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Abdominal acupuncture reduces laser-evoked potentials in healthy subjects ☆

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HIGHLIGHTS

- Acupuncture is able to reduce pain although the exact mechanism is unknown.
- Laser-evoked potential (LEP) is one of the most reliable methods to assess nociceptive pathways.
- Abdominal acupuncture is able to modify LEP.

ABSTRACT

Objective: Acupuncture is known to reduce clinical pain, although the exact mechanism is unknown. The aim of the current study was to investigate the effect of acupuncture on laser-evoked potential amplitudes and laser pain perception.
Methods: In order to evaluate whether abdominal acupuncture is able to modify pain perception, 10 healthy subjects underwent a protocol in which laser-evoked potentials (LEPs) and laser pain perception were collected before the test (baseline), during abdominal acupuncture, and 15 min after needle removal. The same subjects also underwent a similar protocol in which, however, sham acupuncture without any needle penetration was used.
Results: During real acupuncture, both N1 and N2/P2 amplitudes were reduced, as compared to baseline ($p < 0.01$). The reduction lasted up to 15 min after needle removal. Furthermore, laser pain perception was reduced during real acupuncture, although the difference was marginally significant ($p = 0.06$).
Conclusions: Our results show that abdominal acupuncture reduces LEP amplitude in healthy subjects.
Significance: Our results provide a theoretical background for the use of abdominal acupuncture as a therapeutic approach in the treatment of pain conditions. Future studies will have to be conducted in clinical painful syndromes, in order to confirm the analgesic effect of acupuncture in patients suffering from pain.

1. Introduction

The use of acupuncture, as a complementary and alternative medicine, is increasing, although its clinical efficacy is still a matter of debate (Frass et al., 2012). Although the mechanisms underlying the acupuncture analgesic action are far from being known, several elements support the idea that acupuncture can act at the level of the nociceptive pathways. First, a study comparing the effect of

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the stimulation of two different acupoints with the effect of morphine demonstrated that both acupuncture and morphine were able to increase the pain threshold by 80–90%. This effect disappeared after the injection of an anesthetic into the acupoints (Research Group of Acupuncture Anesthesia, 1973). According to this study, the analgesic effect of acupuncture is similar to that of opioid drugs. Second, other studies show that the brain areas involved in acupuncture analgesia belong to the so-called pain matrix, thus suggesting a significant functional overlapping between pain and acupuncture pathways (Treede et al., 1999; Zhao, 2008). In anesthetized rats, Pan and colleagues found that either noxious stimulation or electroacupuncture activate the hypothalamic–pituitary–adrenocortical axis, leading to a marked expression of c-fos in the anterior lobe of the pituitary gland, as well as in the arcuate and some nearby hypothalamic nuclei (Pan et al., 1994). Similar results were achieved by using functional magnetic resonance imaging (fMRI) (Hennig et al., 2000; Hui et al., 2005; Zhang et al., 2003a,b), which showed the important role played by the hypothalamus-limbic system in acupuncture analgesia. Positron emission tomography (PET) studies (Biella et al., 2001; Hsieh et al., 2001; Pariente et al., 2005) showed that acupuncture was able to activate both the hypothalamus and the insula. Third, acupuncture analgesia is possibly mediated by the action of various endogenous neurotransmitters involved in nociception. The effects of acupuncture (and sham acupuncture) on μ-opioid receptor binding have been studied in humans (Harris et al., 2009) and the action of acupuncture in modifying the pain threshold in animal models is reversed by naloxone (Pomeranz and Chiu, 1976). The development of tolerance for acupuncture is probably due to desensitization of opioid receptors in the central nervous system (Han et al., 1979, 1981).

There are studies that investigated the possible site of action of acupuncture, which, however, remains elusive. When the needle is introduced in the skin, it might stimulate the peripheral fibers, including Aδ and C afferents. As these afferents convey the nociceptive input, their stimulation might trigger a conditioning pain modulation (CPM) mechanism, which could reduce the subjective perception of clinical pain (Bing et al., 1990; Fields et al., 2005; Villanueva et al., 1986). However, a recently published study excluded that CPM may explain acupuncture analgesia (Tobbackx et al., 2013). A possible effect of acupuncture at the spinal level is suggested by the segmental specificity of acupoints (Zhang et al., 2003b).

