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Correlations between brain changes and pain management after cognitive and meditative therapies: A systematic review of neuroimaging studies

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ABSTRACT

Background: There are different ways of dealing with pain and cognitive and meditative therapies (CMT) are alternative ways to regulate the emotions associated with pain. Current studies apply neuroimaging techniques trying to elucidate the neural mechanisms of cognitive strategies for pain. This systematic review aimed to summarize the evidence on brain activity changes after CMT, which include cognitive behavioral therapy, mindfulness and/or meditation, for pain management as well as to evaluate clinical pain outcomes.

Methods: Electronic databases – Pubmed, EMBASE, PsycINFO, Science Direct, Scopus – were searched to find randomized controlled trials (RCTs) examining neuroimaging data of CMT for chronic pain patients or healthy individuals with experimental pain. Two reviewers independently selected the relevant trials, rated for quality assessment and extracted all data using a standardized form. Primary outcome was brain activity changes (activation, deactivation or functional connectivity). Secondary outcomes were pain intensity, self-management, pain coping, quality of life, anxiety and depression.

Results: Nine RCTs were included involving 280 adults (18–59 years), 139 chronic pain patients vs. 148 healthy subjects. Three main kinds of intervention were identified: cognitive-behavioral therapy (n = 4), mindfulness meditation (n = 4) and transcendental meditation technique (n = 1). Neuroimaging results revealed distinct patterns of activity, but the main findings were related to increased activation of prefrontal cortex (PFC), specially dorsolateral prefrontal cortex (dlPFC) and ventrolateral prefrontal cortex (vlPFC), orbitofrontal cortex (OBF), somatosensory cortices (SSC) and limbic system in chronic pain population; and increased activation of anterior cingulate cortex (ACC), anterior insular cortex (AI) and decreased activation of thalamus in healthy individuals following CMT.

Conclusion: This result means that regulation of pain by CMT can alter functioning of brain regions in an extensive network including non-nociceptive regions. CMT reduced the affective experience of pain, while reductions of pain intensity ratings were less consistent. Brain changes have been demonstrated as a result of the application of psychological measures and may represent the clinical implications of changes in brain activity or morphology.

1. Introduction

Pain was defined by the International Association for the Study of Pain (IASP) as an unpleasant sensory and emotional experience, associated with actual or potential tissue damage, or described in terms of such injuries.[1] The World Health Organization (WHO) recognizes pain as an important global, public health concern. However, when pain becomes chronic, it has a strong impact on the patient's life and a high cost for the health system. In 2007, WHO identified a need for improved and standardized management of chronic pain (both malignant and non-malignant) and acute pain.[2] Pain affects function, relationships, and behaviour and it is more than a sensory experience; it involves

Abbreviations: ACC, anterior cingulate cortex; AI, anterior insula; CFC, intrinsic functional conectivity; CMT, cognitive and meditative therapies; dlPFC, dorsolateral prefrontal cortex; DMN, default mode network; EEG, electroencephalography; FM, fibromyalgia; fMRI, functional magnetic resonance imaging; lOFC, lateral orbitofrontal cortex; lPFC, lateral prefrontal cortex; PI, posterior insula; RCT's, randomized controlled trials; SI, primary somatosensory cortex; SII, secondary somatosensory cortex; SSC, somatossensory córtices; v1PFC, ventrolateral prefrontal cortex

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immune, endocrine, meaning making, emotional, and behavioral responses.[3]

Since psychosocial factors play important roles in pain and associated physical and psychosocial disability,[4] patients and researchers on the pain field seek therapeutic approaches on pain management involving psychological strategies as such as cognitive and meditative therapies (CMT). CMT is an evidence-based psychotherapeutic method, rooted in behaviorism and cognitive psychological theory,[5] Since the introduction of CMT for chronic pain more than 35 years ago,[6,7] there have been many published reports of symptom improvements in patients with various forms of chronic pain.[8,9,10] A systematic review and meta-analysis of randomised controlled trials (RCT's) of CMT for fibromyalgia patients concluded that CMT improves coping with pain, reduces depressed mood and healthcare-seeking behaviour in such patients.[11]

Brain is a proven source of endogenous modulation of pain and brain imaging studies have contributed to the understanding of cerebral changes associated with chronic pain.[12,13] Recent evidence of neuroimaging studies has established a connection between cognitive dysfunction and specific changes in brain structure[14] and function.[15] Evidence of neural networks that support such modulation has probably opened alternative pathways of treatment and CMT have demonstrated promising options for the multidisciplinar pain management. A better understanding of brain mechanisms underlying therapy can promote improvements in the therapeutic interventions as well as increase our knowledge on the formation and maintenance of symptoms.[16]

Treatments involving CMT have been well investigated by behavioral studies, but few randomized studies bring up the neurological mechanisms involved. This systematic review aimed to analyze the existing data on brain changes recruited throught CMT, including cognitive behavioral therapy, mindfulness and/or meditation, for clinical and/or experimental pain management detected through neuroimaging techniques and to identify the effects of CMT over clinical pain outcomes.

