Using clinical images to study the evolution of mean ADC values and brain volume of healthy pediatric subjects

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Introduction

Diffusion Tensor Imaging measures the water diffusion magnitude and is a surrogate marker for myelin development [1], which undergoes dramatic changes in early neurodevelopment [2].

The aim of this study was to investigate an MRI metric, the Apparent Diffusion Coefficient (ADC), of normative brain development from birth to early childhood.

We used the clinical informatics infrastructure at our institutions in order to identify this pediatric cohort and retrieve images from the Radiology Department archives. Clinical ADC images were then processed with multi-atlas-based skull-stripping tools and brain morphometric measures were extracted.

Methods

We used the Research Patient Data Registry (RPDR) to identify a pediatric cohort and the mi2b2 workbench (mi2b2help.partners.org) [3] to retrieve clinical brain MRI scans.

RPDR (Figure 1) is an analytical database allowing researchers to access clinical information in order to obtain cohorts of patients with IRB approval [4]. It is the foundation upon which the nationally distributed i2b2 (Informatics for Integrating Biology and the Bedside) project was developed (https://www.i2b2.org/).

mi2b2 (Figure 2) is an open-source add-on to RPDR/i2b2 that allows medical images collected during routine clinical practice to be repurposed for research and educational use in a HIPAA-compliant manner [3].

We submitted a request to RPDR for patients aged zero to six years old who had diffusion scans after 2000. It resulted in a cohort of 4745 pediatric patients with a brain MRI. 1765 potentially normative brain MRI studies belonging to 1600 patients were identified.

Expert review of the medical records to exclude any brain trauma or neurodevelopmental abnormality and visual inspection of all images to exclude motion corrupted or artifact-degraded scans, we created a final cohort of n=308 healthy pediatric subjects. This normative cohort was divided into 10 age groups sampling the first two weeks (neonatal stage), quarterly in the first year, and then yearly after six years old to most robustly capture developmental changes. ADC images were processed with multi-atlas-based skull-stripping tools specifically implemented for neonatal and pediatric ADC images [5] [6] and brain morphometric measures were extracted (Figures 3, 4, 5).

Results

Diffusion weighted images were acquired on a Siemens Trio 3T scanner at MGH. Repetition time (TR): 7500~9500 ms, echo time (TE): 80~115 ms, b values: 1000 s/mm², image size: 256x256x60 voxels, voxel size: 0.86x0.86x2.0 mm³. ADC maps were generated by scanner-embedded diffusion tensor imaging software.

ADC characterization of neurodevelopment.

Mean and standard deviation of whole-brain volume in each age-group.

Mean ADC values display a dramatic decrease during the first six months of life (Figure 4) and begin to plateau starting at age one. This is consistent with published reports [7] [8] about rapid myelination during early infancy and its consequent stabilization during childhood.

Figure 5

Morphometric characterization of neurodevelopment.

Mean and standard deviation of whole-brain volume in each age-group. CSF is excluded.

Discussion

In Figure 5, a rapid rise in average brain volume characterizes the first year of life, followed by a steady phase in early childhood. This is in agreement with published literature [9] [10].

Clinically acquired Diffusion MR images were amassed and processed with our neonatal-specific automated brain extraction pipeline. Mean whole-brain ADC and volume values were extracted and used to characterize early life development.

This study demonstrates that clinical ADC images can be used to obtain meaningful quantitative measures of normative brain development in early childhood, confirming that clinical material is of sufficient quality to be used for research. These are the critical initial steps towards the goals of mining and repurposing of institutional big data in order to further neurodevelopmental characterization.

Limitations

There is inevitable risk of inaccuracies when manually reviewing medical records and visually inspecting images. A way to address this issue would be to increase our sample size. However, a rigorous statistical analysis is so far lacking to show how many subjects are sufficient to fully cover the inter-subject variability and effectively represent the normal range of variations.

Lastly, access to multi-institution, multi-vendor and multi-platform data will help improve the representation power of our atlases. In the future we will test our framework’s performances in data from different vendors (GE, Philips) and different magnetic field strengths (1.5T vs 3T).

Conclusions

References

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