Functional MRI of the brainstem and cervical spinal cord of children based on SEEP contrast

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INTRODUCTION

Over the past 6 years a novel method of functional magnetic resonance imaging (fMRI) has been developed based on changes in tissue water content at sites of neuronal activity. Signal Enhancement by Extravascular Protons (SEEP) has been particularly important for imaging regions such as the spinal cord in which traditional BOLD imaging is difficult [1,2]. Within the immature central nervous system there are several factors which may influence the fMRI signal changes that are used to detect neuronal activity. These factors include the proportion of gray/white matter, synaptic density, and differences in resting blood flow and metabolism. The contrast that arises from the SEEP effect in children thus warrants investigation. SEEP was first identified within the spinal cord and higher percentage signal changes are observed in the spinal cord than in the brain. For this reason we investigated the SEEP signal changes in the spinal cords and brainstems of children using a simple sensory task.

METHODS

The brain stem and spinal cord of 10 healthy children, aged 6 to 13, were imaged at 3T (Siemens Magnetom Trio) with subjects supine using a phased-array spine receiver coil. Functional time-course data were acquired using a half-fourier single-shot, fast spin echo sequence (HASTE) (TE 38 msec, effective TR 9000 ms, 20 cm x 10 cm FOV, 192 x 96 matrix). Nine contiguous sagittal slices (2mm thick) were acquired spanning from the thalamus to the C7/T1 disc. The resulting voxel size was 1 mm x 1 mm x 2 mm. Thermal stimulation of the C6 dermatome was produced using a Medoc® TSA-II thermal sensory analyzer and thermal probe placed on the right thenar eminence. In each experiment the stimulator cycled between 32 °C for the baseline condition and either a mildly noxious cold (17°C) or innocuous cold (27°C) temperature for the stimulation condition. Baseline periods were held for 54 to 63 seconds and stimulation periods were maintained for 45 seconds. A total of 54 volumes were acquired. The resulting 3D image data were reformatted to permit smoothing only along the long axis of the cord anatomy, and were normalized to a consistent coordinate space for all studies to facilitate group comparisons of results. Data were analyzed using custom-made software written in MatLab. The peripheral pulse was recorded continuously during acquisition and used (with a general linear model approach) to improve the discrimination between physiological motion and signal intensity changes arising from neuronal activity[3].

RESULTS

Neuronal activity was observed within the thalamus, brainstem and in several spinal cord segments (Fig. 1). Within the spinal cord, active pixels were largely centred in the C6 and C7 spinal cord segments. With both stimuli, the observed lateralization of activity was consistent with known spinal cord anatomy. A greater number of active voxels were observed during the mildly noxious stimulation. Percentage signal changes were lower in the thalamus, midbrain and pons than in the medulla and cervical spinal cord (Fig. 2).

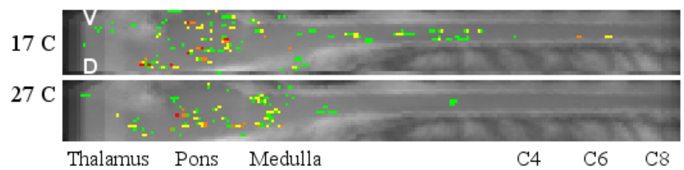

Figure 1. Combined activity maps in one sagittal slice, approximately 3 mm to the right of centre, during 17 °C and 27 °C thermal stimulation applied to the right hand. Images are oriented with the dorsal side at the bottom. The number of subjects showing activity at each voxel is indicated by the color spectrum (green: 6, yellow: 7, orange 8, and red: 9 or 10 out of 10). D indicates dorsal, and V ventral.

DISCUSSION

Previous studies have found lower percentage signal changes in the brain than in the spinal cord in adults. Signal changes are consistently at 2% in the brain[4], and 7%-10% in the spinal cord[1] in healthy adults. In the present study we have also observed lower percentage signal changes at supraspinal levels of the CNS. The percentage signal changes are similar or slightly higher than those previously reported in adults. Within pediatric brain fMRI there are conflicting reports of changes in the BOLD signal with age. Some studies have shown smaller percentage signal changes in children[5], while others have shown greater percentage signal change[6], and there have also been reports of no difference[7]. These results were influenced by subject age, nature of the task employed, and region of interest; therefore, care must be taken in interpretation. A breath holding task has revealed that similar patterns of activity have been observed within the brain between adults and children[6]. Children demonstrated fewer active pixels and higher signal intensities, mainly due to higher levels of noise[6]. Within the present data set, between-subject variability in the signal intensities prevents conclusive differentiation of SEEP signal in the spinal cord of children to adults, suggesting there is no significant difference. Within a pediatric population we have observed a rostrocaudal difference in percentage signal change observed at spinal and supraspinal levels previously observed within adults.

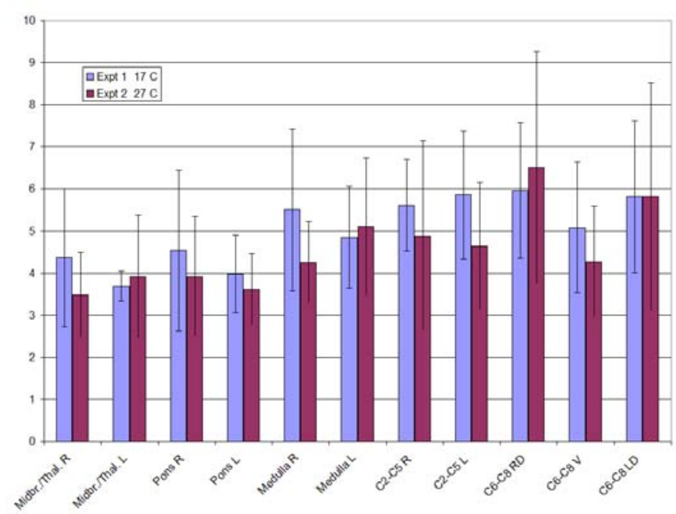

Figure 2. Percentage signal changes observed during 17°C stimulation (blue bars) and 27°C (purple bars). R indicates right side of the subject and L indicates left side. Values are averaged across six subjects (four excluded due to excessive motion). Error bars indicate the standard deviation across subjects.

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