Acupuncture does not influence brainstem auditory evoked potentials: a volunteer crossover study

Taras I Usichenko,1 Peggy Lietz,1 Dragan Pavlovic,1 Reinhardt Schmidt,2 Michael Wendt,1 Alexander Mustea3

Abstract
Background Although acupuncture is effective for treating several conditions, its site specificity is questionable.

Objective To investigate whether acupuncture influences the brainstem auditory evoked potentials (BAEP).

Methods 10 healthy volunteers were enrolled according to inclusion criteria. One of four acupuncture points—TE3, GB43 (both auditory system-specific, according to traditional Chinese medicine) and non-specific acupuncture points HT7 and ST44—was needled during each session. Each volunteer received four sessions of acupuncture, with a 1-week interval between the sessions.

Results Peak latencies and amplitudes of the BAEP were registered before and during each session of acupuncture. Pain intensity and the incidence of paraesthesia (Qi sensation) during acupuncture were also registered. The peak latencies and amplitudes of the BAEP registered during acupuncture had not changed from the baseline levels. Needling of acupoint HT7 was most painful and induced the maximal incidence of Qi sensation.

Conclusions Findings suggest that monitoring the BAEP is not a suitable technique for studying the immediate effects of acupuncture.

INTRODUCTION
Acupuncture—peripheral sensory stimulation of certain predefined sites on the surface of the body—appears to be effective in the treatment of some conditions,1,2 and several physiological mechanisms explaining these clinical effects of acupuncture have been proposed.3 However, the site specificity of acupuncture points, claimed by traditional Chinese medicine (TCM), still remains a challenge to biomedical science.4

Although the evidence for site specificity of acupuncture derives mainly from clinical investigations, recent physiological evaluation of clinical acupuncture effects5 and experts’ recommendations for future research6 suggest that clinical trials are not a suitable arena in which to search for site-specific effects of acupuncture. The use of well-established, non-invasive methods of measuring the physiological response to peripheral sensory stimulation in experimental settings with healthy volunteers might be a more suitable alternative, since such methods allow a study of the site specificity of acupuncture under stringent crossover trial conditions. Recently, using the cortical auditory evoked potentials (CAEP) method on healthy volunteers,7 changes were found in latencies of CAEP components following stimulation of acupoints TE3 and GB43, claimed to be specific for the auditory system in TCM.8 The stimulation of non-specific points—HT7 (receiving the same innervation as TE3) and ST44 (receiving the same innervation as GB43)—produced no changes.

Another technique, the brainstem auditory evoked potentials (BAEP), consists of short-latency electrical signals produced by the nervous system within 10 ms in response to transient acoustic stimuli.9 Normal BAEP are a series of waves with vertex-positive peaks, representing the far-field potentials, generated by groups of neurons of the auditory pathway from cochlea to midbrain. Changes of the BAEP have been registered after acupuncture of patients with chronic pain and in patients with Parkinson’s disease.10,11 BAEP are more stable to functional changes in the body and yield less variable measurements than CAEP or somatosensory evoked potentials, both successfully used to study the influence of acupuncture on the central nervous system in experimental conditions.7,12 In comparison with functional MRI, which is currently the standard technique for investigating the cerebral effects of acupuncture,13 BAEP offer better temporal resolution, while studying immediate effects of peripheral sensory stimulation.

In this study we tried to answer the question, does stimulation applied to ‘auditory-specific’ acupoints TE3 and GB43 produce short-term effects on BAEP and do these effects differ from effects produced by the stimulation of the acupoints HT7 and ST44?

PARTICIPANTS AND METHODS
Subjects
Ten healthy volunteers (age 23–35, five women) naive to acupuncture were enrolled
in the study, which was approved by local ethics committee. The volunteers gave their informed consent to participate in the study and underwent standard audiometric tests (audiogram) to exclude hearing problems. None of the subjects was taking any medication or recreational drugs at the time of the study and clinical examinations revealed no psychological, nervous system or auditory abnormalities previous to the experiment. The volunteers were told that the influence of acupuncture on BAEP would be studied without a detailed explanation of the purpose of this investigation.

