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Acupuncture–brain interactions as hypothesized by mood scale recordings

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ABSTRACT

Mood expressions encompassing positive scales like “activity, elation, contemplation, calmness” and negative scales like “anger, excitement, depression, fatigue” were applied for introducing a new tool to assess the effects of acupuncture on brain structures. Traditional acupuncture points defined in the literature for their effects on task negative and task positive brain structures were applied to chronic disease patients supposed to have dominant negative mood scales. Burn-out syndrome ($n = 10$) and female chronic pain patients ($n = 22$) showed a significant improvement on positive mood scales and a decline in negative mood scales after 10 acupuncture sessions. We observed a direct effect of acupuncture on brain structures in 5 burn-out syndrome patients showing an immediate, fast suppression of unusual slow high amplitude EEG waves in response to acupuncture needle rotation. These EEG waves described here for the first time in awake patients disappeared after 10 sessions but gradually returned after 1–1.5 years without acupuncture. This was accompanied with deterioration of positive mood scales and a return to negative mood scales. Both male ($n = 16$) and female chronic pain patients reported a significant decrease of pain intensity after 10 sessions. Female patients only, however, showed a linear correlation between initial pain intensity and pain relief as well as a linear correlation between changes in pain intensity and mood scales accompanied by a drop of their heart rate during the acupuncture sessions. We hypothesized that mood scale recordings are a sensitive and specific new tool to reveal individual acupuncture–brain interaction.

Introduction

Traditional view of acupuncture

Acupuncture is alongside herbal medicine the basis of the more than 2000 years old Traditional Chinese Medicine (TCM) to treat various types of diseases. For acupuncture metal needles of different size are inserted into the skin tissue at specifically designated acupuncture points. The point nomenclature reflects the microcosmic body representation with words standing for cosmologic, geographic and sociologic phenomena [3]. TCM considers dual fundamental forces maintaining the body: Yang and Yin, the former represents the masculine, kinetic energy and the latter the feminine, structural energy. In the body both are expressed in *qi* (Yang) and blood (Yin) as two separate circulation systems. While blood is pumped by the heart and circulates through the vasculature, *qi* is generated by the lungs and flows through invisible channels called meridians [3,36]. The function of this duality is to promote a normal circulation of blood and *qi* so that the vital essentials derived from man’s food can nourish Yin and Yang for sustaining different organ functions [36]. About 365 traditional acupuncture points are described to give as holes access to the meridians. Loss and mismatches of Yang and Yin due to pathogens like wind, cold, heat and dryness, can be restored to normal balance by acupuncture of specifically related points re-establishing the balanced duality of Yin and Yang and herewith restoring the normal flow of *qi* and blood [3].

The points which are most commonly used in acupuncture research and treatment are located at or below knee and elbow [21,29]. We therefore chose acupuncture points as shown in Fig. 1.

Patients were treated at both arms with LI4 (large intestine 4, hé gú, union valley, dermatome C6) and LI11 (large intestine 11,

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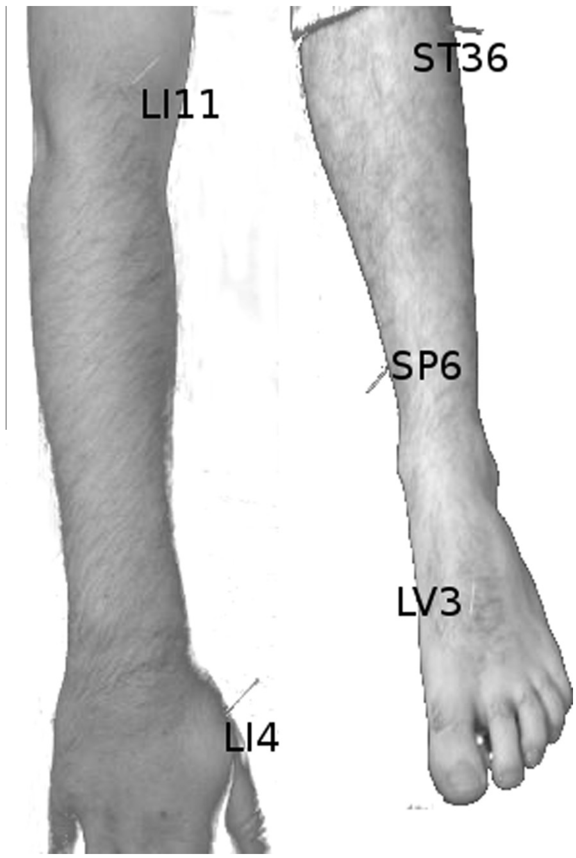

Fig. 1. Traditional acupuncture points on arm and leg chosen for treatment LI4 (large intestine 4, hé gú, union valley, dermatome C6), LI11 (large intestine 11, qū chí, pool at the bend, dermatome C5) ST36 (stomach 36, zú sān lǐ, leg three li, dermatome L5), SP6 (spleen 6, sān yīn jiāo, three yin intersection, dermatome L4), LV3 (liver 3, tài chōng, great surge, dermatome L4).

qū chí, pool at the bend, dermatome C5) giving access to the large intestine Yang channel being disturbed by pain and inflammation; and at both legs with ST36 (stomach 36, zú sān lǐ, leg three li, dermatome L5) giving access to the stomach Yang channel being disturbed by loss of power, SP6 (spleen 6, sān yīn jiāo, three yin intersection, dermatome L4) giving access to the Yin spleen channel being disturbed by loss of power and LV3 (liver 3, tài chōng, great surge, dermatome L4) giving access to the Yin liver channel being disturbed by emotions [3].

