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Research Article

Being Adaptive to Pain Enhances Sham Acupuncture Analgesia: A Crossover Healthy Human Study

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Abstract
We have reported a model that distinguishes pain adaptive individuals (PA) from those who are pain non-adaptive (PNA). The present randomised, cross-over, participant-assessor blinded study aimed to determine the impact of pain adaptability on individuals' response to real and sham acupuncture. Healthy volunteers (nine PA and 13 PNA) were randomly allocated to receive real and sham acupuncture on the left hand and forearm in two separate acupuncture sessions. Pressure pain thresholds (PPTs) were measured at bilateral forearms and right leg before, immediately after and 20 minutes after the end of acupuncture. Ratings to pinprick and suprathreshold PPT were also recorded. The two groups were comparable in their demographic and baseline data. Analgesia induced by real or sham acupuncture did not differ on any outcome measures. PA responded to acupuncture needling better than PNA, and to sham needling (20% increase in PPT) better than to real acupuncture (7.9%). Those differences were at 20 min after

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end of acupuncture in the areas distant to the needling sites. PNA reported little changes in PPT. Being adaptive to pain was associated with enhanced distant analgesia in response to sham acupuncture. Our finding might partly explain varied acupuncture analgesia in clinical practice and trials.

1. Introduction

Acupuncture is increasingly used for pain relief. Many clinical trials have been conducted to assess the efficacy of acupuncture for various clinical pains, including headache [1], low back pain [2], osteoarthritis [3], neck pain [4], and shoulder pain [5,6]. The commonly used control is sham acupuncture, where needles are inserted shallowly into sites that are nonacupoints (but close to the site of real acupoints), and De Qi sensation is avoided. De Qi, a complex sensation of aching, soreness, heaviness, and others [7], indicates the appropriate dose having been achieved. This form of invasive sham acupuncture has been criticized for being noninert as it has real physiological effect [8—10], therefore contributing to the small differences between real and sham acupuncture observed in many clinical trials [11].

It is known that acupuncture exerts its analgesia through activating endogenous pain inhibitory systems. The systems include segmental inhibition, where analgesia is exhibited at the bilateral nerve segmental distributions around the site of the needling [12], and conditioned pain modulation, where analgesia is exhibited at multiple sites over the body away from the needling site [12,13]. For instance, needling Hegu (LI4), increases pressure pain thresholds (PPT) in healthy volunteers on multiple parts of the body, such as the contralateral arm, legs, and abdomen [14]. Electroacupuncture on one of the legs increases pain threshold on the same and opposite legs, but has little effect on pain threshold on the arm [15]. Those studies support the view that acupuncture analgesia relies on the functionality of the endogenous pain controls.

In addition to inhibition, a recent study identifies the dichotomy of pain adaptability, that is, pain adaptive (PA) and pain nonadaptive (PNA) individuals [16]. When undergoing a 5-minute cold pressor test, PA individuals reported a fast increase in pain, then a significant reduction of pain intensity by at least two of 10 at end of the test, whereas PNA had a slower increase of pain to cold pressor and the pain remained high throughout the test. Furthermore, being adaptive to pain was associated with the potency of local pain inhibition, but was not correlated with the potency of conditioned pain modulation. Pain adaptability could be a representation of a facilitation-inhibition circuitry that has rarely been explored before.

This randomized, double-blind (participant and assessor), sham-acupuncture controlled, crossover study involved healthy participants and aimed to investigate (1) if pain adaptability impacted on individual responses to real and sham acupuncture and (2) the spatial distribution of acupuncture analgesia in PA and PNA individuals.

2. Materials and methods

The present study was conducted at the Aalborg University, Denmark, with the approval of the Research Ethics Committee of the North Denmark Region (20120079) and endorsement by the RMIT Human Research Ethics Committee (19156). From March to October 2013, healthy volunteers whose pain adaptability status were previously determined [16] were invited to take part in this study. Twenty-two of them gave written consent to be part of this study. Briefly, the selection criteria were aged between 18 and 50 years, without any ongoing pain or other health issues, fluent in English and without acupuncture experience in the last 3 years. Nine of them were PA with a better pain reduction at the end of the cold pressor test ($\geq$2 from their maximum pain from the cold pressor), and 13 were PNA with less pain reduction at the end of the cold pressor test ($<$2 from their maximum pain). In the present study, they were randomly allocated to receive real and sham acupuncture in two separate sessions (Fig. 1), with half receiving real first then sham, and the other half receiving sham first then real acupuncture. Before the first session, each participant drew a sealed envelope out of a stack of 22, each containing a number corresponding to a random number sequence generated using Excel by an independent researcher (ZZ). This researcher enrolled and allocated the participants. During the tests and interventions, participants were positioned comfortably in a reclining position in a dental chair with arms rested on the armrests and legs elevated to just below hip level.

At baseline, participants were asked to complete questionnaires about their demographics, mental and physical health (SF-36) [17], and level of anxiety (State Trait and Anxiety Test) [18]. Before each acupuncture session, participants were asked about their sleep quality from the night before on a numerical rating scale of 0—10, where 0 means the worst sleep and 10 the best sleep quality, and whether or not they had done any strenuous exercise or taken coffee in the past 24 hours. Female participants were asked about their menstrual cycle. These factors were considered as they are known to affect pain sensitivity [19—21].

2.1. Acupuncture

The real and sham acupuncture protocols followed a credible blinding procedure [22]. LI4 and LI10 were chosen in real acupuncture because of their pain-reduction effect. After insertion, needles were manipulated for 1 minute to achieve De Qi, and this procedure was repeated for a total of three times every 10 minutes. In sham acupuncture, needles were shallowly inserted into sham LI4 and LI10 to