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Different modes of manual acupuncture stimulation differentially modulate cerebral blood flow velocity, arterial blood pressure and heart rate in human subjects

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Abstract

The psychophysiological effect of different modes of manual acupuncture stimulation was investigated in 12 healthy, right handed, male subjects (mean age 29). The cerebral blood flow velocity (CBFV) in both middle cerebral arteries, arterial blood pressure (BP), heart rate (HR) and the perceived intensity of the stimulation were monitored while an acupuncture needle in the right dorsal thenar muscle (point Hegu, Li 4) was repetitively rotated with either high frequency (4–8 Hz) and low amplitude (hf-la) or low frequency (1–2 Hz) and high amplitude (lf-ha). Response patterns induced by hf-la and hf-la stimulation differed significantly ($P < 0.05$) as tested by Student's *t*-test: (1), hf-la stimulation was perceived as more intense and induced a more marked right hemispheric CBFV increase; (2), while hf-la stimulation lead to a slight decrease of BP and HR, lf-ha stimulation induced an initial pressor response (increase of BP, decrease of HR) and a more marked long term decrease of BP. Data indicate that the mode of manual acupuncture stimulation has a differential effect on the perceived stimulation intensity, the cerebral activation and the cardiovascular reflex response.

Keywords: Acupuncture; Cerebral activation; Transcranial Doppler; Somatocardiovascular reflex response

Acupuncture, a treatment modality of traditional Chinese Medicine (TCM), is more and more widely used to treat several diseases. Among other mechanisms changes of the cerebral perfusion [2,7,11,12] and a distinct somatocardiovascular reflex response [6,9,10,18] have been postulated to be evoked by acupuncture. Classical acupuncture literature holds that different modes of manual needle stimulation exert a differential effect on the body [19]. In clinical practice a common mode of needle stimulation is the manual rotation of the needle. A rotation with high frequency and low amplitude (hf-la) is considered as a reinforcing stimulus suitable to treat conditions of depletion (exhaustion, fatigue, etc.). Low frequency and high amplitude (lf-ha) rotation instead is considered as a reducing stimulus being able to adjust conditions of repletion (acute diseases with severe symptoms) [14]. For electroacupuncture (EA) a differential effect of high and low frequency stimulation has been found. In anaesthetized rats EA induces changes of the cardiovascular activation [9] and central endorphinergic mechanisms [20] that vary in relation to the applied stimulation frequency. EA and manual acupuncture (MA) share some similar physiological mechanisms, but they might also exert considerably different effects [13]. It is unknown whether there is a varying psychophysiological response to different modes of manual needle stimulation. Therefore, in the present study, we investigated the effect of hf/la and lf/ha manual acupuncture stimulation on the cerebral activation, the cardiovascular reflex response and the perceived stimulation intensity in healthy human subjects. In order to monitor changes of the cerebral activation, the cerebral blood flow velocity (CBFV) in both middle cerebral arteries (MCA) was measured by functional transcranial Doppler sonography (fTCD) before, during and after acupuncture stimulation. This method has been shown to render information about functional evoked changes of the cerebral perfusion associated with changes of the cerebral activation [1,4]. Additionally the arterial blood pressure (BP) and heart rate (HR) were measured to explore the cardiovascular response

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to acupuncture. The subjects were asked to report the perceived stimulation-intensity at the end of the experiment in order to take into account the introspective perception of the acupuncture stimulation.

Twelve healthy acupuncture-naive, male volunteers (mean age 29 ± 3.6 std), all right handed according to the Edinburgh inventory, participated in the study after giving informed consent. The experiment was performed in a darkened, quiet room and subjects were lying comfortably on a couch. A stainless steel acupuncture needle (Asiamed, ∅ 0.25, length 40 mm) was inserted perpendicularly into the Hegu point (Li 4), which is located on the dorsum of the hand, on the radial side of the midpoint of the second metacarpal bone, in the middle of the right dorsal thenar muscle. In order to make the subjects familiar with the stimulation paradigm, the needle sensation was evoked once before the measurements began. The needle was then twisted every 55 s, ten times in total, each with a duration of 5 s. In six subjects the needle was twisted with a frequency of 4–8 Hz and an amplitude of approximately 0.5–2 rotations (hf-la). In the other six subjects a needle rotation with a frequency of 1–2 Hz and an amplitude of 4–8 rotations (lf-ha) was performed. After the experiment the subjects had to report the subjective intensity of the stimulation. To take into account the variance of the stimulation intensity evoked by manual needle manipulation, subjects were instructed to rate the intensity of the strongest and the weakest stimulation episode. The intensity was represented in a simple way on a visual analogue scale (VAS) with figures from zero to ten, where zero was taken as no sensation and ten was taken as the most intense sensation subjects could imagine. Since acupuncture-naive subjects are unfamiliar with the needle sensation, they were instructed to compare their sensation with the sensation of pain when judging the intensity of the stimulus. Stimulation related changes of the cerebral blood flow velocity (CBFV) in both middle cerebral arteries (MCA) insonated at a depth of 52 mm were measured before, during and after the stimulation. The CBFV was monitored by a commercially available dual transcranial Doppler ultrasonography device (Multi-Dop X, DWL). Two transducer probes (2 MHz) were attached to a headband and placed at the temporal bone windows bilaterally. The correct identification of the arteries was performed according to the clinical standards of TCD examination. The arterial blood pressure was recorded noninvasively at the left middle finger according to the Penaz method (Finapress, Ohmeda, USA) [16]. All measurements were performed in a standardized fashion with equivalent settings for all recordings.

