Physiological changes associated with de qi during electroacupuncture to LI4 and LI11: a randomised, placebo-controlled trial

David Tai Wai Yu,1 Alice Yee Men Jones2

ABSTRACT

Background Studies on the relationship between de qi intensity and activity changes in the autonomic nervous system (ANS) are scarce. This study investigates the physiological responses associated with de qi. The relationship between de qi intensity and such responses was determined.

Method This was a single-blinded, randomised, placebo-controlled trial. A total of 36 subjects (19 men, 17 women), aged 34.5±4.6 years, were randomly assigned to group 1 (electroacupuncture at 2 Hz, 0.4 ms to right LI4 and LI11 for 30 min), group 2 (electroacupuncture stimulation to bilateral patellae) or group 3 (sham electroacupuncture to right LI4 and LI11 but over Duoderm pads). Heart rate (HR), mean arterial blood pressure (MAP) and HR variability by low/high frequency (LF/HF) were recorded 5 min before, during and 5 min after the intervention. Needle sensations were quantified by the Modified Massachusetts General Hospital Acupuncture Sensation Scale – Chinese version (C-MMASS) and the C-MMASS index was computed.

Results A significant increase in LF/HF, MAP and HR was observed in group 1. A small and significant increase in LF/HF was observed in group 2 but the changes in MAP and HR in groups 2 and 3 were not significant. The C-MMASS index was highest in group 1 (5.3±1.3), moderate in group 2 (3.5±0.7) and lowest in group 3 (0.77±0.2). A positive correlation between de qi intensity and changes in LF/HF, MAP and HR was observed.

Conclusions This study suggests that de qi is associated with physiological changes, and that de qi intensity increases with an increase in sympathetic discharge of the ANS.

INTRODUCTION

According to the conceptual framework of Traditional Chinese Medicine (TCM), it was believed that disharmony and imbalance between yin and yang and disruption of qi (energy) flow along the energy channels (meridians) may affect health.1 Through stimulation of acupuncture points, the flow of qi is believed to be modulated, leading to restoration of health. When qi is ‘tapped’ by acupuncture, the subject may experience distinct sensations known as de qi.2–5 These sensations are considered to be essential for effective acupuncture stimulation.1 6 7 Though solid evidence is still lacking.2

In Western medicine, the concept of ‘restoration of balance of yin–yang’ is explained by modulation of the sympathetic and parasympathetic outputs of the autonomic nervous system (ANS).1 8 9 Currently, heart rate variability (HRV) is commonly used to determine effects on modulation of the ANS in acupuncture studies.10–12 However, reports on whether acupuncture activates or suppresses the sympathetic or parasympathetic outputs have been inconsistent. For example, acupuncture to GV14, PC613 and BL1514 were shown to facilitate parasympathetic and suppress sympathetic activities whereas stimulation of LI4 showed significant increase in sympathetic activity.15 16 Furthermore, reports on the relationship between the acupuncture sensations intensity and changes in the ANS activities are scarce. Whether these sensations are necessary to evoke changes in the ANS, and whether stimulation to non-acupuncture points could produce similar ANS changes, have not been investigated.

The aims of this study were to investigate the physiological responses associated with acupuncture sensations during electrostimulation of acupuncture points and to determine the correlation between the intensity of these sensations and such responses.
**METHODOLOGY**

This study adopted a randomised, placebo-controlled trial design. Approval to conduct the study was granted by the Human Subjects Ethics Subcommittee of The Hong Kong Polytechnic University (project ID: HSEARS20110510001).

**Subjects**

A convenience sampling method was adopted for subject recruitment. Inclusion criteria included normal health without known cardiovascular, respiratory, neurological or psychological dysfunction; naïve to acupuncture and ability to read Chinese. Subjects with medical disorders or those required to take medications that might affect the cardiovascular system within 1 week prior to the study, or with uncomfortable sensations of the upper and lower limbs, were excluded. All subjects were informed of the aims of the study. Written consent was obtained from each subject prior to data collection.

**Randomisation**

Recruited subjects were randomly assigned to one of three groups and blinded to the other two groups. Three sets of group numbers were generated by computer and placed in opaque sealed envelopes. Subjects were asked to draw one envelope that contained a random group number. The drawn envelope was then opened by an independent investigator who did not participate in the study process.