Modern view of acupuncture

This traditional view of acupuncture mechanism partly finds its confirmation in recent studies on 1.2.1 Local mechanisms, 1.2.2 Afferent and 1.2.3 Efferent central pathways.

1.2.1 The connective tissue interweaving the whole body is considered as the main local target of acupuncture [28]. Needling or pressure application to acupuncture points might be therefore comparable in mechanism to a massage of the connective tissue which is assumed to stimulate cutaneous–visceral reflexes manipulating the fascial layers within and beneath the skin [19]. Acupuncture meridians and points are physiologically characterized by low electrical impedance and seem to be anatomically associated with connective tissue collagenous planes [2]. It was found that mechanical movement of the needle puncturing traditional points but not sham points generates mechanical waves as measured by ultrasound elastography with subsequent activation of calcium ion channels which leads to beta-endorphin secretion [28,36]. Adenosine, a neuromodulator with anti-nociceptive properties, was released during ST36 acupuncture in mice and its anti-nociceptive actions required adenosine A1 receptor expression [18]. In addition to adenosine, acupuncture triggers the release of other purines, including ATP and ADP that may bind to purine receptors on nearby fibroblasts [17].

1.2.2 Puncturing LI4, ST36 or LV3 and rotating the needle results in immediate changes in the limbic–paralimbic neocortical network (LPNN) as measured by fMRI BOLD (blood oxygenation level dependent). These networks closely match as afferent target the task-negative default mode network (DMN) and the anti- correlated task-positive network as shown in Fig. 2 (adapted from (21)). Clusters of deactivated regions were seen in the medial prefrontal cortex (frontal pole, pregenual cingulate), the temporal lobe (amygdala, hippocampus, and parahippocampus) and the posterior medial cortex (precuneus, posterior cingulate). The sensorimotor cortices (somatosensory cortices, supplementary motor cortex), thalamus and occasional paralimbic structures such as the insula and anterior middle cingulate cortex showed immediate activation by rotating the needle. The amygdala and hypothalamus that is not commonly associated with DMN show decreased activation during acupuncture stimulation. Acupuncture may mediate therefore its anti-pain, anti-anxiety, and other therapeutic effects via this intrinsic neural circuit that plays a central role in the affective and cognitive dimensions of pain as well as in the regulation and integration of emotion, memory processing, autonomic, endocrine, immunological, and sensorimotor functions [13,21,34].

1.2.3 Acupuncture effects might also be related to the hypothala mus–pituitary–adrenal axis mechanism. This efferent mechanism not only shares the well-known central-descending-pain-inhibitory pathway involving endogenous opioids, but also suggests a potential anti-inflammatory mechanism in conjunction with neuro-immune pathways and the cholinergic anti-inflammatory mechanism [9]. The anti-inflammatory effect might be related to a

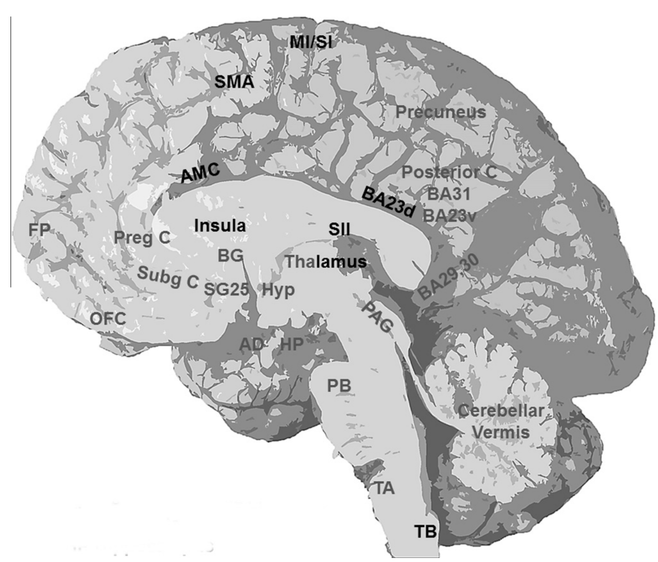

Fig. 2. Task negative, task positive and additional brain centers shown on a brain sketch, with an overlapping of medial and lateral regions being deactivated (gray) and activated (black) respectively by acupuncture of LI4, St36 and LV3. Fig. 2 is adapted from (34). Abbreviations: AMC, anterior middle cingulate; AD, Amygdala; BA, Brodmann area; BA23d, Brodmann area 23 dorsal; BA23v, Brodmann area 23 ventral; BG, basal ganglia; FP, frontal pole; HP, hippocampus; Hyp, hypothalamus; M1/S1, primary motor/primary sensory cortex; OFC, orbitofrontal cortex; PAG, periaqueductal gray; PB, parabrachial nucleus; preg C, pregenual cingulate; SII, secondary somatosensory cortex; SMA, supplementary motor area; SG25, subgenual area 25; Subg C, subgenual cingulate, TA, tract A; TB, tract B.

significant decrease in leukocyte and lymphocyte values after repeated acupuncture treatment [26].

Hypothesis

Mood scales and similarly expressed emotions might be distinguishable in the sense that a mood scale is a low intensity and enduring emotion [7]. Mood scales can be related to consciously felt body emotions which are associated with culturally universal and topographically distinct body sensations [32]. This universal emotional topography might have stimulated ancient TCM physician to define corresponding acupuncture points on the body surface. Patients with chronic diseases have dominating negative mood scales [14] and might probably be especially responsive to brain stimulation by acupuncture. We analyzed here for the first time 8 mood scales to establish a new tool for experimental and clinical studies to document central effects by acupuncture. We could correlate the immediate effect of acupuncture on brain function – as indicated by interruption of slow amplitude EEG waves and decreasing heart rates due to needle rotation – with changes in mood scales. The initial positive mood scale and EEG effects of acupuncture attenuated in burn-out patients as observed in follow up studies up to 1.5 years without acupuncture. The observed mood scale changes might be related to effects on LPNN/DMN brain structures induced by afferent spinal nerve innervated connective tissue mediating acupuncture rotating needle stimulation. The gender difference recorded on chronic pain patients in acupuncture response of mood scales and heart rate as well as the time dependence of the correlation EEG wave amplitude to mood scale strengthen our hypothesis to use mood scales as control of the individual specificity of acupuncture–brain interaction.

