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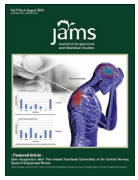

REVIEW ARTICLE

Does Acupuncture Alter Pain-related Functional Connectivity of the Central Nervous System? A Systematic Review

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Abstract
Acupuncture has been studied for several decades to establish evidence-based clinical practice. This systematic review aims to evaluate evidence for the effectiveness of acupuncture in influencing the functional connectivity of the central nervous system in patients with musculoskeletal pain. A systematic search of the literature was conducted to identify studies in which the central response of acupuncture in patients with musculoskeletal pain was evaluated by neuroimaging techniques. Databases searched were AMED, CINAHL, Cochrane Library, EMBASE, MEDLINE, PEDro, Pubmed, SCOPUS, SPORTDiscuss, and Web of Science. Included studies were assessed by two independent reviewers for their methodological quality by using the Downs and Black questionnaire and for their levels of completeness and transparency in reporting acupuncture interventions by using Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) criteria. Seven studies met the inclusion criteria. Three studies were randomized controlled trials (RCTs) and four studies were nonrandomized controlled trials (NRCTs). The neuroimaging techniques used were functional magnetic resonance imaging (fMRI) and positron emission tomography (PET). Positive effects on the functional connectivity of the central nervous system more consistently occurred during long-term acupuncture treatment. The

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results were heterogeneous from a descriptive perspective; however, the key findings support acupuncture's ability to alter pain-related functional connectivity in the central nervous system in patients with musculoskeletal pain.

1. Introduction

Acupuncture is an ancient healing modality used for a range of diseases, including pain disorders [1]. Current evidence demonstrates that acupuncture effects are predominately attributable to its physiological mechanisms rather than to a placebo effect [2,3]. Peripheral, central, and neurohormonal responses are different physiological mechanisms that are triggered in the human body by stimulating muscle afferent fibers during needle manipulation [4].

Since the mid-1990s, the interest in investigating the central response of acupuncture with neuroimaging techniques has been growing [5]. Functional neuroimaging techniques such as functional magnetic resonance imaging (fMRI), positron emission tomography (PET), single photon emission computed tomography (SPECT), electroencephalography, and magnetoencephalography provide a means to monitor the effects of acupuncture on the functional connectivity of the human brain [6].

Functional connectivity is fundamental for understanding the nature of brain function [7]. Neuroimaging has immensely increased the knowledge of pain processing in the central nervous system (CNS) [8,9]. The current evidence indicates that several cortical and subcortical areas constitute the pain matrix: primary somatosensory cortex (S1), secondary somatosensory cortex (S2), insular cortex (IC), anterior cingulate cortex (ACC), amygdala, prefrontal cortex (PFC), and thalamus [10]. However, there is a difference between the brain areas activated during acute pain and during chronic pain [11]. The intensity of pain in chronic pain states such as chronic back pain, fibromyalgia, osteoarthritis, and chronic regional pain syndrome are highly correlated with abnormal plasticity (i.e., functional changes or alterations in the connectivity of brain areas) [12,13].

Neuroimaging acupuncture studies have detected brain activation in the IC, thalamus, ACC, S1, S2, inferior frontal cortex, superior temporal cortex, superior temporal gyrus, and cerebellum; and have detected brain deactivation in the medial prefrontal cortex, subgenual ACC, caudate, amygdala, posterior cingulate cortex, thalamus, parahippocampus, and cerebellum [14]. However, most studies were performed on healthy individuals [6,14—16]. Whether these findings can be extrapolated to patients with pain remains unclear [17]. However, such findings serve as background knowledge and provide a rationale for studies involving patients.

Investigating acupuncture central response will help to underpin the clinical efficacy of acupuncture analgesia, which can be related to an alteration in the functional connectivity of the CNS and restoration of normal plasticity, followed by the reduction of pain. Therefore, the aim of this systematic review was to evaluate the evidence for the effectiveness of acupuncture on influencing the functional connectivity of the CNS in patients with musculoskeletal pain.

2. Methods

2.1. Protocol and registration

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [18]. The protocol was not preregistered.

2.2. Selection criteria

2.2.1. Types of studies

Randomized controlled trials (RCTs) and nonrandomized studies (i.e., observational studies, lab-based experimental studies, case-control studies, cohort studies) published in peer-reviewed journals were included in this review. Non-English language publications were excluded because of the anticipated time constraints of this review.

2.2.2. Types of study participants

Individuals with acute or chronic musculoskeletal pain syndromes were included. There were no restrictions based on sex.

2.2.3. Types of intervention

Studies using acupuncture or electroacupuncture were included. There were no restrictions based on the selection or number of acupuncture points used. Studies using other types of acupuncture such as ear acupuncture, moxibustion, acupressure, laser acupuncture, and dry needling were excluded.

2.2.4. Types of comparators

Studies using sham acupuncture or no intervention as a comparator were included in this review.

2.2.5. Types of outcome measures

Studies that assessed functional connectivity using one of the following brain imaging techniques were included: fMRI, PET, SPECT, electroencephalography, and magnetoencephalography. Brain activity markers (e.g., voxels) were quantified according to the brain imaging technique used in the studies included.

2.2.6. Assessment time frame

No restriction was applied to the assessment time frame.