Time course analysis of paediatric fMRI data with ICA

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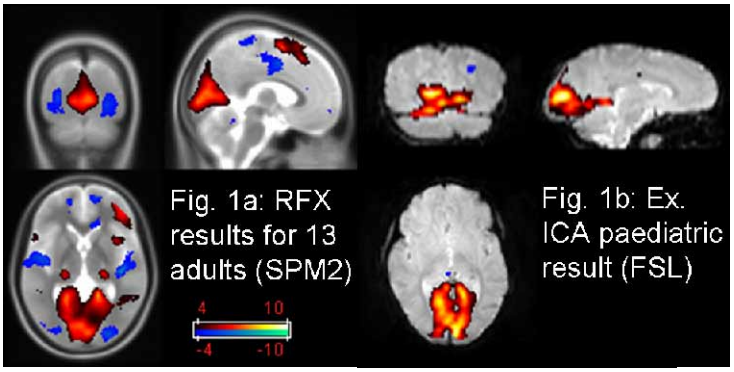
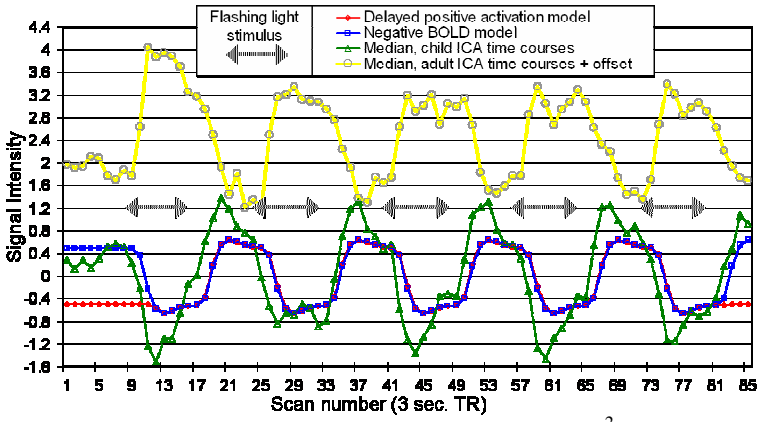
Introduction: The origins of the negative BOLD effect observed in a number of paediatric fMRI studies[1-3] are still a mystery, with theories posited suggesting infants' high synaptic density, anaesthetics/sedative agents, or altered O_2 delivery/extraction balance as possible causes. While the exact haemodynamic response cannot be deconvolved from experiments with manual stimulus delivery, such data can be compared to various activation models. Independent component analysis (ICA) can be used to identify the time course of activation for fMRI studies[4]. The selection of the relevant component is made by correlation with the input stimulus timing, or by matching the spatial component to an anatomical region. In this study, adults were assessed with a paediatric fMRI paradigm in order to determine an anatomical region likely to be activated. Data from the same fMRI experiment performed on young children at 3T were then analysed with ICA. Time courses were isolated from the component with the greatest spatial homology with adult activation areas, and these time courses were compared with two different models of activation. The goal is to determine whether the anti-correlation with stimulus seen in paediatric block paradigm studies is the result of a slow signal increase (delayed positive response) or a synchronised signal decrease.

Methods: Ethical permission approval for this study was granted by the local Research Ethics Committee and written parental consent was obtained prior to scanning. Conventional MRI and fMRI was performed under light sedation with chloral hydrate for 15 paediatric subjects (6-24 months corrected age); only subjects with normal structural imaging (n=12) were included in this study. The fMRI data were acquired in a Philips 3.0 T Intera scanner using 2-D multi-slice EPI scans (TE/TR/θ 30/3000/90, 34 slices, 112 matrix and 260 mm FOV). The stimulus paradigm was 5 blocks of 8 scans with scanner gantry lights manually cycled at 1 Hz alternating with 5 blocks of darkness, with 5 scans before and after the paradigm to reach steady-state magnetization and capture the last haemodynamic response, respectively. Second-order shim gradients and SENSE (r=2) were applied to reduce the susceptibility-based losses common to 3T EPI imaging. FMRI data were also collected on 13 healthy adult volunteers. The Statistical Parametric Mapping toolbox (SPM2, Wellcome Dept. of Imaging Neuroscience, London, UK) predicted time courses resulting from the stimulus using the canonical haemodynamic response. Random effects (RFX) analysis in SPM2 identified the anatomical region most commonly activated in adults (Fig. 1a). Probabilistic ICA evaluations of fMRI data were performed with the MELODIC tool within FSL (FMRIB, Oxford)[4], including a mean-removal step. Independent components from paediatric experiments were identified by similarity of spatial distributions to the adult activations and the individual time courses analysed. To differentiate two possibilities for the negative BOLD effect observed in block paradigm studies, a delayed positive activation model, where the signal increases one whole block after the stimulus onset (Fig. 2, red), was compared with a model with a signal decrease synchronized with the stimulus, after a normal haemodynamic response delay (Fig. 2, blue). Individual time courses were correlated with both models, and the correlation coefficients compared.



Results: Independent component time courses for all 12 children showed signal decreases temporally correlated with the light stimulus, while only 11 of the 13 adults showed positive BOLD responses. Figure 1 shows an example of good correspondence between the activation found in the adult group and the spatial distribution of the independent component. Note that the spatial component in Figure 1b showed signal increases anti-correlated with the stimulus, which would be blue in an SPM-derived display. Figure 2 shows the median time courses (< 10% difference from the mean time course) for the adults (yellow) and children (green) as well as the time courses for the delayed positive (red) and negative BOLD (blue) response models.



While the model time courses only differ for the beginning and end of the experiment, the correlations between the paediatric subject time courses and the negative BOLD model are significantly better than the correlations with the delayed positive trace (corr. coeff. = 0.58 vs 0.50, paired t-test, $p < 0.001$). The triangular shape of the paediatric time course suggests the activation may be inconstant over the stimulus duration, which could indicate habituation to the 1 Hz stimulus or an altered haemodynamic response.

Discussion: Standard fMRI processing allowed the determination in adult volunteers of an anatomical region commonly activated by this paradigm. ICA found time courses in paediatric subjects that correlated significantly with a negative BOLD model. This study demonstrates the utility of ICA for exploratory fMRI research, where the standard haemodynamic response functions may not be valid, such as this initial study of infants with 3T fMRI.

References: [1]Born et al., Visual activation in infants and young children studied by functional magnetic resonance imaging, Pediatric Research 1998. [2]Martin et al., Visual processing in infants and children studied using functional MRI, Pediatric Research 1999. [3]Erberich et al., Functional MRI in neonates using neonatal head coil and MR compatible incubator, Neuroimage 2003. [4]Beckmann and Smith, Probabilistic ICA for fMRI, Trans IEEE Med Imaging 2004.

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