2. Methods

The protocol defined to this systematic review adhered to the recommendations proposed by the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) and the Cochrane Handbook for Systematic Reviews of Interventions.[17,18] The review question was: "What is the neuroimaging evidence and neuromodulatory effects of CMT on pain management?" This current study has been registered at PROSPERO CRD42016046312.

http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016046312).

2.1. Inclusion and exclusion criteria

Study type: only randomised controlled trials (RCTs) that outlined studies on pain management through CMT evidenced by neuroimaging.

Type of participants: individuals of any age, with or without a clinical condition of pain were included in this review.

Type of intervention: Type of intervention.[19] We excluded researches on meditative movement therapies (Qigong, Tai chi, Yoga) or hypnosis.

Type of comparison group: active educacional program, non-practitioners that learned and practiced the technique of meditation, usual treatment, waiting list, other strategies of CMT.

Type of outcome measures: our primary outcome was brain activity changes (activation, deactivation or functional connectivity) proven by fMRI or EEG. Secondary outcomes were pain intensity, self-management, anxiety, physical wellbeing, depression and quality of life (Table 1).

Table 1
PubMed search strategy.

cognitive therapy[MeSH Terms]) OR meditation[MeSH Terms]) OR mindfulness [MeSH Terms]) OR cognitive therap*[Text Word]) OR cognitive behav*[Text Word]) OR meditation[Text Word]) OR mindfulness*[Text Word]) OR mindfulness-based[Text Word]) OR mindfulness[Text Word]) OR cognition therap*[Text Word]
AND
magnetic resonance imaging[MeSH Terms]) OR functional neuroimaging[MeSH Terms]) OR functional magnetic resonance imaging[Text Word]) OR nuclear magnetic resonance[Text Word]) OR brain mapping[MeSH Terms]) OR neurophysiology[Text Word]
AND
pain management[MeSH Terms]) OR pain management[Text Word]) OR chronic pain[MeSH Terms]) OR chronic pain[Text Word]

2.2. Search strategy for the identification of studies

The first search was conducted during December 2016 and updated during April 2018. Five electronic and international databases were searched: Pubmed, Embase, PsycINFO, Science Direct, Scopus. Databases were searched using the following terms in English: cognitive behavioral therapy OR mediation OR mindfulness AND chronic pain OR pain management AND functional neuroimaging. In addition, reference lists of the included studies were examined for additional potentially eligible studies. Terms were combined with the Cochrane MEDLINE filter for controlled trials of interventions. The PubMed strategy, which can be viewed in Table 2, was then adapted for the other listed databases in combination with specific database filters for controlled trials, whenever available. Neither time limit nor language limitation were considered. Surveys were performed immediately before the final analysis and additional studies were retrieved for inclusion.

2.3. Study selection and data extraction

Two reviewers (SSN, LRO) independently selected potentially eligible studies based on title, abstract and full text sequentially, according to the eligibility criteria pre-specified. These authors were not blinded to the journal or authors. Data extraction was performed by the same two reviewers and recorded in a standardized form. Disagreements were resolved by consensus. Data were extracted from randomized controlled trials and an exploratory table includes the following data: population characteristics, treatment intervention / schedule, comparison group, outcome measures/instruments, outcome time assessment.

2.4. Quality assessment and risk of bias

Methodological quality of each study was independently assessed by two authors, who used seven criteria based on the Cochrane Collaboration's tool for assessing risk of bias.[17] Six domains of bias were evaluated in this review: selection bias (randomization sequence generation, allocation concealment), performance bias (blinding of participants), detection bias (blinding of outcome assessor), attrition bias (incomplete outcome data), reporting bias (source of funding bias), and other bias (sample size, stimulation parameters). For each study, each item was rated according to three categories: low risk, high risk and unclear risk (studies without a clear description of these features). Then, the overall risk of bias of individual study for all domains was rated as low, high or unclear. All analyses were carried out using RevMan- Review manager 5.3.

3. Results

3.1. Studies description

Fig. 1 presents flow diagram summarizing the study selection