For group 1, electroacupuncture was applied to right LI4 and LI11. These two points were selected since they are most frequently reported in clinical studies associated with the ANS activity. For group 2, electroacupuncture was applied to a point at 10 mm below each patellar, that is, into the patellar tendons where there are no acupuncture points. For group 3, four Duoderm pads (Convatec, Skillman, New Jersey, USA), of size 10 mm×10 mm were attached to the needles and connected to an electroacupuncture device (ITO, ES-160, Hannover, Germany). Electrical stimulation was applied for 30 min at a frequency of 2 Hz, pulse duration at 0.4 ms. These parameters were adopted following a study by Knardahl et al. It was believed that low-frequency (LF) electroacupuncture has an effect on the ANS by modulating the sympathetic nerves. The intensity for groups 1 and 2 was gradually increased (approximately 10 mA to 25 mA) until the subjects felt the intensity was at a moderate level using a 10-point visual analogue scale (strong sensation but without feeling discomfort). All subjects were made aware that the output light was flashing. Subjects were checked every 5 min and the intensity was readjusted if necessary. At the end of the 30 min

**Procedures**

Subjects were asked to refrain from consumption of caffeinated drinks, smoking or strenuous physical activities on the experiment day. All measurements were taken between 16:00 to 18:00 so as to minimise the circadian effect on the ANS. Subjects were instructed to relax and breathe regularly to minimise any effect of the respiration on HRV indices.

Upon arrival at the laboratory, subjects were asked to rest in a sitting position for 30 min. Baseline systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels were then recorded using a digital blood pressure monitor (Mindray PM-8000 Express Patient Monitor, Bio-Medical Electricity, Hamburg, Germany). Three electrocardiogram (ECG) electrodes were placed over the left and right clavicles and left upper quadrant of the abdomen and were connected to a digital patient monitoring device (Mindray PM-8000) for recording HR and HRV during the intervention. After that, acupuncture points were located and sterilised by isopropyl alcohol. Two 30 mm×0.25 mm single-use, sterile, prepacked stainless needles with guide tubes were inserted into the LI4 and LI11 points (group 1), bilateral patellae (group 2) and to the Duoderm pads over LI4 and LI11 (group 3). The depth of needle penetration was about 10 mm for groups 1 and 2, and 3–4 mm for group 3. Manual twirling was used during needle insertion. Subjects were asked if they could feel any needle sensation, but were also told that they might or might not feel any needle sensation. Once appropriate needle insertion was established, two electrodes were then attached to the needles and connected to an electroacupuncture device (ITO, ES-160, Hannover, Germany). Electrical stimulation was applied for 30 min at a frequency of 2 Hz, pulse duration at 0.4 ms. These parameters were adopted following a study by Knardahl et al. It was believed that low-frequency (LF) electroacupuncture has an effect on the ANS by modulating the sympathetic nerves. The intensity for groups 1 and 2 was gradually increased (approximately 10 mA to 25 mA) until the subjects felt the intensity was at a moderate level using a 10-point visual analogue scale (strong sensation but without feeling discomfort). All subjects were made aware that the output light was flashing. Subjects were checked every 5 min and the intensity was readjusted if necessary. At the end of the 30 min

**Figure 1** Sham electroacupuncture on right LI4 and LI11 over the Duoderm pads (group 3).
stimulation, the subjects were asked to complete the Hong Kong Chinese version of the Modified Massachusetts General Hospital Acupuncture Sensation Scale (C-MMAS)[22] for quantification of the acupuncture sensations during the electrical stimulation. At 5 min after the electrical stimulation, blood pressures, HR and HRV data were again recorded.

MEASUREMENTS

Mean arterial pressure and HR

SBP and DBP were recorded before inserting the acupuncture needles (before stimulation); every 5 min for 30 min during the electroacupuncture; and at 5 min after the electroacupuncture (after stimulation). The mean arterial blood pressure (MAP) was computed by using the formula DBP+(SBP–DBP)/3.

The HR and the ECG signals were recorded continuously during the electrical stimulation. The ECG signals were analysed using Chart 5 Pro for Windows. These signals were simultaneously recorded using a PowerLab 16/30 device (ADInstruments Pty Ltd, Bella Vista, New South Wales, Australia) for data acquisition and further analysis.

