

Atlas-based quantification of diffusion tensor imaging (DTI) and resting-state functional MRI (rs-fMRI) in children with cerebral palsy (CP)

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Target Audience: Pediatric neuroradiologists, pediatric neurologists, and neuroscientists interested in pediatric DTI and fMRI

Purpose: Cerebral palsy (CP) is a heterogeneous group of disorders with different risk factors, causes, and prognoses. In CP, MRI provides important information about the severity and extent of multiple sites of brain injury, and is helpful for understanding pathogenesis and planning clinical intervention [1]. However, the highly variable nature of the location and extent of injuries make objective analysis challenging. Previously, to achieve a systematic description of brain injuries in CP, we applied quantitative atlas-based analysis to whole-brain MRI/DTI to extract anatomical features in two types of CP [2]. In the current study, as a further attempt to integrate multi-modal images systematically, we extended our atlas-based approach to MRI/DTI data by adding resting-state functional MRI (rs-fMRI). We parcellated the brain into 185 structures, obtained scalar measurements using population-based Z-score for MRI/DTI and inter-parcel correlation coefficients for rs-fMRI. Then we used principal component analysis (PCA) to describe the characteristics of CP in a systematic and quantitative manner.

Methods: We studied 23 children diagnosed as spastic-type CP (age 5.1-17.6 years; mean 11.0 years; gross motor function classification system (GMFCS) score I-III), and 20 neurotypical children (age 2-13 years; mean 13.0 years). MRI was performed at 3 T. DTI used 33 gradient directions with 0.83x0.83x2.2 mm³ resolution, and a maximum *b* value of 800 s/mm². Anatomical images were obtained using 3D MP-RAGE with 1x1x1 mm³ resolution. For BOLD rs-fMRI, we used gradient-echo EPI with 2.63x2.63x4 mm³ resolution. The rs-fMRI data were slice-time-corrected, realigned to the first image using rigid body registration to adjust for head motion, and then co-registered to the b0 image using SPM8 rigid body transformation. DTI images were normalized to the JHU-DTI-MNI "Eve" template [3] via a 9-parameter affine transformation using AIR, followed by large deformation diffeomorphic metric mapping (LDDMM) [4, 5]. Inverse transformation of the brain parcellation map led to segmentation of the brain into 159 anatomical structures (Figure 1) [3]. Peripheral white matter and gray matter were separated using Statistical Parametric Mapping (SPM) segmentation of MP-RAGE images. For each subject, we thus obtained DTI outcome measures (fractional anisotropy (FA), mean diffusivity (MD), and volume) for 185 parcels, and a matrix of 185 parcels by 210 time points for rs-fMRI. All measurements were adjusted by age by using batch effect correction. DTI parameters for peripheral gray matter were discarded, and population-based Z-scores were calculated for the remaining 131 parcels. Principal component analysis (PCA) was applied to the Z scores, to extract components that described the characterization of CP and control children. For rs-fMRI, after nuisance removal and filtering [6], inter-parcel correlation coefficients were calculated for the CP and control children by using 46 cortical parcellations; PCA was then applied to the matrix of correlation coefficients.

Results: Figure 2 shows the distribution of CP and control children in three principal components extracted from volume and DTI-derived measures. Figure 3 shows the average inter-parcel correlation coefficients obtained from rs-fMRI in CP and controls.

Discussion: Deep white matter, ventricles, and thalamus were the main structures in which changes in MRI/DTI data were seen in the CP group. PCA using DTI-derived Z scores showed segregation between the CP group and the control group. Regarding the rs-fMRI data, absolute correlation coefficients tended to be smaller in CP children compared with controls, although inter-parcel patterns were similar. PCA using these inter-parcel correlation coefficients showed more concentrated distributions in controls, and more scattered distributions in CP children, consistent with the anatomical variability seen in CP, which cannot be identified by the qualitative analysis.

Conclusion: Atlas-based analysis of multi-modal imaging data, followed by principal component analysis, provides a quantitative means of summarizing inter-group differences, and may lead to approaches to correlate imaging outcomes with individual functional assessments in CP and to measure outcomes of interventions that may affect brain reorganization.

References: 1: Thomas B, et al., Brain 128:2562, 2005. 2: Yoshida S, et al. JMRI (in press). 3: Oishi K, et al., Neuroimage 46:486, 2009. 4: Miller MI, et al., Ann Rev Biomed Eng 4:375, 2002. 5: Beg MF, et al., Int J Comput Vision 61:139, 2005. 6: Faria AV, et al., Neuroimage 61:613, 2012.

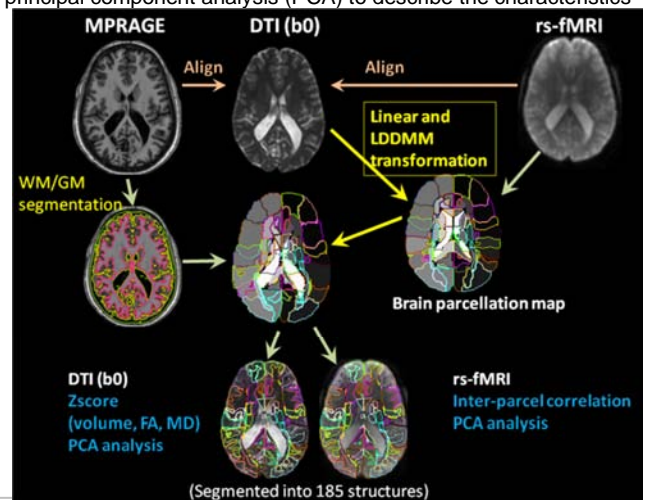


Figure 1: Image analysis. The subject image was linearly normalized, followed by LDDMM. The inverse transformation overlays the white matter parcellation map onto the original DTI image. Combined with white matter / cortical segmentation, the original images are segmented into 185 subregions [2-5].

Figure 2 (right): PCA plot (each symbol is one child) with respect to first three principal components based on volume and DTI-derived measures. Key: Purple: normal; Red: CP, GMFCSI; Blue: CP, CMFCSII; Green: CP, GMFCSIII.

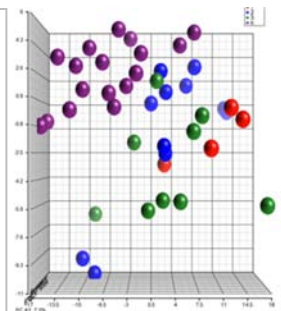


Figure 3 (below): Averaged inter-cortical parcel correlation coefficients map of controls (left) and CP group (right).