Methods

Patients

10 patients (6 women, 4 men, mean age 50.7 ± 10.7 years) being under medication in a general practitioner's practice complained of overload with problems and work in family or profession. They felt emotionally exhausted, lost contact to other people or were less effective in their daily work typical for burn-out syndrome [24] (ICD-10: Z73 [23]). 22 women (mean age 51.9 ± 13.7 years) and 16 men (mean age 52.4 ± 8.1 years) being also under treatment in this practice complained of pain for more than 6 months and unsatisfactory treatment with various medications (chronic pain [12]): 10 women and 13 men with back pain (ICD-10: M54), 6 women and 1 men with migraine (ICD-10: G43) and 6 women and 2 men with arthrosis (ICD-10: M19, M25). All patients were asked to join voluntarily the mood scale study. They were treated in 10 sessions once a week with acupuncture over a period of 3–4 months. During this time all patients followed their daily routine at work and holiday as well as at home. All patients had access to their prescribed medication.

Acupuncture

0.22 × 13 mm single use sterile steel needles (Gushi-zhengzheng, Medical Device, Henang, China) were used for acupuncture. After disinfection of the acupuncture points shown in Fig. 1 needles were superficially inserted about 5 mm deep into the skin by a medical doctor qualified as consultant in acupuncture. Needling started with the right LI4 and finished with the left LV3. The needles were gently rotated clockwise until tissue resistance stopped the rotation. All 10 needles were inserted and rotated within 3 min. Afterwards patients rested in supine position for 10 min. Then the resting needles were rotated again followed by a further rest of 10 min.

The gentle superficial needle rotation is a prerequisite for a correct acupuncture treatment where sharp pain due to needling should be avoided. Instead, our patients reported a sensation of numbness, soreness or heaviness. This sensation is known in TCM as *de qi* and correlates well with the deactivation of the task negative DMN and the activation of the anti-correlated task-positive network [6,21].

Recordings

A mood questionnaire [1] was used to quantify the positive mood scales "activity, elation, contemplation, calmness" as well as the negative mood scales "anger, excitement, depression, fatigue". Each scale is characterized by 5 items which could be answered by yes or No. Digitalized each scale can reach a mean maximal value of 1 or a mean minimal value of 0. The mood questionnaire was completed by the patients before the first acupuncture session, after 10 sessions or later on. Answering the 40 items patients were blinded for the corresponding mood scales.

For pain assessment the Kieler pain questionnaire (http://www.schmerzklinik.de/wp-content/uploads/2009/02/schmerzfragebogen.pdf) was used with a pain intensity scale ranging from 0 to 51. The pain assessment was completed by chronic pain patients before the first acupuncture session and after the last one.

Bipolar frontal-occipital EEG as well as heart rate (beats per minute, BPM) were recorded with Labchart device (ADInstruments, Oxford, UK). EEG recordings were carried on burn-out syndrome patients only. EEG and heart rate recordings of these patients were done during the first acupuncture session. 5 patients (3 women, 2 men) were additionally recorded after 10 sessions, 1 year and one female patient furthermore after 1.5 years. Chronic pain patients got heart rate recordings with NPB-40 device (Nellcor Puritan Bennett Inc., Pleassanton CA, USA) before and after each session.

Statistics

Student's paired two-sided *t*-test with unequal variance was used to calculate significant differences. Significance is reached with $p < 0.05$. Pearson's correlation coefficient r was used to indicate the strength of correlation.

Informed consent was obtained from all individual participants included in the study for a scientific use of their anonymised data.

Results

Burn-out syndrome patients

Table 1 shows the data of positive and negative mood scales of all 10 patients before the first and after 10 acupuncture treatments.

After 10 sessions a highly significant improvement of the positive mood scales as well as the significant decrease of the negative mood scales was observed. Five patients (3 women, 2 men) showed remarkable slow high amplitude EEG waves during the first acupuncture session. The EEG waves were interrupted independently of gender and acupuncture point by rotating the acupuncture needle. This remarkable immediate, fast effect on the EEG waves is demonstrated in Fig. 3.

Fig. 3A shows the recording of a female patient with needle rotation at LI4 left arm, Fig. 3B another female patient with needle rotation at LI4 right arm, Fig. 3C a male patient with the needle rotation at LV3 right foot and Fig. 3D a male patient with the needle rotation at ST36 left leg. With insertion of the needle as indicated by the arrow heart rate starts to drop to different degrees.

Table 1
Mood scale values (Mean) and corresponding standard deviation (SD) of burn-out syndrome patients before and after 10 acupuncture sessions. n = number of patients.

