Characterisation of the BOLD signal Haemodynamic Response Function (HRF) in the neonatal somatosensory cortex

T. Arichi[1], G. Fagiolo[2], A. Melendez[3], N. Merchant[1], N. Tusor[1], S. J. Counsell[1], E. Burdet[3], C. F. Beckmann[4], and A. D. Edwards[1]
[1]Neonatal Medicine Group, MRC Clinical Sciences Centre, Hammersmith Hospital, Imperial College London, London, London, United Kingdom, [2]Imaging Physics Group, MRC Clinical Sciences Centre, Hammersmith Hospital, Imperial College London, [3]Department of Bioengineering, Imperial College London, [4]Mathematical Imaging Neuroscience, Donders Institute, Radboud University, Nijmegen, Netherlands

Aims/Background: Blood Oxygen Level Dependent (BOLD) signal functional MRI (fMRI) allows an indirect assessment of in-vivo neural activity, and therefore offers great potential for understanding human brain developmental following birth. However, technical difficulties inherent to imaging the neonatal population, and inconsistent results from early fMRI studies have prevented widespread use. Key to these difficulties is uncertainty surrounding the effects of developmental changes in neurovascular coupling on the Haemodynamic Response Function (HRF). Although the HRF waveform has not previously been characterised in the human neonatal brain, animal studies have shown that a maturational pattern exists in HRF morphology from birth to adulthood [1]. We hypothesised that developmental changes in the HRF are also seen through early human life, and aimed to characterise the waveform in the neonatal brain using a programmable somatosensory stimulus.

Methods: 11 infants at term corrected gestational age (median 41+1 weeks post menstrual age (PMA), range 38+1 to 45+3 weeks PMA), and 5 adult volunteers (median 30 years old, range 24 to 54 years) were imaged on a 3-Tesla Philips MRI scanner (Best, Netherlands) located within a Neonatal Intensive Care Unit. Infants were sedated with oral chloral hydrate (30-50mg/kg) during image acquisition, and physiological parameters (heart rate, oxygen saturations, temperature) were monitored throughout. Written consent following discussion with one of the investigators and the provision of written information was taken from the parents of infants scanned, and adult volunteers.
The somatosensory system was stimulated with a programmable hand interface, in the form of an appropriately sized MR compatible latex balloon which was intermittently inflated in the right hand of each; with inflation of the balloon causing passive extension of the fingers and deflation resulting in flexion. Synchronisation with image acquisition was achieved via detection of the scanner TTL pulse by a DAQ card and custom-designed software on a standard PC [2].
A short-stimulus event-related experimental paradigm was programmed on the device, with a 1 second balloon inflation followed by a rest period of 41 seconds during which time the BOLD signal was rapidly sampled. A total of 12 stimulation and rest epochs were performed during the acquisition period.
fMRI images were acquired with an 8 channel phased array head coil using a single-shot echo-planar imaging (EPI) sequence with the parameters: TR/TE/FA = 500msec/45msec/90degrees, in-plane resolution 3.13mm^2, slice thickness 3.5mm, 6 slices) lasting 8 minutes and 27 seconds (total 1000 volumes). Data analysis was performed using FSL (www.fmrib.ox.ac.uk/fsl). Functional activation maps were first created using a general linear model (GLM) as implemented in FEAT (v5.98) and FLOBS (FSL's linear optimal basis set, v1.1). The BOLD signal timeseries was then averaged and extracted from a region of interest consisting of voxels with a z-score above the 90th centile in the activation map. The timeseries was then converted to a percentage signal change scale (relative to the mean signal). Peristimulus data analysis and curve fitting with a double gamma probability distribution function was performed using MATLAB (2009b, The Mathworks, Natick, MA).

Results: Data affected by motion artefact during image acquisition was discarded, leaving a total of 92 peristimulus epochs in the infant group, and 85 epochs in the adult group. Adult median peak positive amplitude was 1.823 % (range 0.81-3.48%), with a median time to the positive peak of 5.25 seconds (range 4.5-6.5 seconds), and a negative undershoot amplitude:positive peak amplitude ratio of 0.285. In the infant group, the median positive peak amplitude was smaller at 0.720% (range 0.24-1.83%) with a longer median lag time to the positive peak of 7 seconds (range 4-9.5 seconds). In addition, a proportionately deeper negative undershoot period was seen in the neonatal group (ratio: 0.649).

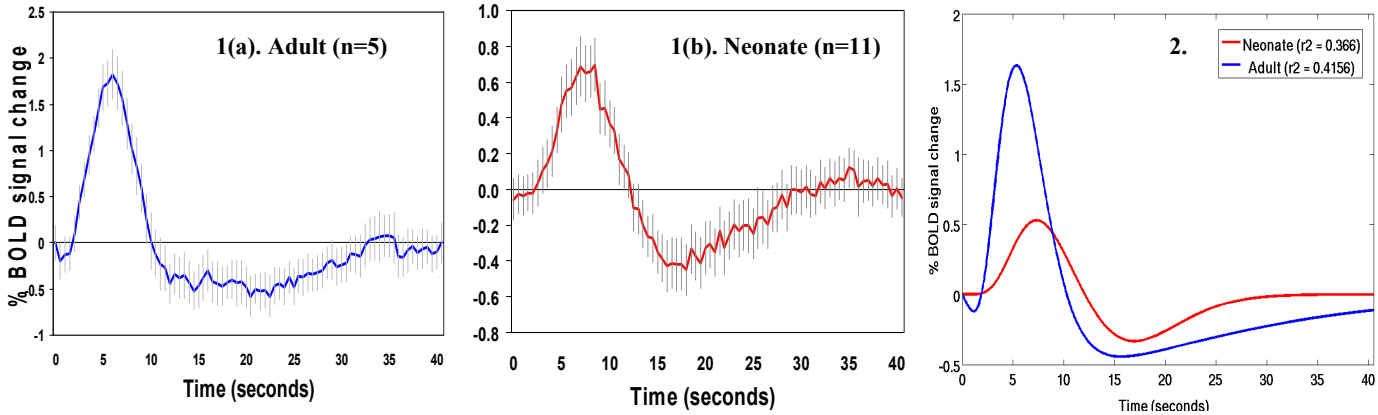

Figure 1(a): Peristimulus plot of mean percentage BOLD signal change against time (error bars represent 2SE from mean) in 5 healthy adult volunteers (median age 30 years, range 24-54 years). The neonatal data from 11 infants (median age 41+1 weeks PMA, range 38+1 to 45+3 weeks PMA) (**figure 1(b)**) shows a smaller peak amplitude, with a longer lag to the positive peak and a proportionately deeper post-stimulus negative undershoot. **Figure 2:** Comparative modelled HRF waveforms for the neonatal (red) and adult (blue) groups following fitting with a double gamma probability distribution function.

Conclusions: This data suggests that there are differences in HRF morphology in the neonatal and adult human brain, which are likely to result from developmental changes in neurovascular coupling. An effect of sedation cannot be excluded. These results may explain previous inconsistent results in fMRI experiments in the neonatal population.

References: [1] Colonnese MT et al. 2008 Nature Neuroscience; 11(1): 72-79. [2] Arichi T et al. 2010 Neuroimage; 49(3): 2063-72.