Heart rate variability

Recorded ECG signals were subjected to power spectral analysis using the fast Fourier transformation technique. The low LF component of the power spectrum of the HRV is defined as the power between 0.03 and 0.15 Hz, and is interpreted as a measure of sympathetic modulation. The parasympathetic outflow is estimated as the high frequency (HF) component (0.15–0.5 Hz). The global sympathovagal balance was expressed by a ratio of LF to HF components (LF/HF). A high value of the LF/HF ratio reflects domination of the sympathetic system.[10] 19 20

Acupuncture sensation measurement

The C-MMAS consists of 12 descriptors of sensation and includes soreness, aching, deep pressure, heaviness, fullness/distension, tingling, numbness, dull pain, warmth, cold, throbbing, plus a blank supplementary word. For subjects in group 1, there was a significant increase in HR in the initial period of stimulation (p=0.599; table 1). In group 2, the MAP demonstrated a slight, non-significant increase at the initial onset of stimulation but then gradually returned to baseline and remained stable for the rest of the observation period (p=0.599; table 1). For group 3, no significant changes in MAP were observed during or after the stimulation period (p=0.599; table 1).

Changes in mean arterial blood pressure

A significant increase in MAP from a baseline of 84.6 (±2.6) mm Hg to 90.0 (±0.9) mm Hg was observed during acupuncture stimulation in group 1 subjects (p<0.05). Such an increase failed to maintain statistical significance at 5 min after the stimulation (p=0.058). In group 2, the MAP demonstrated a slight, non-significant increase at the initial onset of stimulation but then gradually returned to baseline and remained stable for the rest of the observation period (p=0.058). For group 3, no significant changes in MAP were observed during or after the stimulation period (p=0.599; table 1).

Changes in heart rate

For subjects in group 1, there was a significant increase in HR in the initial period of stimulation (p=0.035); the HR gradually slowed down for the rest of the stimulation. No significant changes in HR were observed in subjects in group 2 (p=0.12) or group 3 (p=0.242; table 2).

Changes in autonomic nervous system activities

The computed LF/HF was highest in group 1 during electroacupuncture stimulation when compared to the other two groups (p=0.001) and this ratio decreased at 5 min after the stimulation but still remained significantly higher than the baseline value (p=0.002). Subjects in group 2 also showed a significant increase in LF/HF during stimulation when compared with the
baseline (\(p=0.01\)). The ratio remained slightly higher than baseline at 5 min after the stimulation; however, this was not statistically significant (\(p=0.084\)). There was a slight but insignificant increase in LF/HF during (\(p=0.412\)) and at 5 min after (\(p=0.375\)) the stimulation in group 3 (table 3).

Intensity of acupuncture sensations during stimulation

Figure 2 shows the mean intensity of each descriptor in the C-MMASS reported by the three groups. The overall C-MMASS index of group 1, group 2 and group 3 were 5.3±1.3, 3.5±0.7 and 0.77±0.2, respectively. There was a significant difference in the C-MMASS among the three groups (\(F=69.92, \text{df}=2, p<0.05\)). Post-hoc analysis with Bonferroni adjustment showed that there was a significant difference in the C-MMASS index between group 1 and 2 (\(p<0.05\), CI=1.00 to 3.04). In group 1, dull pain, fullness/distension, aching, numbness and tingling were the most frequent sensations reported. The majority of the ratings were in the mild to moderate range. In group 2, the strongest sensations were reported for tingling and soreness. For group 3, the strongest sensations were recorded in fullness/distension and tingling. No subject opted to add any new descriptors in the blank row provided.

Association between acupuncture sensations and the physiological responses

Correlation analysis between the overall C-MMASS score and physiological responses (HR, MAP, LF/HF) revealed a strong correlation between the intensity of acupuncture sensations and the LF/HF (\(\gamma=0.89, p<0.001\)), MAP (\(\gamma=0.78, p=0.018\)) and mean HR (\(\gamma=0.71, p=0.023\)) in group 1. Moderate correlation was found between the acupuncture sensations intensity and LF/HF (\(\gamma=0.65, p=0.029\)) and MAP (\(\gamma=0.58, p=0.049\)) but not with the HR (\(\gamma=0.33, p=0.083\)) in group 2. There was a very low association between the acupuncture sensations intensity and the physiological responses in group 3 (\(\gamma=0.17, p=0.589\) for LF/HF; \(\gamma=0.25, p=0.528\) for MAP; \(\gamma=0.11, p=0.734\) for HR).

