Central Effects of Menthol-Based Topical Analgesics on Neuropathic Pain

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BACKGROUND: Following nerve injury, neuropathic pain is attributed to peripheral and central pathophysiological mechanisms. Analgesics are often used to manage neuropathic pain, but thorough understandings of the biological mechanisms responsible for pain mediation are necessary to maximize clinical outcomes. Clinicians often use topical analgesics to manage the neuropathic pain associated with carpal tunnel syndrome (CTS). The question of whether a menthol-based topical analgesic mediates neuropathic pain through the central nervous system remains unanswered. Thus, the overall purpose is to establish how menthol-based topical analgesics mediate neuropathic pain through the central nervous system in persons who have CTS.

METHODS/DESIGN: Ten subjects between the ages of 18 and 60 with confirmed mild to moderate CTS will be recruited to participate in this study approved by the human subjects committee. Subjects will be required to consent prior to participation. Subjects will be blinded to treatment and randomly assigned to one of two groups: 1) application of 4% menthol-based topical analgesic, or 2) application of ultrasound gel. Based on the measured surface area, a standardized amount (1 mL per 200 cm2) of menthol or ultrasound gel will be applied over the affected region. The outcome examiners (evaluators), as well as the data managers, will be blinded to group allocation.
Functional magnetic resonance imaging (fMRI) will be used to assess supraspinal hemodynamic changes during sensory stimulation. Median nerve compression test will be used during the fMRI scan to produce a painful stimulus. The sensory-task will involve seven cycles of 20-second periods of painful stimulus alternated with 40-second periods of rest. Pre-determined regions of interest (ROIs) for the fMRI data analysis include the hypothalamus, amygdala, rostral anterior cingulate cortex (rACC), periaqueductal gray region (PAG), and rostral ventromedial medulla (RVM).
Outcome measures include the blood-oxygen-level-dependent (BOLD) fMRI signal used to determine relative changes in deoxyhemoglobin concentration [HHb] and the Numerical Pain Rating Scale (NPRS). The BOLD-fMRI signal represents the primary outcome measure, while the NPRS denotes the secondary outcome measure.
Data analysis will consist of a paired t-test for the BOLD-fMRI and NPRS outcomes. Also, Pearson's correlation test will determine the correlation between the BOLD-fMRI signal and NPRS. A P-value <0.05 will be considered statistically significant.

DISCUSSION: We have presented the rationale and design for a randomized controlled trial to explore the central effects of menthol-based topical analgesics on neuropathic pain.