Different effects of transcutaneous electric nerve stimulation and electroacupuncture at ST36–ST37 on the cerebral cortex

Yu-Tien Kang,1,2 Yi-Sheng Liao,3 Ching-Liang Hsieh4,5,6

For numbered affiliations see end of article.

Correspondence to Professor Ching-Liang Hsieh, Graduate Institute of Integrated Medicine, College of Chinese Medicine, China Medical University, No 91, Hsueh-Shih Road, Taichung 40402, Taiwan; chsieh@mail.cmuh.org.tw

ABSTRACT

Background The effects of transcutaneous electric nerve stimulation (TENS) and electroacupuncture (EA) on the cerebral cortex are largely unclear. The purpose of the present study was to investigate the effect of TENS and EA on the cerebral cortex by examining their effect on the median nerve-somatosensory evoked potentials (MN-SEPs).

Methods Twenty volunteers were studied. The cortical and cervical spinal potentials were recorded by median nerve stimulation at the left wrist. Sham TENS, 2 Hz TENS and 2 Hz EA were applied to both ST36 and ST37. MN-SEPs were recorded during sham TENS, 2 Hz TENS and 2 Hz EA, with at least 1 week interval for each subject. One-way analysis of variance was used to determine the differences in latency and amplitude of the MN-SEPs observed in the stimulation and post-stimulation periods compared with baseline. Scheffe's post hoc correction was employed to identify pairwise differences.

Results No differences in mean latency were found between the stimulation procedures during the stimulation and post-stimulation periods. 2 Hz EA but not sham TENS or 2 Hz TENS caused higher mean amplitudes in N20 and N30 during the stimulation and post-stimulation periods.

Conclusions EA, but not TENS, induces changes in certain components of the signal.

INTRODUCTION

Acupuncture has been used to treat human diseases and relieve pain in China and nearby countries for thousands of years,1 and is becoming popular around the world. The classic medical acupuncture (MA) uses needles typically made of stainless steel, which vary in length for applications on different body parts. The needles may be manipulated in various ways—for example, spun, flicked or moved up and down relative to the skin—or following the recommendations of particular schools.2 While MA is still widely used in clinical practice, the recent development of acupuncture has introduced new techniques using the assistance of electronic devices—for example, electroacupuncture (EA).3 During EA treatment, needle pairs are inserted on acupuncture points and attached to an electric pulse generator in which frequency and intensity of the impulse can be adjusted. Medical scientists have also recently begun to explore the use of another non-invasive technique—transcutaneous electric nerve stimulation (TENS)—in which two or more leads connected to continuous electric pulse generator are stuck on the skin to control certain forms of pain4–6 and to improve other symptoms such as urinary frequency, urgency, nocturia and incontinence.7 However, it remains controversial whether TENS can be used to control pain in the same way as EA. Further understanding of the efficacy and physiological mechanisms of these electrical-based stimulating techniques are needed to make proper use of them.

Evoked potentials are the electrical signals generated by the nervous system in response to sensory stimulation. Because the evoked potentials protocol is a simple, non-invasive and safe method, it has been widely applied in the functional assessment of nervous system disease and as a tool for the study of acupuncture analgesia.8 Somatosensory evoked potentials (SEPs) are widely employed as many SEPs components
have been identified, and are therefore commonly used as an electrophysiological indicator in the evaluation of nervous system disorders. They are generated in afferent pathways, subcortical structures and various regions of the cerebral cortex, either by stimulation of somatic receptors or electrical stimulation of peripheral nerves. Stimulation of the median nerve to create median nerve SEPs (MN-SEPs) is the most common approach for clinical diagnosis and human electrophysiological study, including acupuncture.

ST36 Zusanli is the classically used acupuncture point for treating digestive diseases and other health problems. Many studies have investigated the effect of stimulating ST36 in humans, either by MA or EA. The nearby ST37 Shangjuxu acupuncture point has also been a target of investigation. In a previous study we showed that 2 Hz EA at ST36 and ST37 can enhance excitation of the cerebral cortex. The present study attempted to discern the distinct neuronal actions in the cerebral cortex of EA and TENS when ST36 and ST37 are stimulated bilaterally, using short-latency MN-SEPs recordings.