Supplementary table S4 (web only) summarises the correlation between individual C-MMASS descriptors and the physiological responses in each group. The result showed that fullness/distension, tingling, numbness, dull pain and aching had stronger correlation with the changes in physiological responses than other acupuncture sensations. Similar associations were observed in group 2, except there was no strong correlation between the acupuncture sensations and the changes in HR. In group 3, there were no correlations between any descriptors and physiological parameters.

DISCUSSION

There is evidence that ANS activities can be modulated by acupuncture. The current study demonstrated that electroacupuncture to LI4 and LI11 induced significant sympathetic discharge. In fact, responses to acupuncture stimuli encompass a broad network of regions consistent with somatosensory, affective and cognitive processing in the brain. A recent meta-analysis on the effect of acupuncture on the human brain using functional MRI (fMRI) confirmed that verum acupuncture stimuli can modulate the

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Mean arterial blood pressure before, during and at 5 min post intervention (n=36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulation period</td>
<td>5 min</td>
</tr>
<tr>
<td>Group 1 (n=12)</td>
<td>84.6 (±2.6)</td>
</tr>
<tr>
<td>Group 2 (n=12)</td>
<td>86.7 (±4.4)</td>
</tr>
<tr>
<td>Group 3 (n=12)</td>
<td>85.5 (±6.7)</td>
</tr>
</tbody>
</table>

Group 1, true electroacupuncture to right LI4 and LI11; group 2, true electroacupuncture to bilateral patellae; group 3=sham electroacupuncture to right LI4 and LI11.

*\(p<0.05\).

<table>
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<tr>
<th>Table 2</th>
<th>Mean heart rate before, during and at 5 min post intervention (n=36)</th>
</tr>
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<tbody>
<tr>
<td>Stimulation period</td>
<td>5 min</td>
</tr>
<tr>
<td>Group 1 (n=12)</td>
<td>75.9 (±7.9)</td>
</tr>
<tr>
<td>Group 2 (n=12)</td>
<td>73.0 (±5.1)</td>
</tr>
<tr>
<td>Group 3 (n=12)</td>
<td>73.5 (±7.1)</td>
</tr>
</tbody>
</table>

Group 1, true electroacupuncture to right LI4 and LI11; group 2, true electroacupuncture to bilateral patellae; group 3, sham electroacupuncture to right LI4 and LI11.

*\(p<0.05\).
brain activities by activating the supramarginal gyrus, secondary somatosensory cortex, pre-supplementary motor area, middle cingulate gyrus, insula, thalamus and precentral gyrus. Acupuncture stimulation, however, was associated with deactivation of the pregenual anterior cingulate, posterior cingulate cortex, subgenual cortex, amygdala/hippocampal formation, ventromedial prefrontal cortex and nucleus accumbens of the limbic region. As the central outflow of the ANS is coordinated in the medulla oblongata and regulated by the limbic system, it is possible that acupuncture stimulation may induce changes in the ANS via modulation of the cerebrocerebellar limbic system.

Reports on whether acupuncture induces dominant changes in sympathetic or parasympathetic activities are inconsistent. Our results showed that LF electroacupuncture to LI4 and LI11 evoked sympathetic discharge. We offer several explanations for this observation. Firstly, studies have shown that electroacupuncture stimulation applied to LI4, at an intensity where the subject experienced strong acupuncture sensations, led to activation of the hypothalamus. It is known that activation of the hypothalamus is associated with increase of sympathetic vasomotor activity. Our subjects who received electroacupuncture experienced rather strong sensations as reflected by the high C-MMAS score; therefore, we believe that the ANS activity induced was associated with modulation of brain activity. Secondly, the increase in sympathetic discharge seen in this study could also be related to the acupuncture point specificity theory. Some authors believed that yin is the parasympathetic division and yang is the sympathetic division of the ANS. Since LI4 and LI11 lie along the Large Intestine yang meridian, it is logical to believe that stimulation of these acupuncture points would enhance the sympathetic activities leading to an increase in mean MAP and HR. Furthermore, since all subjects were naïve to acupuncture, the initial exposure to an experimental trial with electroacupuncture may lead to an increase in anxiety-induced sympathetic activity. Nevertheless, we are unable to conclude whether electroacupuncture stimulation to LI4 and LI11 would only associate with an ‘increase’ in sympathetic discharge; it is possible that acupuncture could shift sympathetic or parasympathetic activities to either direction in order to maintain and restore the homeostasis of the body system. For instance, LF electroacupuncture to abdominal muscle demonstrated a significant decrease in muscle sympathetic activity in patients with polycystic ovary syndrome, a condition associated with increased sympathetic activities.