Mood	Activity	Elation	Contemplation	Calmness
Before				
Mean	0.13	0.08	0.34	0.31
SD	0.19	0.14	0.19	0.17
n	10	10	10	10
After				
Mean	0.56	0.62	0.50	0.62
SD	0.32	0.39	0.37	0.35
n	10	10	10	10
T-Test	0.00096	0.00035	0.11881	0.00919
Mood	Anger	Excitement	Depression	Fatigue
Before				
Mean	0.52	0.86	0.70	0.70
SD	0.25	0.19	0.30	0.34
n	10	10	10	10
After				
Mean	0.16	0.26	0.12	0.30
SD	0.22	0.41	0.21	0.40
n	10	10	10	10
T-Test	0.00194	0.00028	0.00005	0.01398

Rotation of the needle as indicated by the horizontal lines in all cases immediately interrupts the high waves which return with needles resting in situ. The slow high amplitude EEG waves were diminished in amplitude after 10 treatment sessions and came gradually back after 1 year. Fig. 4A shows the mean maximal EEG amplitude (EEGA, x-axis) recorded during needling of the acupuncture points shown in Fig. 1 of all five patients during the first session (data point1, DP1), the 10th session (DP2) and after 1 year (DP3). EEGA is correlated with mood indices (MI, y-axis) formed by the difference between the mean of the positive mood scales and the mean of the negative mood scales for each patient. MI is shown as a mean of all five patients at the first session (DP1), the 10th session (DP2) and after 1 year (DP3). Negative values of MI indicate a tendency to negative mood scales and positive MI values a prevailing of positive mood scales. MI can vary between 1 and −1. At the beginning of the acupuncture treatment (DP1) MI dominates with -0.52 ± 0.14 and correlates with EEGA of 100.6 ± 8.3 µV. After 10 sessions (DP2) MI improves to 0.35 ± 0.5 and EEGA decreases to 65.9 ± 32.4 µV. DP1 and 2 are significantly different with EEGA $p < 0.04$ and MI $p < 0.012$. After 1 year (DP3) without acupuncture EEGA values of 52.6 ± 30 µV are statistically significantly different from EEGA at DP1 with $p < 0.02$ whereas

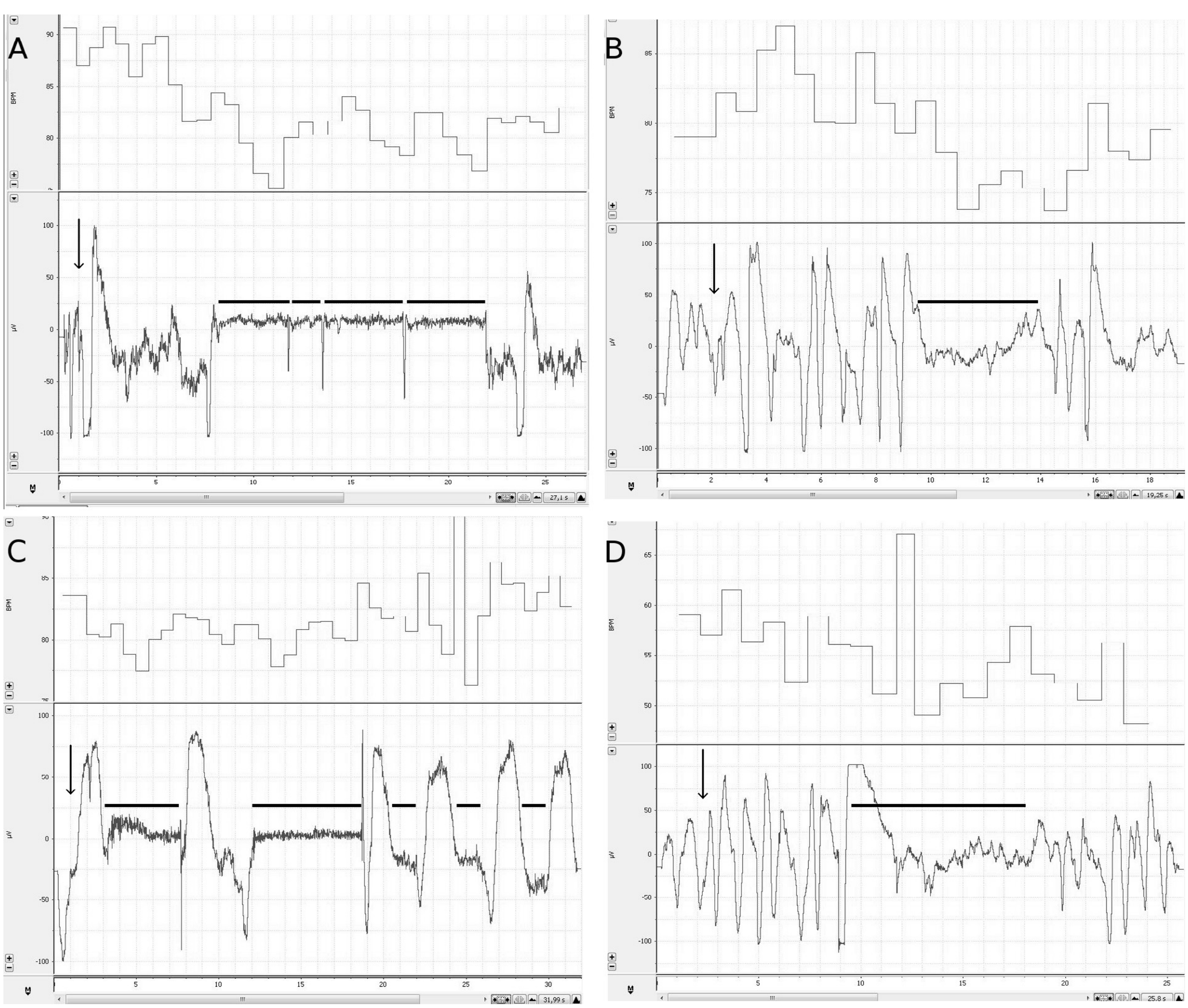

Fig. 3. Original recordings of heart rate (BPM) and slow amplitude EEG waves during the first acupuncture treatment. (A) FEMALE patient, acupuncture LI4 left arm, (B) female patient acupuncture LI4 right arm, (C) male patient acupuncture LV3 right foot, (D) male patient acupuncture ST36 left leg. Arrow indicates time point of needle insertion leading to heart rate (BPM, beats per minute) decrease (upper row), horizontal lines indicate duration of needle rotation interrupting amplitude EEG waves (lower row). EEG is shown in micro Volt (y-axis, µV) and time in seconds (x-axis).

