Assessing White Matter Growth Trajectory of Early Neonatal Development by 3T MR-DTI

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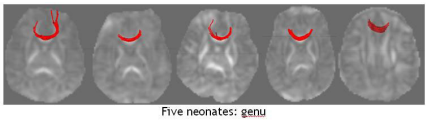
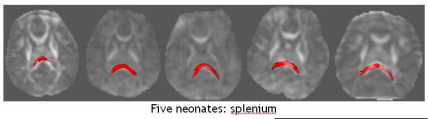
Introduction: Imaging of unsedated newborns is a challenging task in regard to scanning of subjects [Gilmore, 2004] and computer-assisted processing of image data. We present new quantitative analysis of 3Tesla diffusion tensor MRI (DTI) to study white matter development in unsedated newborns. Local diffusion properties in white matter as measured by DTI have been implicated to associate with axon density, degree of myelination and density of fluid. Population statistics of DTI requires reliable measurement of regions at corresponding anatomical locations across subjects, which is challenging due to the complexity of thin white matter bundles as presented in DTI of newborns. Limitations of conventional DTI analysis by manual ROI definition or voxel-based processing are overcome by a novel method that provides analysis of properties of major fiber bundles. We have developed a new set of tools to track white matter bundles between well-defined source and target regions. These bundles serve as complex regions of interest (ROIs) to measure white matter tract properties along tracts and within cross-sections. This gives us the ability to study a tract as a whole and assess research questions in regard to brain connectivity.

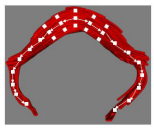
The structural brain abnormalities observed in schizophrenia are thought to arise during very early brain development, though there is little direct evidence to support this hypothesis. We are conducting a prospective study of neonatal brain structure in children at high risk for schizophrenia using 3T MRI and DTI in comparison to matched healthy subjects. DTI of neonates in general present a decrease of fractional anisotropy (FA) and an increase of the apparent diffusion coefficient (ADC) from central to peripheral regions, measured in a representative axial slice [Guihuao 2003]. The new study presented here extends the analysis of diffusion properties to three-dimensions using the novel tract-based statistical analysis.

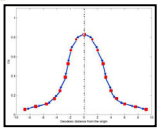


Five neonates: genu



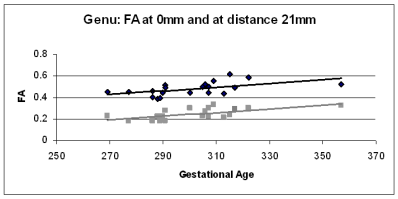
Five neonates: splenium

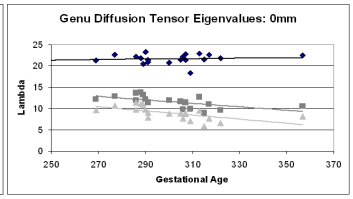


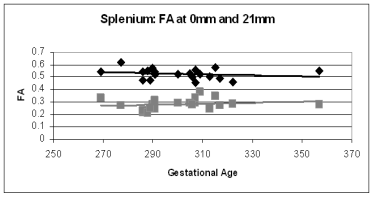


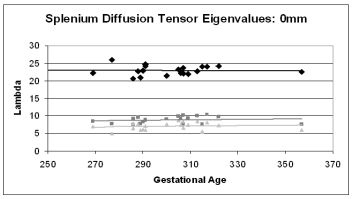
Materials and Methods: Images of 20 unsedated newborns (gestational age at MRI in days: mean 301, stdv 19) were acquired on a Siemens head-only 3T scanner (Allegra). For DTI, we used a single shot echo planar (EPI) diffusion tensor (DTI) sequence with total scan time of approximately 4 minutes. The imaging parameters for the DTI sequence were: TR/TE/TH=4219ms/92.2ms, isotropic voxels with 2mm slice distance and inplane resolution = 2 × 2mm, 4 averages, and 45 slices. Seven images were acquired for each slice, one without diffusion gradient (b=0) while the remaining six with b=1000s/mm^2 and diffusion gradients along the standard orientations as specified by Basser et al. DTI tractography is applied to assess diffusion tensor properties of the commissural bundles of the corpus callosum, in this study specifically to the genu and splenium regions. Seed regions for tractography have been manually defined on the FA image using our SNAP tool. The resulting sets of streamlines have been processed using the new FiberViewer tool [Corouge 2004, Gerig 2004] to provide quantitative diffusion tensor statistics in cross sections along fiber tracts (see right figure with parametrized splenium bundle and FA along the bundle.

Results: Diffusion tensor properties (FA, ADC, eigenvaluesλ_1,λ_2, andλ_3 were calculated along the genu and splenium tract. The graphs show the relationship between measurements (vertical axis) and gestational age at MRI (horizontal). We chose the center as the location of the midsagittal plane and peripheral properties at fiber distances of 21mm from this center, measures along the tracts. Future analysis will extend the statistical analysis to the whole curve. The left two figures show the FA of the genu tract, measured at 0mm and 21mm distance and the associated three eigenvalues at 0mm. The same is shown for the splenium tract (right two figures).









Discussion: The anlysis confirm the earlier findings in regard to decrease of FA and increase of ADC towards peripheral regions (see left figure upper and lower curves, ADC not shown). In the genu, the FA increases with gestational age (correlation 0.54 at center and 0.65 off-center), whereas the ADC decreases quickly (correlation -0.60 at center and -0.72 off-center). Off-center values change more quickly than values measured at the mid-plane. The three associated eigenvalues (second figure, only shown for center location) reveals more insight, namely that this FA increase is due to decrease of λ_2 andλ_3 whereas the diffusion along the major ttensor direction (λ_1) remains constant. The analysis of the splenium tract (right two figures) show a very different result. The FA in the splenium is already at the level reached by the genu at the end of the time window. Also, the values do not change significantly during the time inverval for both, the central and peripheral regions. Further analysis on a larger population with extended age range might reveal more insight into the trajectory of growth as measured by DTI and measured as a function of anatomical location. In conclusion, the extended set of features provided by the new methodology which includes accurate measurement across bundles and along fiber tracts seems to have a good potential to study early development in cross-sectional and longitudinal studies. This might lead to an improved understanding of MRI/DTI findings and its association to normal/abnormal brain development at early age.

References:

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