The analysis was performed off-line with the TCD-analysis-software AVERAGE [5]. The heart rate was calculated by a peak analysis of the envelope curve of the Doppler frequency spectrum in the raw data.

Data were segmented into epochs time locked to the stimulation. The epochs were set from 15 s before to 40 s after the onset of stimulation. As baseline value ($V_{pre.mean}$), the mean velocity in the interval from 15 to 5 s before stimulation onset was taken. The stimulation related changes of CBFV (dV) were calculated by the formula: $dV = (V(t) - V_{pre.mean}) \times 100/V_{pre.mean}$, where V(t) is the CBFV over the course of time [5]. To reduce spontaneous oscillations of the CBFV due to the pulsatility of the TCD velocity curves, they were integrated over the corresponding heart cycles and replaced by a step function [5]. Finally data were averaged time locked to the stimulation for single subjects and for all subjects (Grand average) of the respective group (hf-la versus lf-ha). The velocity values were averaged for each time point and tested for normal distribution by the Kolmogorov–Smirnov test. Differences of CBFV, BP, HR and VAS scores between groups were analysed by the two-tailed Student's *t*-test for unpaired samples. Differences of CBFV changes in the left and the right MCA were analysed by a two-tailed Students *t*-test for paired samples. Differences were classified as significant at $P < 0.05$. To account for the Bonferroni problem only time periods of significant differences longer than 1 s were accepted. Further details of the analysis can be found elsewhere [5].

Lf-ha stimulation was perceived as more intense, reflected by significant ($P < 0.05$) higher maximum (VAS max) and minimum (VAS min) VAS values reported after the experiment. Across subjects the mean reported values at lf-ha stimulation were: VAS min 4.4 (±1.8 std), VAS max 7.4 (±1.1 std), and at hf/ la stimulation: VAS min 1.8 (±1.0 std) and VAS max 4.2 (±1.6 std). The physiological responses to hf-la and lf-ha acupuncture stimulation are shown in Fig. 1. While CBFV at hf-la stimulation initially decreased and then increased slightly above baseline, lf-ha stimulation induced a significantly ($P < 0.05$) stronger increase of CBFV, followed by a significantly ($P < 0.05$) more marked decrease. After needle manipulation CBFV reached baseline values within the observation period across subjects in both stimulation conditions. The side-to-side comparison revealed a significantly ($P < 0.05$) stronger increase in the right MCA after lf-ha stimulation indicating a dominant right hemispheric activation. During hf-la stimulation no significant lateralized activation could be observed. Also the cardiovascular responses varied significantly ($P < 0.05$) dependant on the stimulation mode: While hf-la acupuncture lead to a slight decrease of BP and HR, lf-ha induced a significantly ($P < 0.05$) stronger initial pressor response (increase of BP, decrease of HR) and a significantly ($P < 0.05$) more marked long-term decrease of BP.

Data demonstrate that lf-ha and hf-la manual acupuncture stimulation exerts different effects on the cerebral activation and the cardiovascular reflex response in healthy human subjects. Additionally the sensory stimulation induced by lf-ha acupuncture was perceived as being more intense by the subjects. This could explain the dominant right hemispheric perfusion increase observed only during lf-ha stimulation. Since the right hemisphere is dominant for the processing of attentional tasks and arousal, there might be