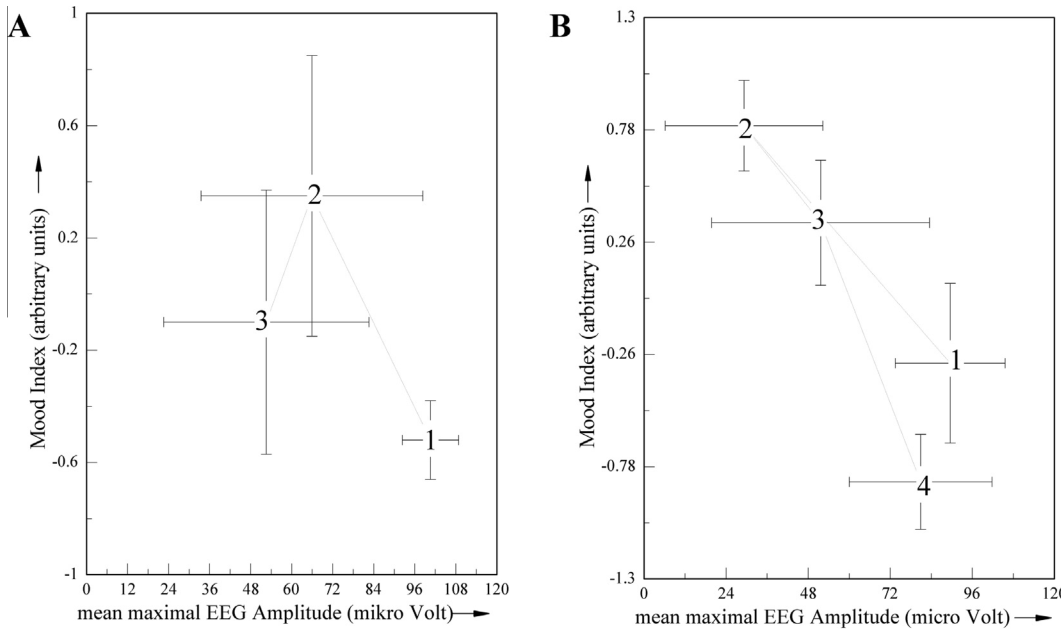

Fig. 4. Relationship between mean maximal EEG amplitude (x-axis, μV) and mood index (y-axis, MI, arbitrary units). (A) Five burnout syndrome patients showing slow high amplitude EEG waves DP1: first recording, DP2: recording after 10 sessions, DP3: recording after 1 year. DP1 and DP2 are significantly different in EEGA and MI $p < 0.012$. After 1 year (DP3) EEGA is statistically different from DP1 with $p < 0.02$ whereas MI with $p > 0.05$ is not. Values of DP2 and DP3 are statically not different. (B) One female patient showing slow high amplitude EEG waves in the first session. EEGA is significantly different between DP1 (first recording) and DP2 (recording after 10 sessions), DP2 and DP4 (recording after 1.5 years) as well as DP 3 (recording after 1 year) and DP 4 with $p < 0.015$. MI is significantly different between DP1 and DP2, DP1 and DP3, DP2 and DP3 as well as DP3 and DP4 with $p < 0.011$.

MI with -0.1 ± 0.47 is rather similar to MI at DP1with $p > 0.05$. Values of DP2 and 3 are statistically not different.

We had the opportunity to examine the female patient shown in Fig. 3A also 1.5 years after the first treatment. Fig. 5 exemplifies the EEG registrations under the influence of needle rotation (bars) of SP6 left leg: 1 during the first session, 2 during the 10th session, 3 after 1 year and 4 after 1.5 years.

Needle rotation interrupts immediately the slow high amplitude EEG waves during the first and the last session. Needles resting in situ have no effect on the EEG waves. Fig. 4B summarizes EEGA as well as MI of four sessions. EEGA with 89.55 ± 16.1 μV dominates during the first session (DP1), EEGA with 29.3 ± 23.1 μV is diminished after 10 acupuncture sessions (DP2), EEGA increases with 51.7 ± 31.9 after 1 year (DP3) and EEGA with 81 ± 20.9 after 1.5 years is comparable to the first registration (DP4). MI has at DP1 a value of -0.3 ± 0.37, at DP2 a value of 0.8 ± 0.21 indicating maximal dominating positive mood scales, at DP3 a value of 0.35 ± 0.29 and at DP4 a value of -0.85 ± 0.22 indicating maximal dominating negative mood scales and worse than the starting values. EEGA is significantly different between DP1 and DP2, DP2 and DP4 as well as DP3 and DP4 with $p < 0.015$. MI is significantly different between DP1 and DP2, DP1 and DP3, DP2 and DP3 as well as DP3 and DP4 with $p < 0.011$.

Chronic pain patients

22 female patients reported pain intensity values of 32.6 ± 6.7 for more than 6 months at the beginning of acupuncture treatment and a value of 17.5 ± 9 after the 10th session. 16 male patients reported pain intensity values 29.1 ± 9 for more than six months at the beginning and a value of 17.5 ± 12 after the last session. Pain intensity of both groups decreased highly significant $p < 0{,}004$ after 10 acupuncture sessions.

Table 2 shows the intensity of positive and negative mood scales of the female patients before the first and after the 10th acupuncture session. Positive mood scales increased and negative mood scales decreased in their intensity highly significant.