MATERIALS AND METHODS

Subjects
Twenty volunteers were recruited as research subjects and all gave their informed consent to participate in the study. None of the subjects was taking any medication during the research period and clinical examinations revealed no nervous system, psychiatric or severe heart diseases. The experiment was performed in a quiet air-conditioned room with a constant temperature of 24–25°C. During the experiment the subjects were awake and relaxed, lying in a supine position on a comfortable bed. Oscilloscope monitoring was conducted to ensure the subjects were awake during the experiment.

MN-SEP recordings
Silver-silver chloride disc electrodes were placed at CV7 (level of the seventh cervical vertebrae) and at the hand representation area of the right somatosensory cortex (2 cm posterior to the Cz point and 7 cm towards the external auditory meatus) to serve as an active recording electrode according to the ‘10–20’ system—that is, the distance between adjacent electrodes se either 10% or 20% of the total distance from front to back and from right to left in the skull. Silver-silver chloride disc electrodes were placed at A1 and A2 point (bilateral ear lobe) as reference recording electrodes. The electrode impedance was maintained at less than 5 kΩ. Square-wave electrical pulse stimuli, 0.2 ms in duration and 4 Hz in frequency, were delivered through surface stimulus electrodes to the median nerve at the left wrist region. The level of intensity (from 7 to 21 mA) was sufficient to cause a 1–2 cm thumb movement. Ground electrodes were placed on the left forearm and forehead to reduce stimulus artefact (figure 1).

The MN-SEP recordings were obtained using a Medelec Synergy averager (Oxford Instruments, UK) with bandpass filter setting between 20 and 3000 Hz.

Figure 1 Position of electrodes of left median nerve-somatosensory evoked potentials. +, anode of stimulator; −, cathode of stimulator; G, ground electrode; Cz, Cz position of international 10–20 system; HRA, hand representation area (2 cm posterior Cz and 7 cm towards external auditory meatus); Cv7, skin surface of seventh cervical spine; A1 and A2, bilateral ear lobe; Medelec Synergy, electrode box of Medelec Synergy machine.
A total of 1000 responses were averaged with an analysis time of 100 ms. In each session, the trial was repeated at least twice to assure reproducibility of N13, N20, P25 and N30 components. The amplitudes were measured from onset of response to their peaks, and the latencies were measured from stimulus artefact to peak (figure 2).

**Stimulation procedures**

Tibial nerve (TN-SEPs) has also been used for detecting particular diseases and in studies of neurophysiology. However, to prevent the production of attenuation or interference when stimulating ST36 and ST37, MN-SEPs but not TN-SEPs were used in this study. Three different stimulation procedures including sham TENS, 2 Hz TENS and 2 Hz EA were performed in each subject over a period of at least 1 week to prevent any residual effect. The order was 2 Hz TENS, then sham TENS followed by 2 Hz EA for each subject because we hoped that starting with a non-invasive intervention may reduce the dropout rate. To perform sham TENS, electrodes were placed on the surface of both ST36 and ST37 bilaterally (located on the fibular side of the tibial tuberosity), but no electrical stimulation was delivered throughout the experiment. For 2 Hz EA, acupuncture needles (sterile stainless needles, 0.30 mm diameter, 50 mm length, Yuguang Corporation, Taiwan) were inserted into both ST36 and ST37 bilaterally and then twisted to obtain de qi, then 2 Hz bidirectional symmetric square wave (0.6 ms pulse width) electrical pulses were applied using the stimulator (Han’s Acupoint Nerve Stimulator (HANS), LH-202, Huawei Co, Beijing, China) between the two adjacent needles. The stimulus intensity (from 1 to 6 mA) was adjusted to generate visible twitching of the anterior tibial muscle. For the high-intensity low-frequency TENS, a portable battery-powered stimulator (HANS, LH-202) was used; 2 Hz bidirectional symmetric square wave electrical pulses were applied via electrodes placed on the surface of both ST36 and ST37 acupuncture points bilaterally. The stimulus intensity (from 12 to 24 mA) was adjusted to generate visible twitching of the anterior tibial muscle.

