) when compared with sham manipulation (SM) as measured by blood oxygenation level–dependent functional magnetic resonance imaging.

Methods: Twenty-four volunteers (67% female) with complaints of acute or subacute mechanical (nontraumatic) neck pain satisfied eligibility requirements and agreed to participate. Participants were randomized to receive TM to the thoracic spine or SM, and then underwent functional magnetic resonance scanning while receiving noxious stimuli before and after TM or SM. An 11-point numeric pain rating scale was administered pre- and postmanipulation for neck pain and to determine perceptions of pain intensity with respect to neck pain and mechanical stimuli. Blood oxygenation level–dependent functional magnetic resonance imaging recorded the cerebral hemodynamic response to the mechanical stimuli.

Results: Imaging revealed significant group differences, with those individuals in the manipulation group exhibiting increased areas of activation (postmanipulation) in the insular and somatosensory cortices and individuals in the sham group exhibiting greater areas of activation in the precentral gyrus, supplementary motor area, and cingulate cortices ($P < .05$). However, between-group differences on the numeric pain rating scale for mechanical stimuli and for self-reported neck pain were not statistically significant.

Conclusions: This study provides preliminary level 2b evidence suggesting cortical responses in patients with nontraumatic neck pain may vary between thoracic TM and a sham comparator. (J Manipulative Physiol Ther 2017;40:625-634)

Key Indexing Terms: *Magnetic Resonance Imaging; Manipulation; Neuroscience; Pain*

INTRODUCTION

A considerable body of evidence has demonstrated that in individuals with mechanical neck pain, a thrust manipulation (TM) to the thoracic spine yields improvements in physiologic range of motion, function, and subjective reports of pain.[1-5] The effects of thoracic manipulation have been associated with both peripheral and spinal neurophysiologic responses.[6-10] Biomechanical theories fall short of explaining how manipulation results in long-term clinical improvements.[11-17] Evidence suggests manual therapies are not segmentally specific, nor is specificity necessary to achieve reductions in pain or improvements in function.[8,17-19] In a sample of patients with nonspecific neck pain, no significant differences in subjective ratings were identified following manual interventions to symptomatic or randomly chosen cervical segments.[20] The biomechanical impulse from a high-velocity, low-amplitude

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thrust likely initiates rapid and sequential involvement of peripheral, spinal, and supraspinal neurophysiologic responses that collectively may better explain the mechanisms accompanying manipulation and hypoalgesia and account for widespread effects that may or may not be segmentally distributed. Alterations have been identified in serum endocannabinoids, beta-endorphins, and monoamines (eg, serotonin, norepinephrine, and dopamine) following manual interventions,[21-23] and recently, investigators have implicated sympathoexcitatory effects including changes in skin conductance[24] and measures of pupil diameter.[9] Furthermore, manipulation may evoke descending inhibition through the interaction of neurotransmitters on subcortical and spinal cord structures.[25] Current research supports both the inhibition of sensory information[26] and the potential for cortical activity governing patient expectation for pain relief.[27-29] These are important considerations, as neuroimaging applications have mapped projections from areas within the cortex to the amygdala, thalamus, periaqueductal gray, and brainstem rostral ventral medulla, indicating an individual's pain experience and response to manual interventions may be modified by a cortical influence on these and other structures.[30-32]

Preliminary functional magnetic resonance imaging (fMRI) evidence has revealed shifts in activation of cerebral areas believed to be involved with the pain experience (premotor and supplementary motor areas; somatosensory areas; insular and anterior cingulate cortices; and subcortical amygdala and thalamus) following TM in healthy individuals.[33] Sparks et al[33] identified a linear relationship between a reduction in the blood oxygenation level–dependent (BOLD) signal in the insular cortex and subjective ratings of stimulus intensity. It is unknown how this response to manipulation in individuals with neck pain differs from that of a sham comparator. We hypothesized that BOLD fMRI would reveal differences in activation in cortical areas associated with the pain experience, specifically within the insular cortex, in response to noxious stimuli in a group of individuals with nontraumatic neck pain receiving TM compared with those receiving a sham manipulation (SM). A linear relationship between a reduction in perceived pain and a reduction in cortical activity in the manipulation group was also expected. Therefore, the purpose of this study was to examine whether cerebral activation in response to noxious mechanical stimuli varies with TM compared with SM as measured by BOLD fMRI.

Methods

A randomized, controlled, parallel-group study with a 1:1 allocation ratio was conducted at the Saint Francis Medical Center medical and research facility. The MRI unit was a Signa HDx 3T GE scanner (GE Healthcare, Waukesha, Wisconsin), which offers ultrafast imaging capability, such as echo planar imaging.

Participants

Right-handed individuals with complaints of mechanical neck pain less than 6 weeks in duration were recruited to participate. Neck pain was defined as generalized idiopathic neck pain, with or without shoulder or periscapular pain, with symptoms provoked by neck postures, neck movements, or palpation of the cervical musculature. Individuals were excluded if they lacked requisite skills in the English language to adhere to the treatment protocol, or if they had any contraindications to MRI including cardiac pacemakers, cochlear implants, metal implants, implanted hearing aids, claustrophobia, and previous injuries involving metal fragments. Furthermore, individuals were not considered if they were pregnant or if, in the absence of an effective form of contraception, they could have conceived since the first day of their last normal menstrual period. Individuals were also excluded if they possessed any of the following: medical red flags suggestive of nonmusculoskeletal origin of pain, such as metabolic disorders, osteoporosis, tumor, and/or rheumatoid arthritis; a history of traumatic neck pain or cervical surgery; a diagnosis of cervical radiculopathy or myelopathy, fibromyalgia syndrome, vascular disease, or Raynaud's phenomenon; or any contraindications to TM of the thoracic spine. Individuals provided written informed consent to participate. The study protocol was funded by the Orthopaedic Section of the American Physical Therapy Association, and approved by the Institutional Review Board at the University Of Illinois College Of Medicine at Peoria, Illinois. The trial was registered with ClinicalTrials.gov (NCT01862705).

Procedures

Randomization. Following recruitment, participants were randomly assigned via computer-generated sequence and concealed allocation with a transilluminate envelope to receive a single session of thoracic TM or SM by the principal investigator. Because of the nature of the study, it was not possible to blind the treating therapist to the intervention group once allocated. However, the assessor and the participants were blinded as to which group they had been assigned.

Between February and October 2014, fMRI studies were performed on 24 individuals with neck pain (67% female) who satisfied eligibility requirements and agreed to participate. Following a baseline assessment of neck pain with an 11-point numerical pain rating scale, (NPRS), participants' heads were positioned inside the high-resolution 8-channel head coil of a 3-T (General Electric, Milwaukee, Wisconsin) magnetic resonance scanner equipped with EPI (echo planar imaging) capabilities. Participants were asked to rate their

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