Table 3 shows the same analysis for the male patients. There was no significant influence of acupuncture on positive or negative mood scales of the male patients except the feeling of fatigue.

Fig. 6 supports the notion of different experience and neuronal processing of pain in women and men.

Fig. 6A shows the correlation between pain intensity at the beginning of the treatment (x-axis) and the reported change in pain intensity at the end of the therapy (y-axis). Women show with $r = -0.5$ a clear correlation meaning that the higher the pain intensity at the beginning the higher the pain relief at the end of acupuncture treatment. Men with $r = -0.2$ show no correlation. The difference in neuronal processing is also presented in Fig. 6B. Women show with $r = -0.7$ a strong correlation between pain intensity (x-axis) and MI (y-axis). Pain intensity and MI at the beginning (filled dots) as well as pain intensity and MI at the end of treatment (open dots) are very well correlated. High pain intensities are linked to more negative and low pain intensities to more positive mood scales. As can be concluded from Table 3 men have no measurable MI change in spite of feeling a significant pain relief at the end of the acupuncture treatment.

A clear difference between female and male chronic pain patients was also observed with the reaction of heart rate to acupuncture. Heart rate was measured before and after the acupuncture treatment in all 10 sessions. For women ($n = 16$) the mean heart rate before treatment was 78.8 ± 9.2 and showed a significant decrease ($p < 0.015$) after the treatment with 71.7 ± 7.8. For men ($n = 7$) the mean heart rate of 85.6 ± 11.4 before and of 78.2 ± 12 after the treatment were not significantly different ($p > 0.05$).

Discussion

Specificity of acupuncture points

To discriminate specific from unspecific effects of acupuncture sham acupuncture points as inert probe are commonly used for comparison with traditional acupuncture points. In a recent

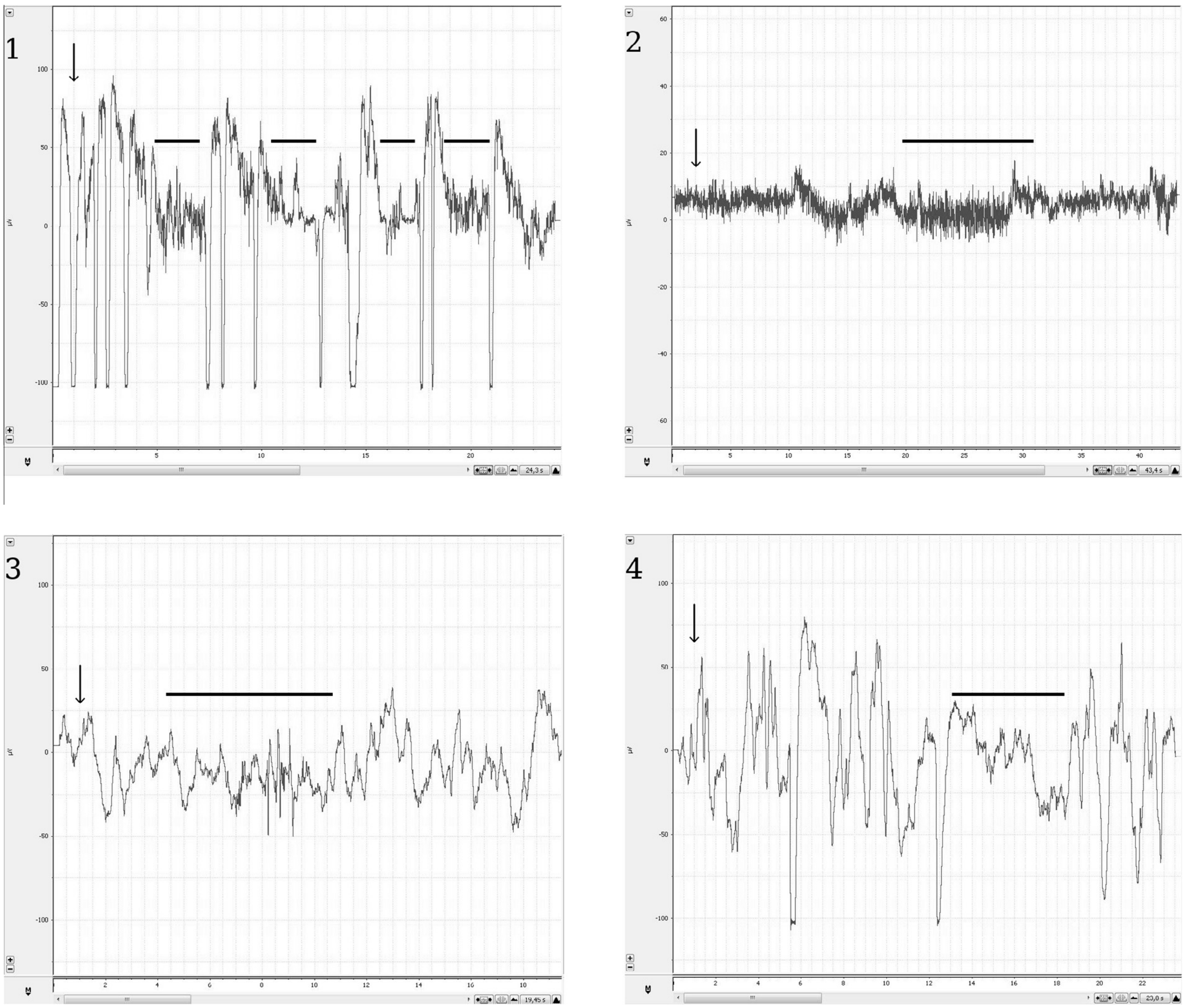

Fig. 5. Original EEG recordings of female patient shown in Fig. 3A and acupuncture at SP6 left leg (1) Acupuncture during the first session, (2) acupuncture after 10 sessions, (3) acupuncture after 1 year, (4) acupuncture after 1.5 years. Arrow indicates insertion of the needle, horizontal lines duration of needle rotation. EEG is shown in micro Volt (*y*-axis, μV) and time in seconds (*x*-axis).