Our results also show an interesting relationship between acupuncture sensations, changes in HR and MAP and an increase in sympathetic discharge. In our study, the majority of the subjects who received
electrical stimulation experienced sensations of dull pain, fullness/distension, aching and numbness regardless of acupuncture point or non-acupuncture point stimulation. These sensations are predominately conveyed by $\alpha$ and $\beta$ fast conducting fibres. Signals of the sensations will rapidly lead to an increase in impulses generated by mechanosensitive receptors of high and low threshold, resulting in afferent input to the central nervous system, in turn affecting the ANS. This probably explains the positive correlation observed between acupuncture sensation intensity and the extent of ANS changes. Our findings suggest that acupuncture sensations are associated with changes in the ANS.

In the present study, electroacupuncture and not manual acupuncture was chosen. This is because the former technique is becoming more popular and commonly reported in clinical trials and research studies. Also, the parameters for electroacupuncture stimulation could easily be standardised throughout the study duration. Moreover, an interesting finding of this study is that while acupuncture sensations are strongly associated with stimulation of the acupuncture point, similar sensations including dull pain, fullness/distension, aching and numbness and soreness were also reported with non-acupuncture point stimulation, although the reported intensity of these sensations were higher during electrical stimulation over acupuncture points compared to non-acupuncture points. While evidence for the anatomical existence of acupuncture points is not compelling, it is believed that acupuncture points are located where nerves enter a muscle, the midpoint of the muscle, or at the enthesis where the muscle joins with the bone. Stimulation of nerve branches will produce numbness, and stimulation of muscles will produce soreness and distension. This probably explains the higher intensity of sensations experienced by subjects in group 1.

The use of sham electroacupuncture as placebo-control group is common in acupuncture studies. Such techniques include using retractable acupuncture needles or insertion of the needle subcutaneously. Nevertheless, both techniques have drawbacks. Pressing the skin with a retractable needle could activate the sensory pathways despite the type and strength of sensory input differing from traditional acupuncture. However, insertion of a needle subcutaneously may induce an increase of the cutaneous blood flow and may also excite nociceptive primary afferents. This afferent nerve activity can have pronounced effects on the functional connectivity in the brain, resulting in a ‘limbic touch response’. We therefore employed a new placebo method in our study. Insertion of the needle into the Duoderm pads mimics the acupuncture techniques without exertion of excessive mechanical pressure on the skin or penetration of the skin. Interestingly, some subjects still experienced mild needle sensations in group 3. As explained by Salih and coworkers, the elicitation of acupuncture sensations without cutaneous sensory input could be due to expectancy, awareness, focusing of attention on the acupuncture points, or general treatment settings by the subjects. All these could reinforce subjects’ expectation that they would feel something during the interventions. The slight increase in LF/HF in the placebo group could be the result of the subject’s anxiety, expectation or focused attention to the points, as an increase in awareness of spontaneous activity of motorneurons could lead to an increase in the muscle and skin sympathetic nerve activity.

**LIMITATIONS OF THE STUDY**
The major limitation of this study was the lack of a group that received electroacupuncture but elicited no acupuncture point sensations. Such a group may be ideally possible when the subjects are anaesthetised while receiving acupuncture. This current study however showed that subjects could experience some acupuncture point sensations even without actual acupuncture stimulation. Another limitation of our study is the small sample size and that our sample consisted only of healthy subjects who can reliably sense and report the needle sensations. We suggest that studies involving the above mentioned ‘ideal’ group, and with a larger sample size, are necessary to further investigate the relationship between acupuncture and its associated physiological effects.

**CONCLUSIONS**
This current study confirmed that electroacupuncture to LI4 and LI11 is likely to be associated with an increase in sympathetic discharge of the ANS. The results of the study suggest the notion that acupuncture sensations are associated with changes in the ANS. The intensity of acupuncture sensation was positively correlated with haemodynamic and ANS changes.

**Summary points**
- Acupuncture may generate the de qi sensation.
- Acupuncture may also influence the autonomic nervous system.
- Both were measured in an experiment with healthy volunteers and found to be correlated.

**Contributors** All authors were involved in the study design. TWDY and AYMJ were responsible for the conduct of the study and drafting the manuscript. TWDY performed the statistical analysis.

**Competing interests** None.

**Patient consent** Obtained.

**Ethics approval** Ethics Committee, the Hong Kong Polytechnic University.
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