MN-SEP recordings were obtained at baseline, during the stimulation period and the post-stimulation period. The baseline MN-SEP recordings were obtained prior to sham TENS, 2 Hz TENS and 2 Hz EA stimulation. For MN-SEP recordings during the stimulation period, the signals were collected 5 min after starting sham TENS, 2 Hz TENS and 2 Hz EA. The application of sham TENS, 2 Hz TENS and 2 Hz EA lasted for 15 min. The acupuncture needles or electrodes were removed immediately afterwards and MN-SEPs of the post-stimulation period were recorded 20 min later.

**Statistical analysis**

The data were presented as mean±SD. One-way analysis of variance was used to determine the differences in amplitude and latency of the MN-SEPs observed in the stimulation period and post-stimulation period compared with baseline in the three stimulation procedures. Scheffé’s post hoc correction was employed to identify pairwise differences. A p value of <0.05 was considered statistically significant.

**RESULTS**

Twenty subjects (7 men and 13 women) completed the study. Their ages ranged from 24 to 32 years with a mean of 28.5±2.4 years, their height ranged from 147 to 183 cm with a mean of 163.1±8.8 cm and their weight ranged from 48 to 106 kg with a mean of 60.4±12.6 kg. Figure 2 shows a typical example of MN-SEP recordings induced by electrical stimulation on the left wrist of a research subject.

The mean latency of MN-SEPs observed in the stimulation and post-stimulation periods compared with baseline in each component during sham TENS, 2 Hz TENS and 2 Hz EA is summarised in table 1 and figure 3. No differences were found between the stimulation procedures. The mean amplitude observed in the stimulation and post-stimulation periods during sham TENS, 2 Hz TENS and 2 Hz EA is summarised in table 2 and figure 3. Differences in mean amplitude were found in N20 and N30 during 2 Hz EA. Subjects treated with EA demonstrated a higher mean amplitude in N20 during the stimulation and post-stimulation periods compared with baseline. These effects were not observed when subjects were treated with sham TENS or 2 Hz TENS. In N30 when treated with EA, the difference only appeared during the stimulation period compared with baseline but not during the post-stimulation period.

No significance differences were observed in other components of MN-SEPs, either for mean latency or amplitude.
DISCUSSION

The application of 2 Hz EA to both ST36 and ST37 increased the amplitudes of the N20 component during the stimulation and post-stimulation periods; the increase was also significant in the N30 component during the stimulation period but not in the post-stimulation period.

Some evidence has suggested that the cerebral cortex plays a modulatory role in the treatment effects of MA and EA. Although most evidence points to the site of action of TENS being in the spinal cord, at the suprasegmental levels as well as at the dorsal horn, recent imaging studies indicated that TENS also acts on the cerebral cortex. For example, Koçyigit et al. conducted a functional MRI (fMRI) study comparing low-frequency TENS and sham TENS and found that low-frequency TENS decreased perceived pain intensity and pain-specific activation of the contralateral primary somatosensory cortex, bilateral caudal anterior cingulate cortex and of the ipsilateral supplementary motor area. Kara et al. showed that the fMRI signal of secondary somatosensory regions, ipsilateral primary motor cortex, contralateral supplementary motor cortex, contralateral parahippocampal gyrus, contralateral lingual gyrus and bilateral superior temporal gyrus of the TENS-treated group decreased in the post-stimulation period compared with baseline, but these changes were not seen in the sham TENS group. Napadow et al demonstrated that 2 Hz EA at common acupuncture points for all patients with carpal tunnel syndrome plus MA at three acupuncture points chosen from a six-point list to resolve individual symptoms showed promise in inducing beneficial cortical plasticity manifested by more focused digital representations.