Table 2
Mood scale values (Mean) and corresponding standard deviation (SD) of female patients with chronic pain before and after 10 acupuncture sessions. *n* = number of patients.

Mood	Activity	Elation	Contemplation	Calmness
Before				
Mean	0.39	0.33	0.31	0.53
SD	0.34	0.29	0.29	0.26
n	22	22	22	22
After				
Mean	0.63	0.72	0.55	0.70
SD	0.37	0.29	0.25	0.24
n	22	22	22	22
T-Test (*P*)	0.01551	0.00003	0.00203	0.01294
Mood	Anger	Excitement	Depression	Fatigue
Before				
Mean	0.23	0.54	0.34	0.38
SD	0.31	0.31	0.34	0.38
n	22	22	22	22
After				
Mean	0.035	0.122	0.043	0.139
SD	0.098	0.178	0.120	0.273
n	22	22	22	22
T-Test (*p*)	0.0035186	0.0000007	0.0001384	0.0082584

Table 3
Mood scale values (Mean) and corresponding standard deviation (SD) of male patients with chronic pain before and after 10 acupuncture sessions. *n* = number of patients.

Mood	Activity	Elation	Contemplation	Calmness
Before				
Mean	0.17	0.29	0.40	0.60
SD	0.2	0.4	0.2	0.3
n	16	16	16	16
After				
Mean	0.33	0.40	0.45	0.63
SD	0.4	0.4	0.3	0.3
n	16	16	16	16
T-Test (*p*)	0.081	0.204	0.296	0.406
Mood	Anger	Excitement	Depression	Fatigue
Before				
Mean	0.18	0.41	0.20	0.50
SD	0.3	0.4	0.3	0.3
n	16	16	16	16
After				
Mean	0.08	0.23	0.09	0.30
SD	0.16	0.33	0.22	0.34
n	16	16	16	16
T-Test (*p*)	0.11	0.07	0.13	0.04

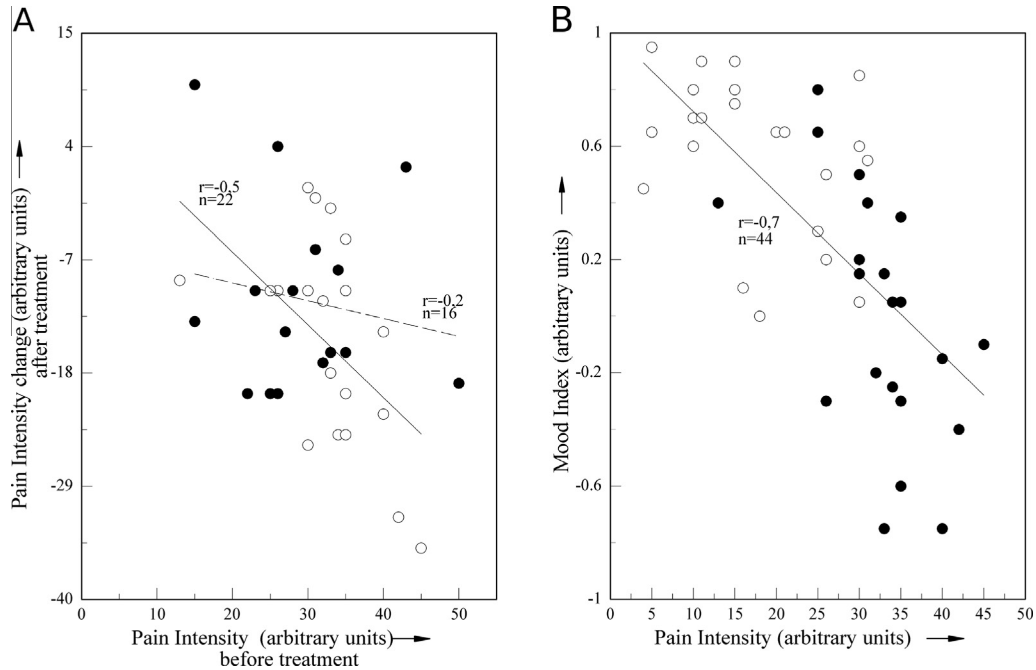

Fig. 6. Pain score and mood index (MI) (A) Relationship between initial pain intensity (*x*-axis, arbitrary units) and pain relief (*y*-axis, arbitrary units) after 10 acupuncture sessions. Open symbols, solid line: female patients; closed symbols, dashed line: male patients. Pearson correlation coefficient (women $r = -0.5$, men $r = -0.2$) and number of participants (women $n = 22$, men $n = 16$) are shown. Women only have a greater pain relief the higher the initial pain intensity. (B) Relationship between pain intensity (*x*-axis, arbitrary units) and MI (*y*-axis, arbitrary units) of 22 female patients before the first acupuncture treatment (closed symbols) and of the same 22 female patients after 10 acupuncture treatments (open symbols). Pearson correlation coefficient (r) and number of participants (n) are shown. $r = -0.7$ highlights the unique linear relationship.

