Gender-Specific Templates of T1, T2 and mcDESPOT Myelin Water Fraction Map Spanning Early Childhood

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Target Audience: Developmental neuroscientists.

Introduction: Infancy and early childhood is a dynamic, yet vulnerable, period of brain development. In response to a complex cascade of environmental and genetic influences, the brain structurally and functionally matures through processes that include myelination, dendritic growth, and axonal pruning and others. It is broadly hypothesized that individual differences in these neurodevelopmental processes yield altered brain networks and functional connectivity patterns that, ultimately, result in differing behavioral and cognitive phenotypes[1-3]. In this context, developmental disorders, such as autism spectrum disorders, represent an extreme deviation from normality. To investigate the development origins of behavioral and other intellectual disorders, comprehensive characterization of normal brain maturation is first needed. In this work, we sought to perform quantitative MRI in a large sample of healthy and typically-developing infants, toddlers, and young children, with the aim of acquiring a series of gender-specific T_1, T_2 and myelin water fraction maps in children 2.5 months through 5.5 years of age.

Purpose: To develop a representative set of age and gender-specific parametric (T_1, T_2 and myelin water fraction, VF_M) maps spanning infant and early childhood brain development, 2.5 months through 5.5 years of age. Using acoustically-modified variants of the mcDESPOT relaxometry approach[4], 424 whole brain T_1, T_2 and VF_M maps were acquired of typically-developing children. From these data, 14 mean male and female T_1, T_2 and VF_M maps were created corresponding to 3, 6, 9, 12, 15, 18, 21, 24, 30, 36, 42, 48, 54 and 60 months of age.

Methods: *MRI Acquisition:* 424 mcDESPOT datasets were successfully acquired from 231 healthy and typically-developing children (113 were scanned 2x; 51 3x; 13 4x; and 3 5x) between the ages of 2.5 months and 5.5 years of age broken down by age group as shown in Table 1. Data were acquired on a Siemens Tim Trio scanner during natural non-sedated sleep (children under 4 years) or while watching a movie using previously described customized 'silent' pulse sequences[5]. Three-pool mcDESPOT post-processing[6], including correction for B_0 and B_1 field inhomogeneity, was used to calculate quantitative T_1, T_2, and VF_M parameter maps. These maps were subsequently non-linearly aligned to a custom study template in approximate MNI space[5]. 14 average male and female T_1, T_2 and VF_M maps were then calculated by averaging the participants within each age and gender demographic (Table 1). Regional masks corresponding to major white matter areas and pathways were derived from the MNI and John Hopkins white matter atlases, superimposed on each participant's T_1, T_2 and VF_M maps, and mean values calculated. Trajectories of these parameters were then plotted to investigate their variation throughout infancy and early childhood.

	3 Months	6 Months	9 Months	12 Months	15 Months	18 Months	21 Months
Male	21	18	26	14	16	16	15
Female	15	17	18	17	14	14	14
	24 Months	30 Months	36 Months	42 Months	48 Months	54 Months	60 Months
Male	13	18	15	15	12	11	15
Female	16	16	14	12	8	11	12

Table 1: Number of subjects in each age and gender category.

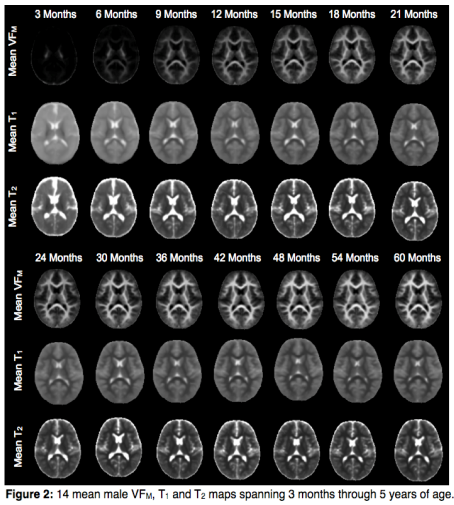

Figure 2: 14 mean male VF_M, T_1 and T_2 maps spanning 3 months through 5 years of age.

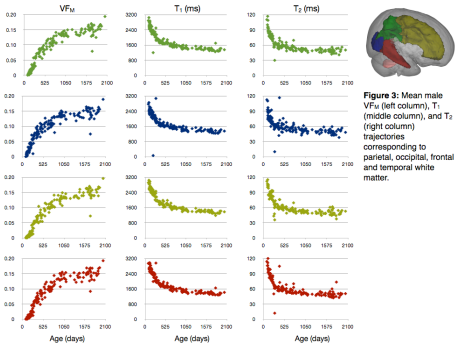

Figure 3: Mean male VF_M (left column), T_1 (middle column), and T_2 (right column) trajectories corresponding to parietal, occipital, frontal and temporal white matter.

Results & Discussion: Representative axial slices through the 14 mean male and female template T_1, T_2 and VF_M maps are shown in Fig. 1. These maps, and the corresponding raw data, are freely available to the research community at babyimaginglab.com/research.htm. Parameter trajectories, corresponding to frontal, occipital, parietal and temporal white matter regions are shown in Fig. 2. As has been shown previously, T_1 and T_2 decrease with age in approximate exponential fashion, whilst VF_M increases according to a sigmoidal function. The observed changes in T_1, T_2, and VF_M reflect a wide array of neurodevelopmental processes, including changes in axonal density and structure, water compartmentalization and, perhaps more specifically in the case of VF_M, myelination. These results provide the first consistent set of quantitative parametric maps spanning this dynamic, yet vulnerable, period of neurodevelopment that coincides with the onset of many social, emotional, cognitive, and behavioral functions. The data represents a valuable resource, offering a normative template to which suspected at-risk populations may be compared, or for use in optimizing acquisition protocols for more conventional volumetric studies.

References: [1] Akshoomoff A et al. (2002). Dev. Psychopathology. 14: 613-634. [2] Hazlett HZ, et al. (2005). Arch. Gen. Psychiatry. 62: 1366-1376. [3] Krain AL, et al.. Clin. Psychol Rev. 26: 433-444. [4] Deoni SC, et al. (2008). Magn. Reson. Med. 60: 1372-1387. [5] Deoni SC, et al. (2012). NeuroImage. 63: 1038-1053. [6] Deoni SC, et al. (2013). Magn. Reson. Med. 70: 147-154.