fMRI of Very Premature Infants (<32 weeks GA) at Birth

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Introduction: The survival rate of very premature infants, born at less than 32 weeks gestational age (GA), has increased in the last decades due to improvements in neonatal intensive care. However, half of this population continue to experience significant disability, many of whom suffer from cognitive deficits that will emerge only at school-age. To date there are no early predictors as to which children will suffer cognitive dysfunction [1]. Consequently, there is a vital need to develop accurate prognostic tools for long-term outcome in preterm infants. As part of a large multimodal longitudinal study, investigating advanced neuroimaging techniques to study the structure and function of the preterm brain, this research explores the functional MRI of preterm infants at birth. Initial fMRI experiments using typical adult parameters, based on those reported in Erberich et al. [2], did not find task-related BOLD activity reliably. Rivkin et al. [3] has suggested that the use of a longer TE, closer to the long T2* values found in preterm infants, may improve signal detection. This work focuses on efforts to better understand the scan parameters necessary for obtaining fMRI in very preterm infants.

Methods: fMRI data were collected with a 1.5T MRI system (Signa EXCITE HD, GE Medical; T2* weighted, EPI, axial, sequential, 64 x 64 voxels (2.5 x 2.5 x 4mm), TR = 3000ms, FA = 90°) with a neonatal head coil, part of an MR-compatible incubator (AIR Inc., Cleveland). Data were collected with TE=60ms and 21 slices with full brain coverage, as well as with TE=130ms and 17 oblique slices oriented to cover the occipital lobe. A block design paradigm was used, alternating between blocks of 1 Hz visual flashes and rest blocks of darkness with no stimuli. Following an initial rest block, 4 ON-OFF blocks were presented. Block length was 20s for the TE60 runs and 30s for the TE130 scans, for total scan times of 3 or 4.5 minutes respectively. Infants were not sedated; the fMRI scans were conducted within an extensive multimodal protocol. fMRI data at both TE60 and TE130 were acquired in 12 infants: mean GA at birth (GA-b) 29.5±2.2 weeks, at scan (GA-s) 30.8±2.4. Data acquisition for T2* quantification was recently added to the study protocol. Scan parameters were adapted from Rivkin et al. [3] (T2* weighted SPGR, 5 slices same dimensions as above, FA=30°, TR=100ms, TE = 7, 24, 48, 64, 91ms). These data were acquired for 3 infants.

Prior to analyses, fMRI data were motion corrected and spatially smoothed (5mm FWHM) using AFNI [4]. Data were analyzed using the general linear model – 1st and 2nd order legendre polynomials (detrending) and motion parameter estimates were included as components of no interest. In the absence of a hemodynamic response model for preterm infants, the first scan between ON/OFF, OFF/ON transitions was omitted from analysis; outliers and the first two scans per run were also omitted.

Results: Six of the infants had structural images with significant brain abnormalities. Two infants had reduced cortical volumes in the occipital lobes. Excessive motion (>5mm) was found in 3 of the TE60 and 3 of the TE130 runs. Datasets with no fMRI signal in the occipital lobe or high motion were discarded, leaving 7 infants at each TE. Evidence of task-related activity was found in the occipital lobe in 1 of 7 infants at TE60 and 3 of 7 infants at TE130. One infant (GA-b 28, GA-s 29 3/7) exhibited activation at both TE60 and TE130. The activation location and signal found in this infant are plotted in Figures 1 and 2 respectively. The TE130 signal plot in Figure 2b is from a voxel ~5.5 mm from the location identified in Figure 1. Similar activation was found in the other two infants. As expected, signal dropout due to subject induced field inhomogeneities were more pronounced at TE130 than at TE60. The T2* values calculated within manually defined ROIs in the occipital lobe for the 3 neonates were 148, 163 and 196ms. These values agree with the findings of Rivkin et al [3] that T2* values in preterm neonates are significantly greater than those of normal adults (~70ms).

Conclusions: Despite the difficulties in detecting task-related fMRI signal in very preterm infants, this research is the first of its kind to show BOLD activity in this population. Longer TE values appear to improve signal detection, at the risk of greater signal loss due to field inhomogeneities. Data acquired as part of this large multimodal longitudinal study will help identify and resolve the technical challenges associated with the use of fMRI in very preterm infants.

Figure 1 (right) – T-statistic image, TE60, p<10⁻⁶ uncorrected
Figure 2 (below) - Voxel signals, at TE60 (A) and TE130(B)