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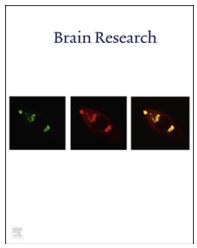

Research Report

Maturational differences in thalamocortical white matter microstructure and auditory evoked response latencies in autism spectrum disorders

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ABSTRACT

White matter diffusion anisotropy in the acoustic radiations was characterized as a function of development in autistic and typically developing children. Auditory-evoked neuromagnetic fields were also recorded from the same individuals and the latency of the left and right middle latency superior temporal gyrus auditory ~50 ms response (M50)[1] was measured. Group differences in structural and functional auditory measures were examined, as were group differences in associations between white matter pathways, M50 latency, and age. Acoustic radiation white matter fractional anisotropy did not differ between groups. Individuals with autism displayed a significant M50 latency delay. Only in typically developing controls, white matter fractional anisotropy increased with age and increased white matter anisotropy was associated with earlier M50 responses. M50 latency, however, decreased with age in both groups. Present findings thus indicate that although there is loss of a relationship between white matter structure and auditory cortex function in autism spectrum disorders, and although there are delayed auditory responses in individuals with autism than compared with age-matched controls, M50 latency nevertheless decreases as a function of age in autism, parallel to the observation in typically developing controls (although with an overall latency delay). To understand auditory latency delays in autism and changes in auditory responses as a function of age in controls and autism, studies examining white matter as well as other factors that influence auditory latency, such as synaptic transmission, are of interest.

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[1]M50: superior temporal gyrus auditory 50 ms response; FA: fractional anisotropy; WM: white matter; MEG: magnetoencephalography; DTI: diffusion tensor imaging; ASD: autism spectrum disorder; TD: typically developing.

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1. Introduction

During typical development, myelination of white matter (WM) confers electrical insulation to allow more efficient axonal signal conduction. This myelination is a critical determinant in processing basic sensory information as well as increasing processing speed during more complex cognitive tasks (Dockstader et al., 2012; Kandel et al., 1991; Stufflebeam et al., 2008). Due to the importance of myelination during development, an investigation of white matter maturation and its consequences in individuals with developmental disorders is of interest. Diffusion tensor imaging (DTI) allows indirect measurement of white matter maturation and of the microstructural properties of WM through fractional anisotropy (FA), a measure of the organization of water diffusion (Beaulieu, 2002; Harsan et al., 2006).

Whereas DTI provides measures of brain structure, magnetoencephalography (MEG) permits recording of neural activity with high temporal resolution. Thus MEG's functional complement to DTI's microstructural data offers insight into the relationship between brain anatomy and function (Dockstader et al., 2012; Roberts et al., 2009, 2010; Stufflebeam et al., 2008). DTI studies have found an increase in FA with age throughout childhood (Ashtari et al., 2007; Hasan et al., 2007; Schmithorst et al., 2002), and other studies have shown an inverse relationship between age and the latency of evoked responses in children (Paetau et al., 1995; Roberts et al., 2009, 2010). The maturational relationship of FA and latency with development has prompted examination of an association between these measures (Dockstader et al., 2012; Roberts et al., 2009; Stufflebeam et al., 2008), with studies indicating a link between increasing FA and decreasing latency as a biophysical feature of developmental change (Roberts et al., 2009).

Previous studies have demonstrated atypical white matter FA and delayed auditory responses in children with ASD versus typically developing (TD) children (Lange et al., 2010; Lee et al., 2007; Gage et al., 2003a, 2003b; Oram Cardy et al., 2008; Roberts et al., 2008, 2010). Furthermore, a previous study observed associations between FA of the acoustic radiations (a critical WM pathway extending from the medial geniculate nucleus of the thalamus to the primary auditory cortex in the superior temporal lobe) and the latency of the 100 ms auditory response (M100) in TD children, with both FA and M100 latency showing age-dependent developmental changes (Roberts et al., 2009).

The present study builds on previous studies, (Reite et al., 1988), examining the earlier "middle latency" cortical 50 ms auditory response (M50) and M50 latency associations with age and FA of the thalamocortical projections (see Fig. 1). Some ($N=24$) of the TD individuals reported by Roberts et al. (2009) are included in the present cohort (although the MEG paradigm and auditory response of interest differ between the studies). It was hypothesized that group differences would be observed in the rate of maturation of the M50 latency and WM thalamocortical projections, as well as group differences in associations between these measures, with the ASD population demonstrating a weaker relationship between M50 latency and FA.

2. Results

Seven subjects were excluded from final analyses because they were unable to complete the MRI exam (2 ASD) or because of excessive metal artifact in the MEG data (2 TD, 3 ASD). Useable data was obtained from 39 TD children/adolescents (mean age=11.02, SD=2.68) and 53 children/adolescents with ASD (age=10.42, SD=2.43). In this slightly reduced sample, groups did not differ in age ($p=0.23$).

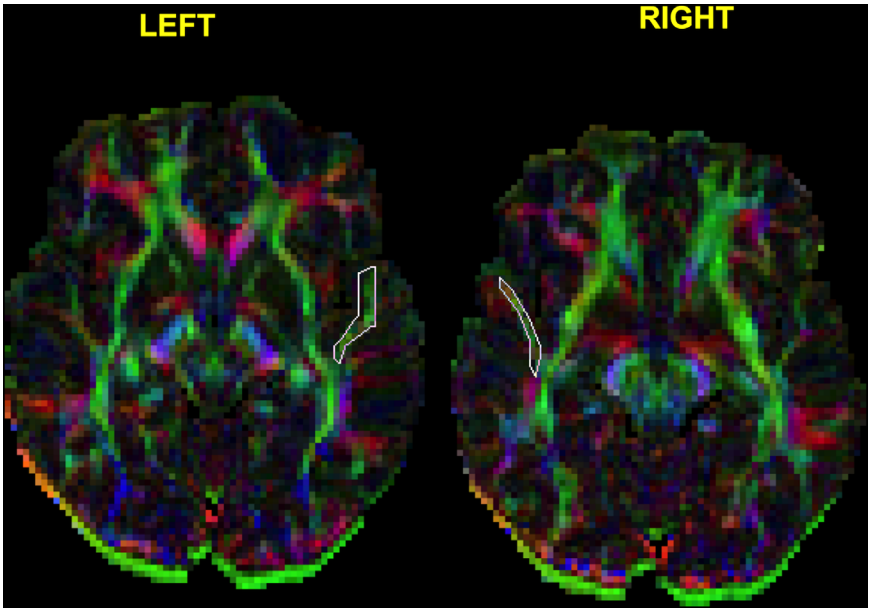

Fig. 1 – *Auditory radiation*: An example of a ROI drawn around the auditory radiation (in this case, the left) on a participant's MRI.