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Research Paper Review

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Cerebral Hemodynamic Responses to Pain Following Thoracic Manipulation in Subjects with Neck Pain

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ABSTRACT

INTRODUCTION: *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: *Significant group differences with those individuals in the manipulation group and individuals in the sham group.*

DISCUSSION: *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.*

***CONCLUSION**: 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.*

ANALYSIS

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Background Information

Thrust manipulation (TM) to the thoracic spine has shown improvements in physiologic range of motion, function, and subjective pain (1) in individuals with mechanical neck pain. These effects have been associated with both peripheral and spinal neurophysiological responses, with evidence suggesting that manual therapies are not segmentally specific, nor do they require specificity to achieve reductions in pain or improvements in function (2).

It is likely that thrust manipulation initiates rapid, sequential involvement of peripheral, spinal, and supraspinal neurophysiological responses which may account for the widespread effects that may or may not be distributed segmentally. As well, manual interventions have been shown to be followed by changes in serum endocannabinoids, beta-endorphins, and monoamines (3) and may evoke descending inhibition through the interaction of neurotransmitters on subcortical and spinal cord structures (4). Both the inhibition of sensory information (5) and potential for cortical activity governing patient expectation for pain relief (6) are supported in the current literature. These are all important, as neuroimaging applications have mapped projections from areas within the cortex to the amygdala, thalamus, periaqueductal gray, and rostral ventral medulla of the brainstem. This indicates that the individual's pain experience and response to manual therapy may be modified by the influence of the cortex on these structures (7). Preliminary functional magnetic resonance imaging (fMRI) studies have shown changes in activation of cerebral areas believed to be involved in the pain experience following TM in healthy subjects (8).

This study looked at differences in activation in cortical areas associated with the pain experience (specifically the insular cortex) in response to noxious stimuli in individuals with non-traumatic neck pain receiving thoracic thrust manipulation (TM) compared to those receiving sham manipulation (SM).

Pertinent Results:

All participants completed the study protocol with no adverse effects. Mechanical noxious stimuli at the hand and foot showed significant areas of activation in the cerebellum, amygdala, thalami, insula, putamen, central operculum, parietal operculum, precentral gyrus, and postcentral gyrus.

Following thoracic thrust manipulation (TM), a 35% decrease in activation was seen. After the sham manipulation (SM), an 11% increase in activation was observed. Between-group comparisons showed increased areas of activation in the insular and sensorimotor cortices in the TM group, while increased activation was seen in the anterior and posterior cingulate, supplementary motor area, and precentral gyrus in the SM group. There were no significant between-group differences in rating of stimulus intensity on the NPRS for hand or foot pain, however, individuals in the TM group showed a reduction in neck pain following the intervention, while individuals in the SM group reported a non-statistically significant increase in symptoms following the intervention.

CLINICAL APPLICATION & CONCLUSIONS

The experience of pain is highly variable and depends on a number of factors that likely includes interplay among a network of areas within the brain dependent on attention, type of pain, and fears and emotions that may be tied to the stimulus (10). This study showed decreased areas of activation in response to noxious mechanical stimulation in the insular cortex following manipulation to the thoracic spine. The insular cortex is believed to have a role in cognitive-emotional processing, detection and evaluation of stimulus quality and intensity, and discriminate transmission of this information to other cortical and subcortical areas (11). Levels of activation in the insular cortex and the dissemination of signal from the insular cortex to the cingulate, somatosensory, and prefrontal cortices and the subcortical amygdala and parahippocampal gyrus (12) may be the stimulus for inhibition or facilitation of a painful output or response.

This study showed quantifiable changes in the brain's response to nociceptive information following spinal manipulation, when compared to sham. These reductions in cortical activity do not always correlate to a reduced perception of pain. Being aware of this reduced activity, but also considering that the perception of pain is generally tied to a unique and emotional response, can be useful when considering when to use manipulation in clinical practice. This study adds to our body of knowledge on this topic, while at the same time reminding us that we have much work left to do in our quest to fully understand the neurophysiological effects of thrust manipulation.

STUDY METHODS

A randomized, controlled, parallel-group study with a 1:1 allocation ratio was conducted. Right-handed participants with mechanical neck pain (generalized idiopathic neck pain, with or without shoulder or periscapular pain, with symptoms provoked by neck postures, neck movements, or cervical muscle palpation) of less than 6 weeks duration were recruited. Individuals were excluded if they:

- lacked the necessary skills in the English language to adhere to the treatment protocol,
- had contraindications to MRI,
- were pregnant or could be pregnant,
- had medical red flags suggestive of non-musculoskeletal origin of pain,
- had a diagnosis of cervical radiculopathy or myelopathy, fibromyalgia, vascular disease, or Raynaud's phenomenon, or
- had contraindications to TM of the thoracic spine

Participants were randomly assigned to receive a single session of thoracic thrust (TM) or sham (SM) manipulation from the principle investigator via computer-generated sequence and concealed allocation. It was not possible to blind the treating therapist, but the assessor and the participants were blinded. The 24 eligible participants all received a baseline assessment for neck pain using an 11-point numerical pain rating scale (NPRS) applied after the patient was positioned in the MRI machine. Patients were provided with ear plugs and their heads were padded with foam and secured to minimize head and neck motion.