meta-analysis [35] on 17922 patients with chronic pain significant differences between traditional and sham acupuncture could be shown disagreeing with a study on 2201 patients with no statistical difference in successful treatment of chronic pain using traditional acupuncture points or sham acupuncture [12]. In a meta-analysis of 18 randomized controlled trials traditional acupuncture was shown to be an appropriate adjunctive treatment for chemotherapy-induced nausea and vomiting [16]. A randomized controlled single-blind pilot study indicated that treating traditional acupuncture points may improve submaximal exercise tolerance of patients with chronic heart failure in contrast to sham points when given in addition to optimized standard heart failure medication. This improvement was associated with an optimized respiratory efficacy, post-exercise recovery, autonomous balance and reduction of inflammatory cytokines [27]. This effect might be related to highly significant activation of endothelial and neuronal nitric oxide synthase by ST36 electro-acupuncture as shown in animal experiments [22]. Combined acupuncture and placebo studies indicate that although traditional acupuncture plus high expectation and sham acupuncture plus high expectation induced subjective reports of analgesia of equal magnitude, fMRI analysis showed that traditional acupuncture produced greater fMRI signal decrease in pain related brain regions. This might hint to the existence of different mechanisms underlying traditional or sham acupuncture analgesia and expectancy evoked placebo analgesia [25]. When body self-recognition was disrupted by rubber hand illusion technique local blood flow to the site of LI4 acupuncture stimulation was reduced and brain activation was significantly decreased in the insula, a key brain region involved in the interoceptive system [8]. Traditional acupuncture points seem to have according to this discussion a high specific interaction with brain structures. Sham points however seem to have an interaction with lower intensity excluding their application as inert probe.

Brain function of acupuncture points

In awake burn-out syndrome patients the immediate fast interruption of unusual slow high amplitude EEG waves due to rotation of the acupuncture needle was unexpected (Figs. 3 and 5). The velocity of this response – probably mediated by afferent spinal nerve fibers of the connective tissue [33] – is comparable to the fast effects on cerebral circulatory response to needle rotation as measured by the fMRI-BOLD technique [13,21]. Slow high amplitude EEG waves are characteristic as delta waves for NREM (non rapid eye movement) sleep and are observed in EEG recordings of major depression patients after ketamine infusion or sleep deprivation [11]. Delta waves are described to be associated with activation of brainstem as well as inferior frontal gyrus, posterior cingulate cortex and precuneus [15], which are part of the DMN displaying the highest structure–function connectivity in the brain [20]. The task negative DMN is described to enable internal construction of mental models that support self-reference assessment and is involved in pain reception and emotion processing [21]. This set of functions seems to contrast with task positive goal-directed brain activities. Increased activity of DMN might represent a mechanism whereby certain cognitive deficits and/or symptoms may be exacerbated in neuropsychiatric disorders [4]. We hypothesize on the basis of the balance between task negative and task positive brain centers acupuncture might lead by long term facilitation to the improvement of mood scales of our patients.

Treatment with acupuncture points

Burn-out syndrome is associated with a deficit of executive functions that promote the ability to focus on relevant aspects of the environment and maintain a high level of task readiness. Burn-out patients have been described to show reduced P300 amplitudes and a lower alpha peak frequency as well as a reduced beta power. These EEG findings in burn-out patients differ from those described for depression and chronic fatigue patients suggesting that burn-out should be considered as a separate clinical syndrome [23,30]. We describe here for the first time slow high amplitude EEG waves recorded from five awake burn-out syndrome patients. The magnitude of the waves seems to correlate with the improvement of the mood scales (see Fig. 4). A significant improvement of the mood scales was observed after 10 treatments concomitant with a decrease in EEG wave amplitude. After 1–1.5 years without acupuncture mood scales significantly worsen again concomitant with a return of the EEG wave amplitude. The mood improvement was also observed after 10 sessions for the other five burn-out patients without slow high amplitude EEG waves (see Table 1). No gender difference was observed. This more accidently obtained result of slow EEG waves gave us the opportunity to evidence the very fast acupuncture–brain interaction. Furthermore this observation let us conclude a direct influence on task negative and task positive brain centers in all 48 patients treated for different diseases by our acupuncture rotating needling technique.

In spite of having equal pain relief by acupuncture treatment emotional and pain related brain structures seem to be differently affected in women and men. We quantify here for the first time a linear relationship between initial pain intensity and pain relief (see Fig. 6A) as well between initial pain intensity and mood scale improvement for women (see Fig. 6B) but not for men. This gender difference might be reflected by the differences in BOLD response to acupuncture. Needle rotation during acupuncture evoking *de qi* sensations induced significantly stronger deactivation of the LPNN/DMN system especially at the posterior cingulate, precuneus and angular gyrus in females but stronger activation at the sensorimotor network in males [34]. In support of our results of gender difference experimental pain studies have shown a significantly greater activation of blood flow in the left, contralateral, prefrontal, primary and secondary somatosensory, parietal, and insula cortices in male subjects compared with female subjects and a greater response in the perigenual cingulate cortex in female subjects [10]. Furthermore the BOLD response signal amplitude to experimental pain was significantly lower for women in the primary somatosensory cortex, the midanterior cingulate cortex, and the dorsolateral prefrontal cortex than for men [31].

The heart rate response to acupuncture point treatment highlights the interaction with the autonomic nervous system balancing sympathetic and parasympathetic activities. A significant parasympathetic stimulation by acupressure in female but not male patients underlines the proposed balancing effect [5].

Conclusion

The basis of the response to acupuncture seems to be related and explicable on the basis of differences in regional brain blood flow patterns. The traditional acupuncture points described for over 2000 years seem to allow physical treatment procedures with greater impact than sham acupuncture points. Not the needle insertion nor the resting needle in situ but the needle rotation seems to be the key physiological parameter to facilitate the acupuncture point brain interaction. We hypothesize this interaction to be revealed by mood scales recordings significantly correlated to EEG patterns as well as gender specific to pain intensity, pain relieve as well as heart rate characteristics.

Conflict of interest statement

None.

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