**BAEP recordings**

The experiments were performed in a standard audiometric, soundproof and air-conditioned room. An interval of 10 min was provided for each volunteer to adapt to the environment before beginning the experiment. Throughout the investigation session, the participants were in a supine position on a stretcher, with their eyes closed, to prevent interference with measurements due to eye movements.

The stimulation and registration of BAEP was performed with an ERA-Diagnostic System *evoselect* (Pilot GmbH, Blankenfelde, Germany). BAEP were elicited by 1000 clicks with a length of 150 μs, given monaurally via headphones with an intensity of 80 dB and 70 dB (HL), following the rate of stimulus at 20 Hz. The contralateral ear was exposed to a masking white noise at 30 dB lower

**Figure 1** Flow diagram of the study session. Each study session began with a 5 min preparation period, 5 min baseline BAEP recording before acupuncture (1. BAEP), 3 min of rest and 5 min of a second BAEP recording during the acupuncture procedure. BAEP, brainstem auditory evoked potentials.

**Figure 2** Acupuncture points, stimulated in the study. (A) TE3 acupoint is situated on the dorsum of the hand between the fourth and fifth metacarpal bones. (B) HT7 is located at the ulnar end of the transverse crease of the wrist. (C) Acupoint GB43 is situated on the dorsum of the foot, between the fourth and fifth toe and acupoint ST44 is located between the second and third toes, proximal to the web margin.
than the intensity of stimulation clicks. The recorded signals were averaged by the ERA-Diagnostic System computer program.

Standard Ag/AgCl electrodes were used for recording the procedures. The active electrode was placed at the vertex, the negative electrode was placed on the mastoid of the monitored side and the ground electrode at the right side of the forehead in accordance with the standard 10/20 electrodes system by the International Federation of Societies for Encephalography and Clinical Neurophysiology.14

Each study session began with a 5 min preparation period (sticking the electrodes), 5 min of baseline BAEP recording before acupuncture, 3 min of rest and 5 min of a second BAEP recording during the acupuncture procedure (figure 1).

### Acupuncture

Each subject received acupuncture four times—once at each of the ‘auditory-specific’ acupoints TE3 and GB43 and once at each of the auditory non-specific acupuncture points HT7 and ST44. The TE3 acupoint is situated on the dorsum of the hand between the fourth and fifth metacarpal bones, in the depression proximal to the metacarpophalangeal joint (figure 2A). Acupoint GB43 is situated on the dorsum of the foot, between the fourth and fifth toe, proximal to the margin of the web (figure 2C). HT7 is located at the ulnar end of the transverse crease of the wrist, in the depression on the radial side of the tendon of M. flexor carpi ulnaris (figure 2B). Acupoint ST44 is located between the second and third toes, proximal to the web margin and lateral to the second metatarsophalangeal joint (figure 2C). Each pair of acupoints: TE3/HT7 and GB43/ST44 (specific/non-specific) received the innervation from the same dermatome. The pair TE3/HT7 received the innervation from dermatome C8-Th1 via the ulnar nerve and pair GB43/ST44 received innervation from L4/5-S1 via the superficial peroneal nerve. The sequence of acupuncture points to be stimulated with simultaneous registration of the BAEP was chosen at random. In each subject, only one point was punctured during a session, so that for each patient the entire experiment consisted of four study sessions. Randomisation of the sessions was achieved by tossing a coin: twice before the very first session—to choose ‘auditory-specific’ versus non-specific and ‘hand’ acupoint versus ‘foot’ acupoint. Before the second and third session the coin was tossed only once. The recovery interval between the sessions was at least 1 week, to avoid the influence of residual acupuncture effects.15

The acupoints on the left side were used for puncture with stainless steel needles, sized 0.25×25 mm (Asia Med GmbH, Suhl, Germany). The needles were inserted into each participant 2 min after the first registration of BAEP, perpendicular to the skin surface, to a depth of 5–10 mm and rotated once forward and backward. The needles were retained in situ during the second BAEP registration without manual stimulation and withdrawn after registration was terminated.


