# Investigating Cortical Myelination and Maturation using Quantitative Myelin Water Fraction and Relaxation Time Imaging

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**Target Audience:** Developmental neuroscientists.

**Introduction:** Early childhood is a rapid period of brain development. Myelination, dendritic sprouting, and synaptic pruning yield the optimized brain networks that underly cognitive, behavioral, and motor functioning. While several studies have sought to investigate white matter maturation and myelination across childhood [1-3], cortical myelination remains understudied. Cortical changes have traditionally been investigated via cytoarchitecture, however, myeloarchitecture has seen increased attention with the introduction of methods proposed to be sensitive to cortical myelin[4]. However, these techniques are qualitative and, thus, may be unable to reveal individual differences, or identify associations with cognitive or behavioral outcomes. In this work, we sought to use quantitative imaging techniques (namely, myelin water fraction and $T_1$ relaxation time imaging) to investigate the maturation of cortical myeloarchitecture in a large cohort of healthy and typically developing children.

**Purpose:** To investigate the use of quantitative myelin water fraction and $T_1$ relaxation time imaging to map the evolution of cortical myelo and cyto-architecture in older infants, toddlers, and young children, 1 to 6 years of age.

**Methods:** *MRI Acquisition:* Whole-brain myelin water fraction (MWF) and $T_1$ maps were acquired of 215 (105 female) healthy and typically developing children using mcDESPOT [5], DESPOT1, and DESPOT2[6], with incorporated $B_1$ inhomogeneity correction[7]. Age optimized protocols were used[1], providing a constant voxel resolution of (1.8x1.8x1.8)mm$^3$. Children ranged from 363 to 2198 days (approx. 1 to 6 years) of age, corrected to a 40 week gestation. A high resolution (1.2x1.2x1.2)mm$^3$ $T_1$-weighted anatomical image was also acquired. All data collection was performed on a Siemens Tim Trio with a 12-channel head RF array. *Cortical Projections of $T_1$ and MWF:* Each child's high resolution anatomical image was intensity normalized [8] and freesurfer[9] analysis performed to delineate the cortical ribbon and segment the cortex into 48 distinct regions per hemisphere. Each child's $T_1$ and MWF maps were linearly co-registered[10] to their high resolution image, and at each cortical vertex, the mean orthonormal $T_1$, $T_2$ and MWF values calculated through the cortical ribbon was projected onto the surface. Age-averaged $T_1$ and MWF surfaces were then calculated by registering all children's surfaces to a custom mean template and averaging those between: 363-712 days (1.5 Years); 718-1099 days (2.5 Years); 1102-1442 days (3.5 Years); 1469-1814 days (4.5 Years); and 1836-2198 days (5.5 Years). Developmental Trajectories of Cortical $T_1$, $T_2$ and MWF: From the individual surface projections, plots of regional mean $T_1$ and MWF vs. age were constructed for 11 bilateral regions, including the inferior and middle temporal, lingual, inferior and superior frontal, and pre and post-central gyri; occipital and temporal poles; precuneus and cingulum[11].

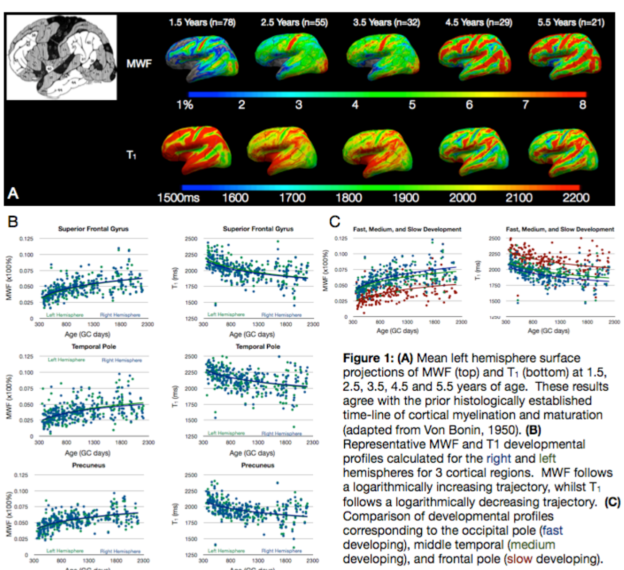


**Figure 1: (A)** Mean left hemisphere surface projections of MWF (top) and $T_1$ (bottom) at 1.5, 2.5, 3.5, 4.5 and 5.5 years of age. These results agree with the prior histologically established time-line of cortical myelination and maturation (adapted from Von Bonin, 1950). **(B)** Representative MWF and T1 developmental profiles calculated for the right and left hemispheres for 3 cortical regions. MWF follows a logarithmically increasing trajectory, whilst $T_1$ follows a logarithmically decreasing trajectory. **(C)** Comparison of developmental profiles corresponding to the occipital pole (fast developing), middle temporal (medium developing), and frontal pole (slow developing).

**Results & Discussion:** Figure 1A shows the age-averaged cortical surface MWF and $T_1$ projections at 1.5, 2.5, 3.5, 4.5, and 5.5 years of age. Shown for comparison in Fig. 1A is the map of subcortical myelination during development (originally produced by Flechsig and modified by Von Bonin). We find a similar pattern of myelination and maturation, with primary motor, somatosensory, visual, and auditory cortices developing first, and prefrontal cortex developing slowest. Figure 1B displays developmental profiles (MWF vs. age and $T_1$ vs. age) across childhood for a series of cortical regions, calculated for right and left hemisphere. Here, we found MWF follows a logarithmically increasing function, whilst $T_1$ follows a logarithmically decreasing profile. For both MWF and $T_1$ for these regions, we found no significant right-left hemisphere asymmetry in rate or trajectory. Figure 1C demonstrates the different trajectories associated with a fast, medium, and slower developing region (occipital pole, middle temporal gyrus, and frontal pole, respectively). These results represent the first non-invasive quantitative investigation of cortical myelination using myelin water and relaxation image imaging, and closely agree with prior histological data and findings. The quantitative nature of this approach lends it directly to studies investigating differences associated with developmental disorders (e.g., autism) or intellectual ability.

**References:** 1.Deoni SCL, et al. Neuroimage. 2012;63:1038–53.2.Barkovich AJ, et al. 1988;166(1 Pt 1):173–80.3.Brody BA, et al. J. Neuropathol. Exp. Neurol. 1987;46:283–301.4.Glasser MF, Van Essen DC. J Neurosci. 2011. 5.Deoni SCL, et al. Magn Reson Med. 2008;60:1372–87.6.Deoni SCL, et al. Magn Reson Med. 2005;53:237–41.7.Deoni SCL. J Magn Reson Imaging. 2009;30:411–7. 8.Boyes RG, et al. Neuroimage. 2008;39:1752–62.9.Fischl B. FreeSurfer. Neuroimage. 2012;62:774–81.10.Jenkinson M, et al.. Neuroimage. 2002;17:825–41. 11.Shaw P, et al. Am J Psychiatry. American Psychiatric Association; 2011;168(2):143–51.