Investigating the Age Modulation of Functional Connectivity in a Pediatric Population Using Multi-echo EPI

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PURPOSE

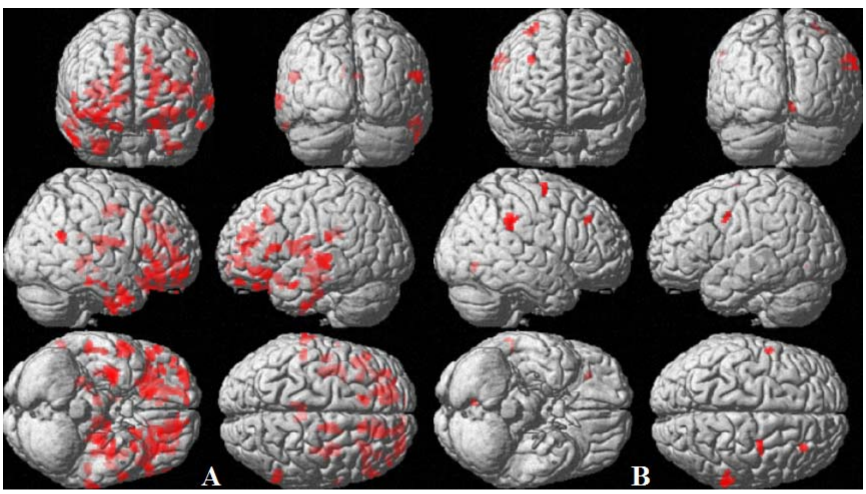
Functional connectivity MRI (fcMRI) has attracted a tremendous amount of interest among neuroscience researchers in recent years. In particular, the technique is potentially an effective tool for studying the maturation of the human brain. Indeed, fcMRI has recently been used to improve our understanding of the maturation of neuronal networks [1]. Clinical applications based on fcMRI are also being investigated for several diseases including epilepsy [2] and autism [3]. In the current study, we used single shot, multi-echo fcMRI data to investigate the age dependence of local and remote functional connectivity in a normal pediatric population. This knowledge benefits both our understanding of cerebral development and could also have implications for clinical applications of fcMRI.

METHODS

Subjects: 25 right-handed normal volunteers range 8 to 21 years (mean age 15.6 ±4.3 years, 12 males, 13 females) with no prior history of neurological diseases were recruited and consented for the current study. All subjects were native English speakers. They participated in a MRI scanning session and were also administered a neuropsychological exam which included WASI, OWLS and EOWPVT tests. ***MRI:*** Participants were scanned in a 3 Tesla Philips Ingenia scanner equipped with a 32-channel head coil. They were instructed to stay still during the whole scanning session, and asked to keep their eyes open during the resting state fcMRI scan. The MRI scans included anatomical T1 MPRAGE and resting state fMRI, along with several other sequences. A single-shot, four-echo EPI sequence was used to acquire the fcMRI data with primary imaging parameters listed as follows: TR=3300ms, TE=8.67, 24.36, 40.05, 55.74ms, FA=90°, resolution=3.5x3.5x3.5mm^3, a parallel imaging factor of 2 and 106 dynamics. ***Analysis:*** For each participant, the raw fcMRI dataset was first separated based on echo number and preprocessed in the sequence of motion correction, spatial smoothing, temporal filtering, and normalization to the MNI space using SPM 8. Following that, the estimated motion parameters, as well as the mean signal from ventricles, were regressed out of the dataset for each individual echo. The four fcMRIs (with different TEs) were then combined into a single 4 dimensional dataset using a weighted average scheme [4]. The echo-combined fcMRI data was then masked with a thickened gray matter template to exclude sub-cortical tissues. Finally, both local and remote connectivity maps were computed on the masked data using an approach similar to that described by Stufflebeam et al [2]. In the local connectivity map, each voxel's value was calculated by averaging the Pearson's correlation coefficients (thresholded at 0.01) between the time courses of the current voxel and its surrounding voxels (radius < 4mm). For remote connectivity, each voxel's value in the map was determined by the averaged correlation coefficients (thresholded at 0.01) between the time courses of the current voxel and its distant voxels (radius > 26mm). The local and remote connectivity maps for each participant were then entered into a group level GLM to study the effect of age on the functional connectivity. Demeaned full scale WASI score was treated as a nuisance covariate in the GLM to regress out linear IQ effects. For local and remote connectivity maps, both +age and –age contrasts (uncorrectly p<0.001, cluster size>20 voxels) were generated by the GLM analysis. The +age contrast captures positive correlations between age and connectivity, whereas the –age contrast reveals any negative correlations.

RESULTS AND DISCUSSION

No abnormalities were detected on the anatomical MRI scans for any of the subjects by an experienced neuroradiologist. None of the fcMRI datasets showed severe motion (mean displacement>3mm). Local connectivity exhibited an age dependent decrease (Fig. A) in the (bilateral) frontal and temporal lobes, but did not display any age dependent increases. In contrast, remote connectivity showed age modulated increase in the frontal-parietal network (primarily on the right hemisphere) but showed no areas of decreased modulation with age. This result echoes the findings of a study which used graph theory to analyse fcMRI and which concluded that the functional networks evolve from high degree local connections to distributed networks as brain matures [1]. Our observations also demonstrate the importance of including age in the analysis when developing fcMRI based clinical applications such as identifying surgical targets in epilepsy [2]. The current study is obviously limited by the relatively small sample size. We are continuing the enrollment for this research and exploring means to better utilize the multi-echo data such as automated elimination of nuisance components in ICA analysis based on the pattern of signal decay across multiple echoes [5].



A. The -age contrast shows local connectivity decreases as the brain develops; **B.** The +age contrast shows remote connectivity increases as the brain develops.

CONCLUSION

The current study shows a decrease in local connectivity with age, and a corresponding increase in remote connectivity with age in a pediatric population.

REFERENCES

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