Simultaneous CBF and BOLD Mapping of Electrical Acupoint Stimulation Induced Brain Activity

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Introduction:

Acupuncture has long been used worldwide in pain-relief treatment with a growing interest developed recently in its neurological effects [1]. A number of studies utilized blood oxygenation level dependent (BOLD) fMRI to map brain activity related to acupoint stimulation. Given the well-known concern with the poor specificity and reproducibility of BOLD fMRI, the present work investigated the effects of acupuncture using cerebral blood flow (CBF) mapping with arterial spin labeling (ASL) [1-4], which provides more spatial specificity and consistency within and between subjects [5]. This study aims to map brain activity elicited by electroacupuncture using simultaneous BOLD and CBF contrasts and inter-subjects' variation was compared between the two techniques.

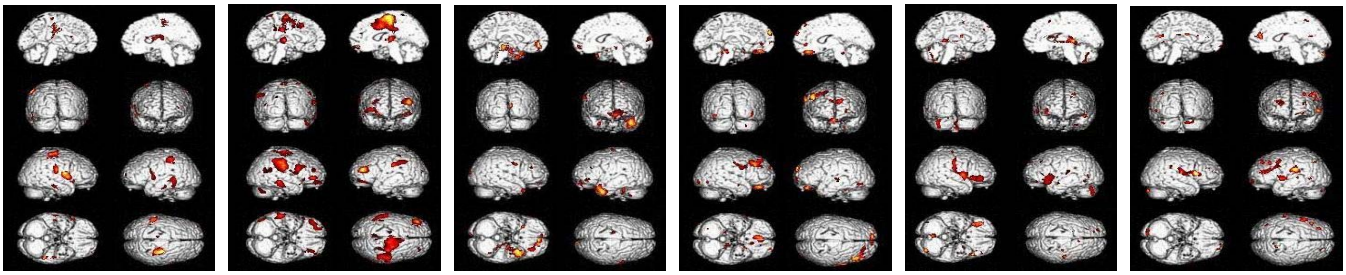
Materials and Methods：

Twenty-three healthy right-handed subjects (12 males and 11 females, age 20–30 years) participated in this study. Thirteen participants (7 males and 6 females) received electrical acupoint stimulation (EAS) at maximal intensity without pain and the remaining 10 subjects (5 males and 5 females) received minimal-EAS (minimal detectible intensity) for control stimulation. All subjects received 100 Hz stimulation through a pair of skin electrodes placed on the left LI4 acupoint. In compliance with guidelines of human experiments from the ethical committee, all subjects provided informed consent with thorough understanding of study's purpose and procedures. Simultaneous acquisition of BOLD and CBF was performed for 7 minutes comprised of alternating 1-minute blocks of rest and EAS. EAS was delivered with an MRI-compatible HANs 200 electric acupoint stimulation device (Nanjing Gensun Medical Technology Co. Ltd., Nanjing, China). All experiments were performed on a General Electric 3T Signa MRI system with a standard head coil. Functional data were acquired using a double readout spiral-out sequence with simultaneous CBF and BOLD acquisition [7]. CBF/BOLD readouts were acquired at TE of 3.1/30 ms covering 10-12 axial slices of the cerebrum and most of the cerebellum. Statistical T-Test was used to identify regions with statistically significant correlation to the stimulation paradigm (cluster corrected $p<0.05$, contiguous voxels > 10). T score maps were used for inter-subject evaluation of CBF and BOLD results. First, T values were discretized by assigning each voxel value to 0 if its absolute value was subthreshold ($t=1.66$, $p=0.05$) and 1/-1 if it was higher/lower than the positive/negative threshold. For each voxel, the discretized value (0, 1 or -1) was counted across all subjects. Then the total number of -1,0,1 of each voxel were calculated for all subjects. The highest total number was chosen for a normalized group map. A higher group map value corresponded to higher consistency between subjects or smaller inter-subjects' variation.

Results：

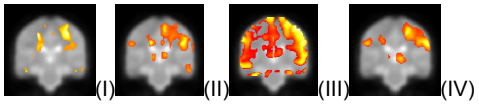
Robust BOLD and CBF responses was found contralateral to EAS including right MI, SI and SII (Fig 1(a~d)) with more CBF activated and fewer deactivated brain areas compared to BOLD. Common BOLD and CBF activation ipsilateral to EAS included left caudate and cingulate gyrus (Brodmann area 24, which is considered to play a complex pivotal role in the affective-motivational component of pain [8]). EAS BOLD activation was found in insula and bilateral claustrum alone, while CBF activation was found in right cingulate gyrus (Brodmann area 24), caudate and bilateral thalamus. BOLD deactivation was seen in the parahippocampal gyrus, uncus, substania nigra of midbrain, culmen, and cerebellar tonsil, as well as regions in the default mode network, such as medial frontal gyrus (MFG), whereas CBF deactivation included contralateral middle frontal gyrus, superior frontal gyrus and orbital gyrus. Minimal-EAS activation was similar for BOLD and CBF contrasts (Fig 1(e) and Fig 1(f)). Neither activations in Brodmann area 24 nor deactivations were found for minimal-EAS BOLD and CBF.

Meanwhile, increased signal change ratio between EA and rest state was found in CBF according to the time course of the voxel, suggesting higher sensitivity than BOLD. Surprisingly, group CBF activations were more spatially extensive than group BOLD activations while results in single subject followed the opposite trend (Fig.2). One possible interpretation was that the inter-subjects' variation was decreased in CBF response. To prove this, individual T-score maps were used to quantify inter-subjects' variation for BOLD and CBF contrasts (Fig.3). We calculated the ratio of voxel count with greater CBF group value divided by that of greater BOLD group value. The ratio was 38.1:1, indicating a smaller inter-subjects' variation for CBF.



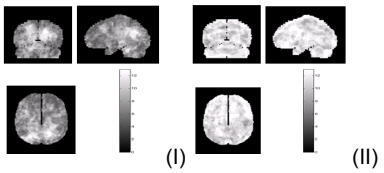
(a) (b) (c) (d) (e) (f)

Fig.1: Group results of activation based on (a) EAS BOLD; (b) EAS CBF; deactivation based on (c) EAS BOLD; (d) EAS CBF; activation based on (e) minimal-EAS BOLD and (f) minimal-EAS CBF.



(I) (II) (III) (IV)

Fig.2: Group results of activation based on (I) EAS BOLD; (II) EAS CBF and a typical subject activation result based on (III) EAS BOLD; (IV) EAS CBF.



(I) (II)

Fig.3: Reproducibility maps for EAS BOLD(I) and CBF (II) using normalized t values.

Conclusion：

This study provided the first evidence of CBF response to EAS. The group results suggested that the sensitivity and specificity to sensory and pain-related regions were consistent with previous EAS observations [6]. Improved inter-subjects' variation relative to BOLD suggested that CBF might be advantageous in studies requiring high reproducibility. One potential source of BOLD signals variation could be its sensitivity to hemoglobin and veins, while CBF signals were specific to arteries and capillaries [9]. Previous study claimed that the arterial distribution was more consistent between subjects relative to that of veins, which might explain the observed differences [10].

References:

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