Functional imaging was used to record cerebral hemodynamic response (HDR) while von Frey filaments were used to produce noxious stimuli. Noxious stimuli were applied to the cuticle of the right index finger at a rate of 1 Hz for 15 seconds, followed by 15 seconds of rest, for a period of 5 minutes. This process was then repeated at the great toe. Patients then received either a TM consisting of a high-velocity, end-range, anterior-to-posterior force (patient supine) directed at the mid-thoracic spine in cervicothoracic flexion, or a SM where the practitioner's hands were placed in the same positions but then slid across the skin with minimal pressure, providing no counterforce or thrust directed toward a motion segment. This method has been identified as an adequate sham comparator to TM in the thoracic region (9). Following the intervention (within 5 minutes), participants immediately underwent reimaging with a second delivery of noxious stimuli to the same index finger and great toe. Patients were then asked to rate the stimulus intensity of the noxious stimuli using the same 11-point NPRS, and finally given the 11-point NPRS for neck pain at the completion of their scans.

STUDY STRENGTHS/WEAKNESSES

Strengths:

- This study revealed quantifiable changes in the brain's response to nociceptive stimuli after thoracic spinal manipulation, thus adding to this body of literature.

Weaknesses:

- The No attempt was made to investigate long-term clinical responses associated with a single session of TM in individuals with neck pain – having only one treatment session was necessitated by the use of fMRI, but additional treatments may have a different effect compared to one.

- Participants were only given the NPRS during the delivery of the stimulation, not during the off intervals. As a result, it is unknown if individuals felt an increase in stimulus intensity as the intervals progressed.

- No specific pain center in the brain has been identified in the literature, so we have no standard area to evaluate for activity due to pain. Thus, physiological imaging data cannot be directly interpreted as a proxy for a given patient's pain experience. This alone may influence reproducibility and reliability during fMRI studies like this one.

Additional References:

1. Boyles RE, Ritland BM, Miracle BM, et al. The short-term effects of thoracic spine thrust manipulation on patients with shoulder impingement syndrome. Man Ther 2009; 14(4): 375-380.
2. Cleland JA, Fritz JM, Kulig K, et al. Comparison of the effectiveness of three manual physical therapy techniques in a subgroup of patients with low back pain who satisfy a clinical prediction rule: A randomized clinical trial. Spine (Phila Pa 1976) 2009; 34(25): 2720-2729.
3. Degenhardt BF, Darmani NA, Johnson JC, et al. Role of osteopathic manipulative treatment in altering pain biomarkers: A pilot study. J Am Osteopath Assoc 2007; 107(9): 387-400.
4. Wright A. Hypoalgesia post-manipulative therapy: A review of a potential neurophysiological mechanism. Man Ther 1995; 1(1): 11-16.
5. Bialosky JE, Bishop MD, Robinson ME, et al. Spinal manipulative therapy has an immediate effect on thermal pain sensitivity in people with low back pain: A randomized controlled trial. Phys Ther 2009; 89(12): 1292-1303.
6. Bialosky JE, Bishop MD, Robinson ME, et al. The influence of expectation on spinal manipulation induced hypoalgesia: An experimental study in normal subjects. BMC Musculoskelet Disord 2008; 9: 19.

7. Hadjipavlou G, Dunckley P, Behrens TE, et al. Determining anatomical connectivities between cortical and brainstem pain processing regions in humans: A diffusion tensor imaging study in health controls. Pain 2006; 123(1-2): 169-178.
8. Sparks C, Cleland JA, Elliott JM, et al. Using functional magnetic resonance imaging to determine if cerebral hemodynamic responses to pain change following thoracic spine thrust manipulation in healthy individuals. J Orthop Sport Phys 2013; 43(5): 340-348.
9. Michener LA, Kardouni JR, Sousa CO, et al. Validation of a sham comparator for thoracic spinal manipulation in patients with shoulder pain. Man Ther 2015; 20(1): 171-175.
10. Apkarian AV, Bushnell MC, Treede RD, et al. Human brain mechanisms of pain perception and regulation in health and disease. Eur J Pain 2005; 9(4): 463-484.
11. Sparks C, Cleland J, Elliott J, et al. Supraspinal structures may be associated with hypoalgesia following thrust manipulation to the spine: a review of the literature. Phys Ther Rev 2013; 18(2): 112-116.
12. Menon V, Uddin LQ. Saliency, switching, attention and control: A network model of insula function. Brain Struct Funct 2010; 214(5-6): 655-667.