The N20 component is generated in the thalamo-cortical projection or at the posterior bank of the central sulcus, corresponding to area 3b of the primary somatosensory cortex. P25 and N20 originate from two different cortical sources. P25 is a radial dipole while N20 is a tangential dipole of the primary somatosensory cortex. The source of the N30 component has been attributed to the motor cortex or the supplementary motor area. It is reasonable to conclude that 2 Hz EA but not 2 Hz TENS on ST36 and ST37 induced excitability of the somatosensory or motor cortex, or supplementary motor area, as evidenced by the MN-SEP recordings. However, it should be noted that the electrodes of 2 Hz TENS in this study were placed on the surface of both ST36 and ST37 bilaterally. The distance between the TENS electrodes and the deep peroneal nerve was greater than EA with needles inserted into the muscle layer and, thus, TENS might have stimulated a different set of nerves. Stasis in MN-SEPs during 2 Hz TENS suggests that the stimulation technique does not share a similar electrophysiological action with that of 2 Hz EA in the cerebral cortex. The N13 component is

<table>
<thead>
<tr>
<th>Components</th>
<th>Sham TENS</th>
<th>2 Hz TENS</th>
<th>2 Hz EA</th>
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<tbody>
<tr>
<td>N13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>11.99±0.78</td>
<td>12.00±0.80</td>
<td>12.01±0.89</td>
</tr>
<tr>
<td>Stim</td>
<td>11.97±0.76</td>
<td>12.02±0.83</td>
<td>11.93±0.89</td>
</tr>
<tr>
<td>Post-stim</td>
<td>12.03±0.78</td>
<td>11.98±0.82</td>
<td>11.92±0.86</td>
</tr>
<tr>
<td>N20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>17.73±0.91</td>
<td>17.69±0.85</td>
<td>17.66±0.88</td>
</tr>
<tr>
<td>Stim</td>
<td>17.77±0.91</td>
<td>17.78±0.81</td>
<td>17.79±0.87</td>
</tr>
<tr>
<td>Post-stim</td>
<td>17.85±0.92</td>
<td>17.80±0.79</td>
<td>17.84±0.88</td>
</tr>
<tr>
<td>P25</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>22.19±1.78</td>
<td>22.48±1.85</td>
<td>22.56±2.10</td>
</tr>
<tr>
<td>Stim</td>
<td>22.16±1.74</td>
<td>22.51±1.81</td>
<td>22.51±1.83</td>
</tr>
<tr>
<td>Post-stim</td>
<td>22.25±1.76</td>
<td>22.42±1.78</td>
<td>22.53±1.82</td>
</tr>
<tr>
<td>N30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>30.02±1.78</td>
<td>29.42±2.20</td>
<td>30.42±1.86</td>
</tr>
<tr>
<td>Stim</td>
<td>30.05±2.18</td>
<td>29.69±2.30</td>
<td>30.34±1.90</td>
</tr>
<tr>
<td>Post-stim</td>
<td>30.43±1.89</td>
<td>29.83±2.18</td>
<td>30.42±1.92</td>
</tr>
</tbody>
</table>

N13, N20, P25 and N30 are four components of MN-SEPs. Post-Stim, post-stimulation period; Stim, stimulation period.
generated in the dorsal column of the cervical cord.28
Because the mean amplitude of N13 did not change, the relationship of the spinal cord with EA and TENS requires further study.

The major strength of this study is in using ST36 and ST37 which are 3 cm apart, suiting the need to form a circuit during electrical stimulation for EA and TENS. This study was not without limitations. Its main drawback is that modulation of monosynaptic reflex activity in the spinal cord (eg, H-reflex) was not examined and thus it was not possible to conclude whether TENS acted on the spinal cord when stimulating on ST36 and ST37. Second, MN-SEP recordings do not resolve detailed functional changes as does fMRI—that is to say, the lack of evidence in MN-SEPs does not necessarily mean that no changes would be observed in fMRI.