The scarce knowledge on the acupuncture mechanisms of action can be due to the almost exclusive use of somatic acupuncture. Indeed, using somatic acupuncture, it is difficult to compare the effects of acupuncture with those obtained in a real sham condition. Sham acupuncture is difficult to obtain, as the needle has to induce a pinprick and/or dull sensation (‘‘De Qi’’ sensation) in order to work. This problem can be solved by using ‘‘abdominal’’ acupuncture (AA). It is an ancient technique based on the stimulation of abdominal points, according to a ‘‘turtle representation’’ of the somatosensory areas (Fig. 1). With respect to ‘‘somatic’’ acupuncture, in AA, the needle is superficially driven and no stimulation is needed. Moreover, while in somatic acupuncture treatment is based on differentiation among syndromes, AA is merely driven by the symptom location, thus allowing the treatment to be more standardized than in somatic acupuncture.

The most reliable laboratory tool for assessing nociceptive pathway function is laser-evoked potential (LEP) recording (Haanpää et al., 2011; Valeriani et al., 2012). LEPs are related to the activation of type II AMH mechanothermal nociceptors. The afferent volley is conducted along the small myelinated (Aδ) primary sensory neurons and the spinothalamic pathway (Bromm and Treede, 1991). LEPs consist of a temporal lateralized component (N1), with an almost simultaneous frontal positive potential (P1). These are followed by a larger vertex biphasic potential reaching its maximal amplitude on the Cz vertex (N2/P2). Intracerebral recording studies and dipolar modeling studies agree in suggesting that the N1 and P1 potentials are probably generated in the opercular (SII/insula) area (Valeriani et al., 1996, 2000; Frot et al., 1999). The N2 and P2 potentials have a topographical distribution very similar to the vertex potential obtained in other modalities (Mouraux and Iannetti, 2009), and they probably originate from different sources including the midcingulate cortex and insula (Garcia-Larrea et al., 2003; Dowman et al., 2007; Frot et al., 2008).

In order to verify whether AA is able to modify the LEP amplitudes and laser pain perception, we recorded LEPs in healthy subjects during abdominal acupuncture. The results were compared with those obtained during sham acupuncture, in order to separate the possible acupuncture-related analgesic effect from the placebo effect. We expected to find a reduction of both LEP amplitude and laser pain perception during real acupuncture, as compared to the sham condition.

2. Methods

The study protocol was approved by the local ethics committee. The study was designed as a single-blind, crossover protocol that allowed us to consider each subject as his/her own control. Ten normal subjects (five male and five female, mean age 38 years, age range 25–49 years) were asked to sign an informed consent form to participate in the study. The subjects were naive to all types of acupuncture. Only volunteers with no historical symptoms nor signs of focal upper limb entrapment, cervicobrachialgia, or polyneuropathy were enrolled. Each subject underwent two separate sessions of real and sham AA. All subjects did not know that there would be a sham acupuncture, and all of them were told that the aim of the study was to investigate the effect of two different kinds of acupuncture on LEPs. Each session included three times: (1) baseline, in which LEPs to stimulation of the skin of both the right and left dorsal wrist were recorded before real or sham AA; (2) acupuncture, in which LEPs were recorded to stimulation of the same sites during real or sham AA; and (3) post, in which LEPs were recorded 15 min after needle removal (Fig. 2).

The order of the sessions was randomized across subjects, and the time interval between sessions ranged from 28 to 40 days. We ensured that female subjects underwent both sessions in the same menstrual period, as hormonal changes can influence pain perception (de Tommaso et al., 2009). All subjects were treated by the same acupuncturist (SL). Only the acupuncturist was aware of the type of acupuncture (i.e., real or sham), while all the other experimenters were blind to it.

2.1. Laser stimulation and LEP recording

Laser pulses (wavelength, 1.34 μm) were delivered on the dorsum of the right and left wrist separately by a YAP Stimul 1340 (Electronic Engineering, Florence, Italy). The order of side stimulation was counterbalanced across subjects. The laser stimulus intensity was fixed at 38 mJ/mm^2, which was perceived by all subjects as a painful pinprick (Cruccu et al., 2003; Valeriani et al., 2002). The interstimulus interval varied randomly between 9 and 11 s. In order to avoid nociceptor fatigue, the laser spot was slightly moved from one stimulus to another.

LEPs were recorded from two scalp electrodes placed along the midline (Fz and Cz positions of the 10–20 international system), and one electrode in the left temporal region (T3/T4), contralateral to the stimulation. The reference electrode was placed on the nose, and the ground on the forehead (Fpz). Both vertical and horizontal eye movements and eye blinks were monitored by an electroocu-