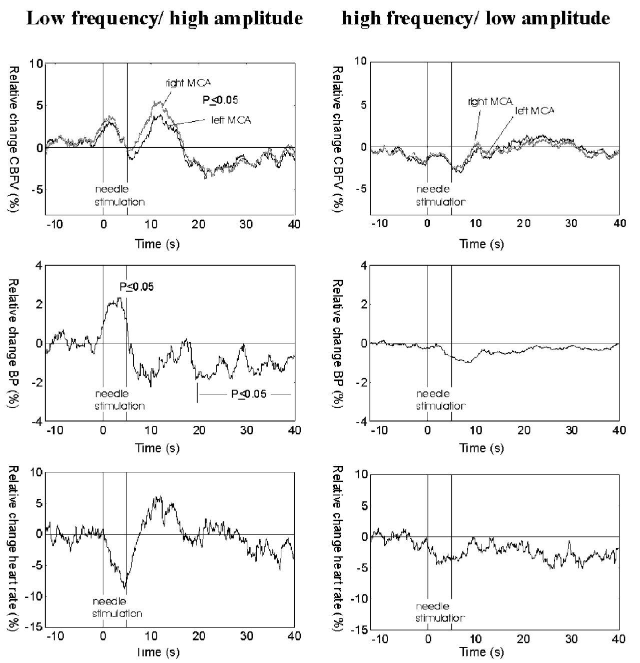

Fig. 1. Grand average of the physiological response to low frequency/high amplitude (left panel) and high frequency/low amplitude (right panel) manual acupuncture stimulation. Note: data for grand averages shown on the right and the left panel are derived from respectively six different subjects ($n = 12$), each being stimulated repetitively ten times for a duration of 5 s. Upper panel: relative changes of the cerebral blood flow velocity in the right and the left MCA (CBFV), middle panel: relative changes of arterial blood pressure, lower panel: relative changes of heart rate. Vertical bars represent onset and offset of the needle stimulation.

a stronger right hemispheric activation when a stimulus is considered to be more aversive [15]. Other functional imaging studies which investigated the anatomy of the cerebral processing of acupuncture by fMRI and positron emission tomography (PET), have shown divergent results. While Hui and co-workers [7] found decreases of activation in mainly subcortical structures, Biella and co-workers [2] observed an activation of structures usually involved in the processing of pain. Data acquired by fTCD are comparable with PET and fMRI [4]. Since the present data indicate that the way of acupuncture stimulation might considerably influence the cerebral activation, differences of needle stimulation could account for divergent results in previous functional imaging studies.

The CBFV changes observed in the present study might be partly induced by changes of the arterial blood pressure, since BP changes show a somehow parallel modulation pattern. BP changes in the 'lf-ha condition' consisting of an increase during the stimulation and a decrease after the stimulation might be due to a biphasic response of the autonomous nervous system to acupuncture, which has been described previously [6,18]. An acupuncture induced BP-increase was explained by a higher sympathetic vasoconstrictor tone mediated by different supraspinal mechanisms [10], while a baroreflex response could account for the parallel-observed decrease of HR. In the later post stimulation phase (20–40 s after the end of stimulation) there might have been a dominant parasympathetic tone or a decreased sympathetic tone, since a decrease of both BP and HR could be observed. The clinical experience that patients report to be more relaxed after an acupuncture treatment might be due to the long-term increase of the parasympathetic tone or decrease of the sympathetic tone. It has to be mentioned however, that the present data gained from event related averaging reflect only short lasting changes within the observation period of 55 s. There might additionally be tonic or long-term effects beyond the time frame of 55 s, which however were not explored by the present paradigm.

Since lf-ha stimulation was perceived as being more intense than hf-la stimulation, the perceptual condition was quite different. Strong aversive stimuli are known to evoke a 'fight-or-flight-response', a condition of general alertness, which is accompanied by an increase of the sympathetic tone during the confrontation with the stimulus and a post-stimulation decrease of the sympathetic tone [8]. In contrast weaker stimuli may induce a decrease of BP and HR when attention is directed to an impending stimulus ('orienting response') [3]. Additionally more intense stimuli might elicit a stronger post stimulation decrease of the sympathetic tone. This must be taken into account in clinical acupuncture practice, since patients might faint more easily, when the needle stimulation is too strong.

Changes of the CBFV during acupuncture have been studied previously by fTCD [11,12]. Litscher and co-workers found an increase of CBFV in the right MCA, which was paralleled by an increase of regional cerebral oxygenation, as measured by near infrared spectroscopy. In this study a combination of points were needled which, according to TCM, should lead to a 'general increase of Qi-energy'. Litscher and co-workers concluded that acupuncture would enhance the oxygenation of the cerebral tissue [11]. It has to be mentioned that because these researchers did not monitor physiological parameters from both hemispheres they could not monitor lateralized cerebral activation. Based on the present data the increase of CBFV and oxygen saturation in the right hemisphere might have been caused by a right hemispheric activation due to the processing of the acupuncture stimuli. During regional cerebral activation there is a relative increase of oxygen saturation in the tissue since the increase of oxygen supply (caused by an increase of perfusion) exceeds the increase of oxygen demand due to the neurovascular coupling [17]. Compared with the present study however, the acupuncture scheme and needle manipulation applied by Litscher and co-workers were different, thus data have to be compared with caution. Changes of the cerebral perfusion induced by acupuncture may vary with the selection of acupoints. This is indicated by another study of Litscher and co-workers [12], who found an increase of CBFV in the ophthalmic artery during acupuncture of 'vision related acupoints' whereas under the same acupuncture scheme CBFV in the MCA remained unchanged.

To summarize, the present study shows that different modes of manual acupuncture stimulation exert a differential psychophysiological response in healthy subjects. In clinical practice, as proposed in TCM, it might be beneficial to adapt the mode of acupuncture stimulation to the clinical condition and the functional (vegetative) state of the patient.

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