Cortical connectivity observed in normal and healthy neonates, 1 year and 2 years old children using low-frequency BOLD fluctuation

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INTRODUCTION

While fMRI has been widely employed for the study of how the brain works, relatively few fMRI studies have been conducted in the pediatric population, particularly in the very young age group (0-2yrs)(1). The lack of studies in this age group is not surprising since external sensory/cognitive inputs and the cooperation of the subjects to perform or sense the specific sensory/cognitive inputs that are required for fMRI are clearly difficult for subjects in these age groups. As a result, our understanding of the brain function in these age groups is relatively lacking. Recently, Biswal et al (2) have observed the synchronization of low frequency blood oxygen level dependent (BOLD) signal in the brain. With rapid acquisition of a series of T2*-weighted images while subjects lie resting inside the MR scanner and the use of a low pass filter (cutoff frequency ~0.08Hz), the resulting signal in a specific cortical region exhibits a high correlation with other brain regions which are functionally similar. For example, the low pass filtered signal in the primary motor cortex exhibits high temporal correlation at the motor cortex areas in both hemispheres. Therefore, Biswal et al suggested that the observed BOLD synchronization (BOLDs) in functionally similar brain regions may represent cortical connectivity. To this end, BOLDs was employed in this study to investigate the development of cortical connectivity in neonates (2-4wks), 1 yr and 2yrs old children. Results demonstrate an increase of "cortical connectivity" from neonates, 1yr to 2 yrs old children.

MATERIALS AND METHODS

All images were acquired on a 3T head-only MR scanner (Allegra, Siemens Medical Systems Incs). A total of 36 normal and healthy children were recruited for this study. These children were divided into three sub-groups depending on age: 14 neonates (2-4 wks), 11 1yr olds and 11 2yr olds. Informed consent was obtained from the parents prior to the imaging studies. Since all of the subjects were normal and healthy, no sedation was employed. All of the subjects were imaged during sleep. A T2*-weighted EPI sequence was used to acquired images. In addition, 3D MP-RAGE images were also acquired, used for co-registration among subjects and utilized for defining ROIs. The pre-processing of the experimentally acquired data included, motion correction, correcting baseline drift, correcting time shift between different slice locations, low-pass filtering of the experimental data (cutoff frequency = 0.08 Hz), and rigid body registration between the MR-RAGE and the T2*-weighted images of each subject. In addition, the MP-RAGE images from one of the subjects of each age group were chosen as the template and the MP-RAGE images of the remaining subjects in the same age group were co-registered onto the template so as to allow group analysis. After the preprocessing, a board certified neuroradiologist manually drew 3 ROIs including the primary motor (ROI-M), somatosensory (ROI-S) and visual (ROI-V) cortex, respectively for each subject. Cross correlation was then conducted throughout the entire brain using the averaged signal of each ROI as the reference signal. The cross correlation coefficients were converted to z-scores with a normal distribution using the approaches proposed by Lowe et al(3). Pixels with a z-score > 1 were considered as the "activated" voxels and a 3D Gaussian low pass filter was applied to the activation maps to improve SNR. Finally, the group average maps for each ROI and each age group were obtained.

RESULTS

Substantial motion artifacts were observed in 7 neonates, 5 1yr olds and 5 2yr olds; these were excluded from final data analysis. 7 neonates, 6 1yr olds and 6 2yr olds were included for the final data analysis. Figure 1 shows the average z-score maps for the neonate, 1yr and 2yr groups for the motor, sensory and visual ROIs, respectively. It is immediately apparent that activated regions are functionally similar to the pre-defined ROIs. For example, the primary motor and sensory cortices exhibit high correlation when the signal in the ROI-M and ROI-S were used as the reference functions while the primary visual cortex exhibits high correlation when the signal in ROI-V was used. These findings are consistent with that reported in the literatures based on adults. Quantitative measures of the average number of activated voxels for the three age groups are shown in Fig. 2. The number of "activated" voxels increase as a function of age although it appears to be non-linearly dependent on the age. The number of activated voxels are more comparable between the neonate and 1 yr old groups whereas a marked increase of activated voxels is observed for the 2yr olds, suggesting potentially more advanced cortical connectivity. In addition, our results also suggest that the visual cortex has fewer activated voxels when compared with that in motor and sensory cortices.

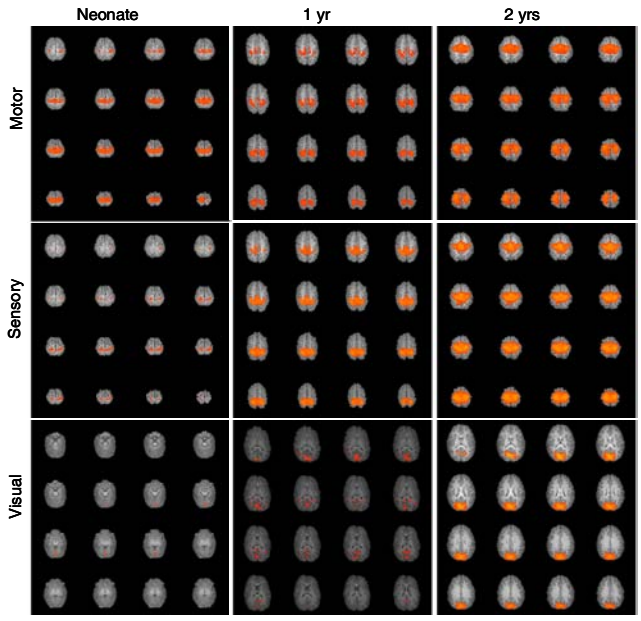

Fig. 1

DISCUSSION

We have demonstrated that it is feasible to obtain BOLDs in normal and healthy pediatric subjects without sedation, including neonates between 2-4 wks, 1 yr and 2yr old children. Our results are consistent to that reported in the literature in adult subjects – regions exhibited high correlation are functionally similar to the pre-defined ROI where the reference function was derived for correlation analysis. More importantly, our results suggest that although the development of the "putative" cortical connectivity is age-dependent, there is a marked increase in the number of "activated" voxels from 1 to 2 yr of ages.

1. Anderson AW, et al. Magn Reson Imaging 2001;19(1):1-5.
2. Biswal BB, et al. NMR Biomed 1997;10(4-5):165-170.
3. Lowe MJ, et al. Neuroimage 2000;12(5):582-587.