The gate control theory is used to explain part of the mechanism of acupuncture analgesia. In this theory, the pain perception fiber transmits the pain signal into the brain cortex: somatosensory evoked potentials.31 Acupuncture at GB34 can increase postsynaptic dopamine neurotransmission to improve motor function in 1-methyl-4-phenyl 1,2,3,6-tetrahydropyridine (MPTP)-induced Parkinson’s disease mouse model.32

Effective mechanisms of acupuncture are therefore mediated via multiple pathways in the CNS including signal transmission, neuropeptides release and synaptic transmission.

In summary, we compared the cortical responses to TENS and EA using SEPs and found EA but not TENS induced changes in certain components of the signal.

<table>
<thead>
<tr>
<th>Components</th>
<th>Sham TENS</th>
<th>2 Hz TENS</th>
<th>2 Hz EA</th>
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<tbody>
<tr>
<td>N13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>1.09±0.40</td>
<td>1.15±0.37</td>
<td>1.12±0.38</td>
</tr>
<tr>
<td>Stim</td>
<td>1.09±0.24</td>
<td>1.14±0.28</td>
<td>1.14±0.45</td>
</tr>
<tr>
<td>Post-Stim</td>
<td>1.01±0.39</td>
<td>1.07±0.26</td>
<td>1.22±0.42</td>
</tr>
<tr>
<td>N20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>1.38±0.67</td>
<td>1.23±0.64</td>
<td>1.31±0.66</td>
</tr>
<tr>
<td>Stim</td>
<td>1.42±0.73</td>
<td>1.27±0.67</td>
<td>1.47±0.61*</td>
</tr>
<tr>
<td>Post-Stim</td>
<td>1.32±0.73</td>
<td>1.28±0.65</td>
<td>1.42±0.53*</td>
</tr>
<tr>
<td>P25</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>1.13±0.91</td>
<td>0.96±0.84</td>
<td>1.34±0.97</td>
</tr>
<tr>
<td>Stim</td>
<td>1.13±1.01</td>
<td>0.94±0.93</td>
<td>1.37±1.34</td>
</tr>
<tr>
<td>Post-Stim</td>
<td>1.22±1.12</td>
<td>0.98±0.91</td>
<td>1.37±1.24</td>
</tr>
<tr>
<td>N30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>0.93±0.62</td>
<td>0.90±0.46</td>
<td>0.98±0.68</td>
</tr>
<tr>
<td>Stim</td>
<td>1.10±0.77</td>
<td>0.99±0.40</td>
<td>1.15±0.71*</td>
</tr>
<tr>
<td>Post-Stim</td>
<td>1.09±0.82</td>
<td>1.08±0.45</td>
<td>1.07±0.72</td>
</tr>
</tbody>
</table>

N13, N20, P25 and N30 are four components of MN-SEPs. *p<0.05 compared with baseline. Post-Stim, post-stimulation period; Stim, stimulation period.

Summary points

- Standardised nerve stimulation produces signals in the brain cortex: somatosensory evoked potentials.
- We tested whether TENS or EA influenced these signals.
- EA, but not TENS, influenced the amplitude but not the latency of the signals.

Author affiliations
1Graduate Institute of Chinese Medicine, College of Chinese Medicine, China Medical University, Taichung, Taiwan
2Department of Traditional Chinese Medicine, Taichung Veterans General Hospital, Taichung, Taiwan
3Department of Neurology, Taichung Hospital, Ministry of Health and Welfare, Taichung, Taiwan
4Graduate Institute of Integrated Medicine, College of Chinese Medicine, China Medical University, Taichung, Taiwan
5Department of Chinese Medicine, China Medical University Hospital, Taichung, Taiwan
6Research Center for Chinese Medicine and Acupuncture, China Medical University, Taichung, Taiwan

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Contributors Y-TK performed the experiment. Y-SL participated in the discussion and helped with the experiment. C-LH and Y-TK designed the study protocol and prepared the manuscript. All the authors have read and approved the final manuscript.

Competing interests None.

Patient consent Obtained.

Ethics approval The research protocol of this study was approved by the Research Ethics Committee, China Medical University and Hospital, Taichung, Taiwan (DMB95-IRB-167, ICF Version date 29 November 2006).

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