The volunteers and investigators who performed the registration of BAEP and other outcome measures had no previous knowledge of acupuncture and thus were blinded to the location and the specificity of acupuncture points.

### End points and data analysis

The absolute peak latencies of waves I, III and V, interpeak latencies I–III, I–V and III–V were registered automatically. The amplitudes of waves I, III and V were subsequently measured manually from the curves on the acquired graphs. At the end of each study session the volunteers were asked to report the intensity of pain, felt immediately after insertion of the acupuncture needle, according to a 100 mm visual analogue scale and their subjective sensations, matching the Qi description in TCM (heaviness, fullness, warmth, cooling, tingling, numbness, pressure).

Normally distributed data were analysed using the Student t test for paired samples, non-parametric data were analysed using Wilcoxon signed rank, both tests with subsequent Bonferroni adjustment for repeated comparisons (SPSS 13 for Mac OS X). Dichotomous data were
Table 1  Peak latencies and amplitudes of BAEP, stimulated with 80 dB intensity, before acupuncture (BAEP1) and after insertion of the acupuncture needle (BAEP2) in acupoints TE3, HT7, GB43 and ST44

<table>
<thead>
<tr>
<th></th>
<th>Peak latencies (ms)</th>
<th>Amplitudes (nV)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
<td>III</td>
</tr>
<tr>
<td></td>
<td>R</td>
<td>L</td>
</tr>
<tr>
<td>TE3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BAEP1</td>
<td>1.78±0.14</td>
<td>1.64±0.11</td>
</tr>
<tr>
<td>BAEP2</td>
<td>1.76±0.18</td>
<td>1.62±0.08</td>
</tr>
<tr>
<td>p Value (uncorrected)</td>
<td>0.72</td>
<td>0.44</td>
</tr>
<tr>
<td>HT7</td>
<td></td>
<td></td>
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<tr>
<td>BAEP1</td>
<td>1.74±0.08</td>
<td>1.53±0.17</td>
</tr>
<tr>
<td>BAEP2</td>
<td>1.75±0.13</td>
<td>1.51±0.09</td>
</tr>
<tr>
<td>p Value (uncorrected)</td>
<td>0.66</td>
<td>0.49</td>
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<tr>
<td>GB43</td>
<td></td>
<td></td>
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<tr>
<td>BAEP1</td>
<td>1.71±0.13</td>
<td>1.59±0.08</td>
</tr>
<tr>
<td>BAEP2</td>
<td>1.73±0.14</td>
<td>1.64±0.11</td>
</tr>
<tr>
<td>p Value (uncorrected)</td>
<td>0.32</td>
<td>0.25</td>
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<tr>
<td>ST44</td>
<td></td>
<td></td>
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<tr>
<td>BAEP1</td>
<td>1.67±0.12</td>
<td>1.56±0.12</td>
</tr>
<tr>
<td>BAEP2</td>
<td>1.74±0.14</td>
<td>1.61±0.10</td>
</tr>
<tr>
<td>p Value (uncorrected)</td>
<td>0.26</td>
<td>0.43</td>
</tr>
</tbody>
</table>

Statistically significant p values are shown in bold. Comparison BAEP1 vs BAEP2 is analysed using Student’s t test for paired samples (latencies) and Wilcoxon signed rank (amplitudes). p Values are given uncorrected. BAEP, brainstem auditory evoked potentials; L, stimulation of the left ear; R, stimulation of the right ear.
analysed using Fisher’s exact test. The differences occurring with p<0.05 were considered statistically significant.

RESULTS
The peak latencies and amplitudes of the waves I, III and V (table 1) and interpeak latencies I–III, I–V and III–V (data not shown) of the BAEP registered during acupuncture had not changed from the baseline level. Analysed as single tests for paired samples, the latency of wave V during stimulation of the left ear was reduced after acupuncture of GB43 in comparison with baseline (p=0.03); the amplitude of wave V under stimulation of the right ear was reduced after acupuncture of HT7 (p=0.031) and increased after ST44 acupuncture (p=0.03) in comparison with baseline. However, after Bonferroni correction for multiple comparisons these changes appeared to be accidental.

