# Brain Mechanisms Underlying Electro-Acupuncture-Induced Analgesia: A functional MRI study

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**Introduction:**

The CNS responses associated with acupuncture stimulation have been detected using fMRI [1, 2, 3, and 4]. However, using the BOLD technique, the brain responses underlying acupuncture-induced analgesia have not been reported. In this study, we employed a continuous 25-min Electro-Acupuncture (EA) stimulation to examine the brain responses associated with attaining acupuncture-induced analgesia using the BOLD method.

**Material and Methods:**

Twelve subjects (7 male, 5 female) were enrolled in this study. The study consisted of three conditions: one experimental condition and two control conditions. For the experimental condition, subjects received continuous 25 min, 2 Hz EA on acupoints LI-4 (R. hand) and St-36 (R. leg). A 5 min rest period was used before and after this long-duration stimulation and resulting in an overall duration for 35 min. For the Sham point control, the identical EA parameters were applied to two non-acupoints about 10 cm posterior to ST 36 and ST 37, respectively. For the 2$^{nd}$ control, subjects received no stimulation for the entire 35 minutes. Before and after each imaging session, a pain threshold was measured using a Medoc TSA-2001 (Medoc, Ramat Yishai, Israel) heat-pain instrument outside the scanner, in order to determine the post acupuncture analgesia. The subjects were scanned sequentially for the three conditions on three different days, at least 3 weeks apart, to prevent the interference of the effects from the prior study. All 12 subjects experienced the experimental condition; 7 subjects also experienced the sham point control and 4 subjects experienced all three conditions.

A Siemens 3T head only (Allegra) scanner was employed for brain imaging. The functional images were acquired using TR/TE=2000/40 ms, 22 cm FOV, 5 mm slice thickness, 32 trans-axial slices to cover the entire brain. The data were analyzed in two ways: a) SPM99 [5] to determine the activation location and volume during stimulation for each 5 min period and b) AFNI [6] to examine both the time course changes over the entire 25 min stimulation period and at every 5 min step. For activation, the data were first realigned to correct for head motion, then normalized and smoothed. The activated areas of each 5 min period were generated quantitatively by comparing the averaged signal magnitude of that specific period to the baseline, i.e., the initial 5 minute period. The activation volume for the following ROIs were calculated: 1) primary sensorimotor, 2) secondary sensorimotor, 3) anterior cingulate, 4) insula, 5) limbic 6) basal ganglia and 7) thalamus. Then, the activated volume of each ROI was plotted versus time to determine the dynamic volume changes during the 25 min stimulation.

For the time course changes, the time courses (35 min duration) were examined visually first to determine any changes in oscillation frequency and/or amplitude during the stimulation around the ROI of the primary sensorimotor area. Then, the time courses in the ROI were extracted and analyzed using FFT. The first 5 highest peaks in the frequency domain were obtained for every 5 min and the frequency changes were examined.

**Results:**

a. Activation: a transient effect of activation volume during the 25 min stimulated period was observed in the ROIs in most of the subjects. This effect is characterized as a gradually increasing activated volume that reaches its maximum at about 20 minutes and then decreases significantly at the end of the stimulation period, despite continued stimulation. This result is seen with both positive and negative activation. Stimulation of the sham points generally produced smaller activated volumes; occasionally, some of the ROIs also showed the transient effects.
b. Frequency: a characteristic low frequency enhancement was found in all the subjects. This enhanced frequency was typically approximately 0.01 Hz with increased amplitude. The maximum amplitude appeared at 15-20 min after the EA onset. The enhancement in the sham point condition was less evident.
c. Analgesia: All the subjects except three of them showed a pain-threshold temperature increase after acupuncture, which indicated the successful elicitation of analgesia. The average temperature increase for analgesia was 2.1 degrees C and the temperature decrease was 1.6 degrees C.

**Conclusions:**

BOLD fMRI can be used to detect changes in cerebral oxygenation during EA- induced analgesia. The strong correlation between the maximum activated volume and the maximum amplitude of the oscillation may shed some light on the brain mechanisms underlying the elicitation of analgesia. The enhanced low frequency oscillation may be related to the reduced activity and warrants to further investigation.

**References**

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