Acupuncture Mediated Brain Activity Demonstrated with fMRI at 4 Tesla

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Purpose
A demonstration of regionally specific, quantifiable acupuncture effects on relevant structures of the human brain might facilitate acceptance and integration of acupuncture into the practice of Western medicine.\textsuperscript{1} Previous reports from the imaging literature indicate the limbic system reacts to acupuncture in healthy subjects, however, the methodology used in these studies (e.g. sham acupuncture and arbitrary control conditions) has been questioned.\textsuperscript{2,4} Point injection (PI) is an alternative method of acupuncture stimulation that shows promise to overcome these methodological issues. We hypothesised that incrementally stimulating an acupuncture point used empirically to induce analgesia with PI would produce central nervous system (CNS) responses similar to those documented to result from analgesic agents.\textsuperscript{5,6}

Methods
Using functional magnetic resonance imaging (fMRI) we assessed the effects of linearly incrementing stimulation of acupoint LI4 by PI in 21 healthy male subjects (average age 26.2 years). Local pressure at the acupoint, measured by manometer was used as a regressor of interest. Using functional magnetic resonance imaging (fMRI) we assessed the effects of incrementally stimulating an acupuncture point used empirically to induce analgesia with PI would produce central nervous system (CNS) responses similar to those documented to result from analgesic agents.\textsuperscript{5,6}

Results
Paired samples t-tests demonstrated significant decreases in HR (p=0.006) and PRP (p=0.002) indicative of an effect of stimulation. Subjectively, on a 10 point Likert scale, deqi was rated at 4.8 (SD: 2.6; range: 0-8). An expected linear effect of incrementing stimulation was not observed in the manometer measurements, although pressure did trend toward a significant increase between initial and final (fifth) point injections (p=0.06). Analyses of grouped imaging data with SPM2 demonstrated inverse correlations between measured acupoint and blood oxygen level dependent (BOLD) signal in the cerebellum (lingula) and insula ipsilaterally and the contralateral supplementary motor area (SMA) and cingulum, as shown in Table 1 and Figure 2.

Discussion
An acupuncture effect may be inferred from the subjective and physiological results. The brain regions demonstrating significant inverse response to acupuncture stimulation are those known to respond to pain stimuli and are consistent with the distribution of µ-opioid receptors. Evidence from analgesia studies indicates that acupuncture stimulation and µ-opioid receptor agonists decreases response to noxious stimuli. The extensive, robust connections of the insula suggest a vital role in the motivational-affective valuation of sensory experience. Any method that reduces response in these regions might well modulate response to pain or its expectation. Additionally, insular modulation may explain the often reported sensation of well-being following acupuncture. Intense stimulation of the skin by acupuncture or PI may invoke diffuse noxious inhibitory control where the reduced pain sensation is assumed to be the result of inhibition of multi-receptive neurons to the brain.\textsuperscript{7}

Conclusion
This study demonstrated reduced activity in a sub-set of the currently understood pain network, namely the cerebellum, insula and cingulum; a pattern previously associated with pharmacological analgesia.

Table 1

<table>
<thead>
<tr>
<th>Label</th>
<th>x, y, z (mm)</th>
<th>Z</th>
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<tbody>
<tr>
<td>(i) Insula</td>
<td>-24 24 18</td>
<td>4.02</td>
</tr>
<tr>
<td>(i) Cerebellum (crus)</td>
<td>-36 -57 -27</td>
<td>3.99</td>
</tr>
<tr>
<td>(c) SMA, cingulum</td>
<td>6 -27 63</td>
<td>4.00</td>
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</tbody>
</table>


\textsuperscript{2} Anzai M S. Does the choice of placebo determine the results of clinical studies on acupuncture? A meta-analysis of 100 clinical trials. Forschende Komplementarmedizin 1998;5:8-11.


\textsuperscript{5} Adler LJ, Gyulai FE, Diehl DJ, Mintun MA, Winter PM, Firestone S, Adler LJ, et al. Combining fMRI with a pharmacokinetic model to determine which brain areas activated by painful stimulation are known to respond to pain stimulus. The brain regions demonstrating significant inverse response to acupuncture stimulation are those known to respond to pain stimuli and are consistent with the distribution of µ-opioid receptors. Evidence from analgesia studies indicates that acupuncture stimulation and µ-opioid receptor agonists decreases response to noxious stimuli. The extensive, robust connections of the insula suggest a vital role in the motivational-affective valuation of sensory experience. Any method that reduces response in these regions might well modulate response to pain or its expectation. Additionally, insular modulation may explain the often reported sensation of well-being following acupuncture. Intense stimulation of the skin by acupuncture or PI may invoke diffuse noxious inhibitory control where the reduced pain sensation is assumed to be the result of inhibition of multi-receptive neurons to the brain.

\textsuperscript{6} Wise RG, Rogers R, Painter D, Bantick S, Ploghaus A, Williams P, et al. Combining fMRI with a pharmacokinetic model to determine which brain areas activated by painful stimulation are known to respond to pain stimulus. The brain regions demonstrating significant inverse response to acupuncture stimulation are those known to respond to pain stimuli and are consistent with the distribution of µ-opioid receptors. Evidence from analgesia studies indicates that acupuncture stimulation and µ-opioid receptor agonists decreases response to noxious stimuli. The extensive, robust connections of the insula suggest a vital role in the motivational-affective valuation of sensory experience. Any method that reduces response in these regions might well modulate response to pain or its expectation. Additionally, insular modulation may explain the often reported sensation of well-being following acupuncture. Intense stimulation of the skin by acupuncture or PI may invoke diffuse noxious inhibitory control where the reduced pain sensation is assumed to be the result of inhibition of multi-receptive neurons to the brain.