

## Developmental Increase of Diffusion Anisotropy in the Acoustic Radiations Measured by DTI Correlates with Maturational Shortening of Auditory Evoked Neuromagnetic Field Response Detected with Magnetoencephalography (MEG)

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**INTRODUCTION:** Auditory cortex evoked responses rely on conduction of impulses from the ear, through brainstem, thalamus (medial geniculate nucleus) to superior temporal lobe. Emerging theories of neuropsychiatric disorders such as autism spectrum disorders (ASD) suggest anomalies of connectivity between functional areas with commensurate electrophysiological disturbances. Additionally, developmental changes occurring through childhood and adolescence are associated with both structural and electrophysiological changes, reflecting maturation of pathways. The purpose of this study is to investigate diffusion tensor imaging (DTI) of the auditory/acoustic radiations in children and adolescents in terms of the fractional anisotropy (FA) changes during development and to associate these changes with the latency of an electrophysiological marker of auditory cortex response – the “M100”, recorded by magnetoencephalography (MEG).

**MATERIALS AND METHODS:** 28 children and teenagers (6-18yrs old) underwent MRI including DTI as well as MEG examinations. DTI consisted of whole-brain 2x2x2mm isotropic acquisitions with 30 directions and b-value of 1000s/mm<sup>2</sup>. Postprocessing, including calculation of fractional anisotropy (FA) and fiber tracking, was performed using DTIStudio using an FA threshold of 0.25 and an angle cutoff of 70°. Visualization was performed using Siemens Neuro3D/DTI package. MEG recordings were made during auditory stimulation (40dB SL) with sinusoidal tones of frequency 300Hz and 500Hz using a 275-channel whole-head biomagnetometer. Determination of the latency of the major auditory evoked field component (the “M100”) occurring ~100ms post stimulus onset was made for each hemisphere.

**RESULTS:** Fractional anisotropy (FA) in the acoustic radiations increased linearly with age, in the range FA=0.39 to FA=0.58. The correlation coefficient was  $r=0.78$ ,  $p<0.05$  and the slope was 0.014 per year in the age range 6-18years. MEG measures of cortical auditory evoked responses, characterized by the latency of the “M100” response, varied in the range 112-166ms over the same age range for responses elicited by 500Hz tone stimuli, with a correlation coefficient of  $r= -0.76$  ( $p<0.05$ ), indicating a significant shortening of the M100 latency with increasing age with a slope of ~5ms per year of age. Similar correlation was obtained for 300Hz stimulus tones ( $r=-0.84$ ,  $p<0.05$ ). Comparing FA and M100 latency directly revealed a negative correlation of  $r=-0.68$  ( $p<0.05$ ) for the 500Hz tone stimulus and  $r=-0.69$  ( $p<0.05$ ) for the 300Hz stimulus, with a slope of ~20ms per 0.1 change in FA.

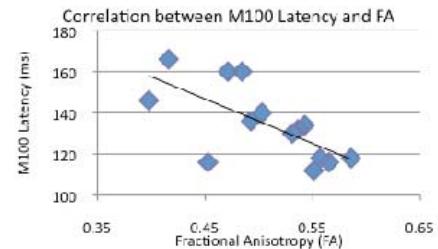
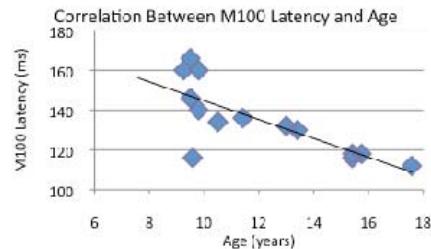
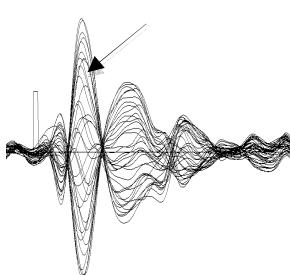
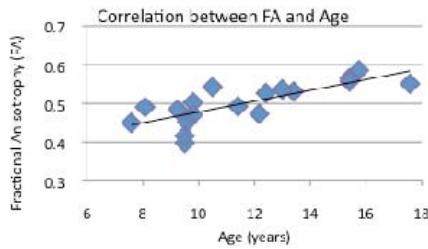
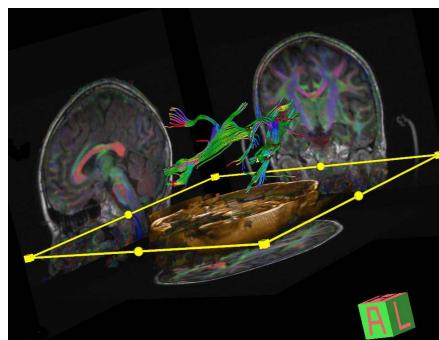


Figure: (far left): DTI Fiber tracking allows tract based computation of FA. (left) Auditory evoked neuromagnetic field, detected by MEG. The major component (M100) occurs at approximately 100ms post stimulus (arrow). Below: (left) increasing FA with age, (middle) decreasing M100 latency with age, (right): negative correlation between FA and M100 latency.

**DISCUSSION:** This study establishes a positive correlation of FA with age during development, and a negative correlation of M100 latency with age. Furthermore, FA and M100 latency are significantly negatively correlated, suggesting a biophysical mechanism (white matter myelination, reflected in increasing FA) to explain the electrophysiological observation of evoked response latency shortening with age.