There were no differences in the effects of stimulation produced on the BAEP between ‘auditory-specific’ TE3/GB43 acupoints and non-specific HT7/ST44 acupoints.

The intraindividual pain intensity varied during needling of the different acupoints (p=0.032; Friedman’s test). Needling of acupoint HT7 was most painful (median 21 mm; 100 mm visual analogue scale) and induced Qi sensation in six out of 10 volunteers in comparison with only one volunteer during needling of GB43 and ST44 acupoints (p<0.05; Fisher’s exact test). The needling of TE3 was less painful, even though it produced the same incidence of Qi sensation as the needling of HT7 (figure 3).

DISCUSSION
This crossover investigation in healthy volunteers failed to provide the expected immediate changes in the BAEP during acupuncture applied to ‘auditory-specific’ acupoints. The BAEP, generated by neurons of the auditory pathway, are the most commonly used evoked brain responses, being applied to study the integrity of the peripheral and brainstem auditory system. The BAEP are strongly dependent upon stimulation parameters and the morphology of the auditory system and can be modified by lesions of the brainstem derived from tumours, trauma, haemorrhage, ischaemia, demyelination or metabolic insult. The BAEP are only minimally affected by the level of consciousness, sedatives and general anaesthesia; however, significant changes of BAEP were described in patients with neuropathies of various origin (diabetic, toxic—aminoglycoside antibiotics and cytostatic drugs), in patients with Alzheimer’s disease and multiple sclerosis. In healthy people, age, hypobaric hypoxia (mimicking high altitude) and physiological oestrogen fluctuations influence the latencies of BAEP.

Kumar et al found an increase in peak latencies and a decrease in amplitudes of BAEP waves, in correlation with reduced intensity of clinical pain following 10 sessions of electroacupuncture in patients with chronic cervical and lumbar pain. Their findings were strengthened by results of Wang et al, who described a decrease of the absolute and interpeak latencies in patients with Parkinson’s disease after acupuncture treatment. In their study manual acupuncture was applied every second day for 3 months. Interestingly, those changes in the BAEP waves correlated with the clinical improvement score. The absence of an effect of acupuncture on the BAEP in our investigation might be due to the short monitoring period and the investigation of healthy volunteers only, rather than patients, as in previous clinical investigations.

During the acupuncture, acupoint HT7 was the most painful and needling of both hand acupoints HT7 and TE3 was associated with a maximal incidence of Qi sensation, in comparison with the needling of acupoints GB43 and ST44 on the foot; this corresponds to the anatomy of regional innervation, with a higher-density of nerve fibres in the hands and glabrous skin and a lower density in the feet. The limitations of our investigation are (1) the effects sought were the immediate effects of acupuncture on BAEP, whereas the potential delayed effects, which were beyond the scope of this investigation, were not studied; (2) follow-up investigations at only few time-points; (3) lack of control for the menstrual cycle, which might have influenced BAEP, in the five female volunteers in our study. These limitations, however, do not prevent the conclusion that monitoring the BAEP is probably not an appropriate method for searching for immediate effects of peripheral sensory stimulation (acupuncture) in healthy subjects.

CONCLUSIONS
The findings of this investigation show that acupuncture does not have an immediate effect on BAEP. Thus the question of site specificity of acupuncture points cannot be solved with this technique using the present design. However, in the light of previous investigations, the pain-modulating effects of acupuncture at the level of brainstem (due to its action on the diffuse noxious inhibitory control system) might be the potential object of BAEP monitoring in future studies with experimentally induced pain.

Summary points

▶ Brainstem auditory evoked potentials have some advantages in exploring the mechanisms of sensory stimulation
▶ We made recordings while stimulating four acupuncture points in 10 healthy volunteers
▶ We found no change in the evoked potentials

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Competing interests None.

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