T2 Relaxometry of Normal Pediatric Brain Development

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Objective: The NIH MRI Study of Normal brain Development [1] is a large ongoing multi-center study of brain and behavior development in healthy children. As part of that study we have established normal age-related changes in quantitative MR relaxometry parameters. We report here on the T2 relaxation time constant evolution in several brain regions for children within the range of birth to 4-years, 5-months. The goal of this study is to provide a publicly available normative pediatric MRI and behavior database, which can subsequently be used in studies assessing normal brain development and deviation due to various neurological disorders.

Methods: The sampling plan consisted of acquiring both cross-sectional and longitudinal T2 relaxometry data for 75 subjects between the age of 0 and 4-years, 5-months, with a total of 201 scans. Data acquisition consisted of two sets of dual contrast fast/turbo spin echo (FSE/TSE) images on GE and Siemens 1.5T scanners, resulting in four effective echo times (TEeff~15, 80, 120, 160 ms). T2 relaxation time constants were estimated on a voxel-by-voxel basis using a single exponential model. Regions of interest (ROIs) were selected on the resulting parametric T2 maps to investigate the dependence of this tissue-specific parameter on age. A mono-exponential was also used to model the measured T2 as a function of age in specific ROIs, using the equation proposed by Engelbrecht et al. [2]:

$$T2 = T2_0 + T2_1 e^{-Ct}$$

where T20, T21 are in ms, C is in 1/months, and t is the age in months. The bi-exponential approach of Ding et al. [3] was also investigated. For this approach, it was determined whether the addition of the extra parameter is justified through the adjusted coefficient of correlation: R_a^2 (takes into account the number of parameters and only increases if the fit is improved). Inter and intra-site variability were assessed using an ACR phantom and a living phantom (healthy adult) both scanned periodically at the participating sites.

Results: The coefficients of variation in the T2 estimates were less than 3% and 5% for the ACR and living phantoms respectively. For the children, grey and white matter regions showed a continuously decreasing T2 value with age, with more pronounced changes occurring in the first few months of life. For infants up to 1 month of age, the average T2 in white matter was approximately 423±13 ms for major (occipital) and minor (frontal) forceps and 236±7 ms for the corpus callosum. In the case of deep grey matter structures, the average time constant was 226±6 ms. These values can be contrasted with those for adults, where T2 is expected to reach approximately 80ms for white matter and 100ms for grey matter. For the 6 ROIs shown in Figure 1, the quality of fit for the mono-exponential model, as given by the adjusted coefficient of correlation were R_a^2 = 85-89% in white matter and R_a^2 = 84-86% in grey matter. No significant increase in R_a^2 was observed for the bi-exponential model of T2 changes with age.

Discussion: Since T2 values in this study were evaluated using slice selective RF pulses and "effective" echo times, the accuracy of any T2 measurement is slightly less (4-15%) than found in phantoms using a "gold standard" 32 echo hard pulse CPMG sequence (data not shown). Nevertheless, the technique reliably detected T2 changes with age. The T2 values at birth are consistent with those reported by Ding et al. [3] for both white (T2~400 ms) and grey matter (T2~200 ms) for a similar TSE acquisition. In terms of the age-regression, a mono-exponential model is well suited to the dataset and additional terms do not significantly increase the quality of fit. This is perhaps due to the smaller age range used here than that by Ding et al. [3] (0-4.5 years vs. 3 weeks-39 years). The decline in T2 reflects changes in water content in addition to the progression of myelination in white matter and cell maturation in grey matter. The pattern of T2 evolution parallels known caudal-to-rostral timing of myelination [4], whereby the rate of decline is faster in occipital than in frontal white matter (Cmf < CMF) and faster in the splenium than the genu of the corpus callosum (CgCC < CsCC). The relatively slower rate in the corpus callosum could indicate an already advanced degree of myelination due to a high concentration of early myelinating fibers [5]. In order to investigate regions beyond the ROI analysis on a scan-by-scan basis, we have also developed a pediatric brain model. It consists of 8 co-registered age-range specific models, created by applying iterative linear and non-linear registration to all subject scans. This model facilitates the investigation of T2 evolution in the pediatric brain as a whole and is thus an important tool for future studies on early brain development and behavior.

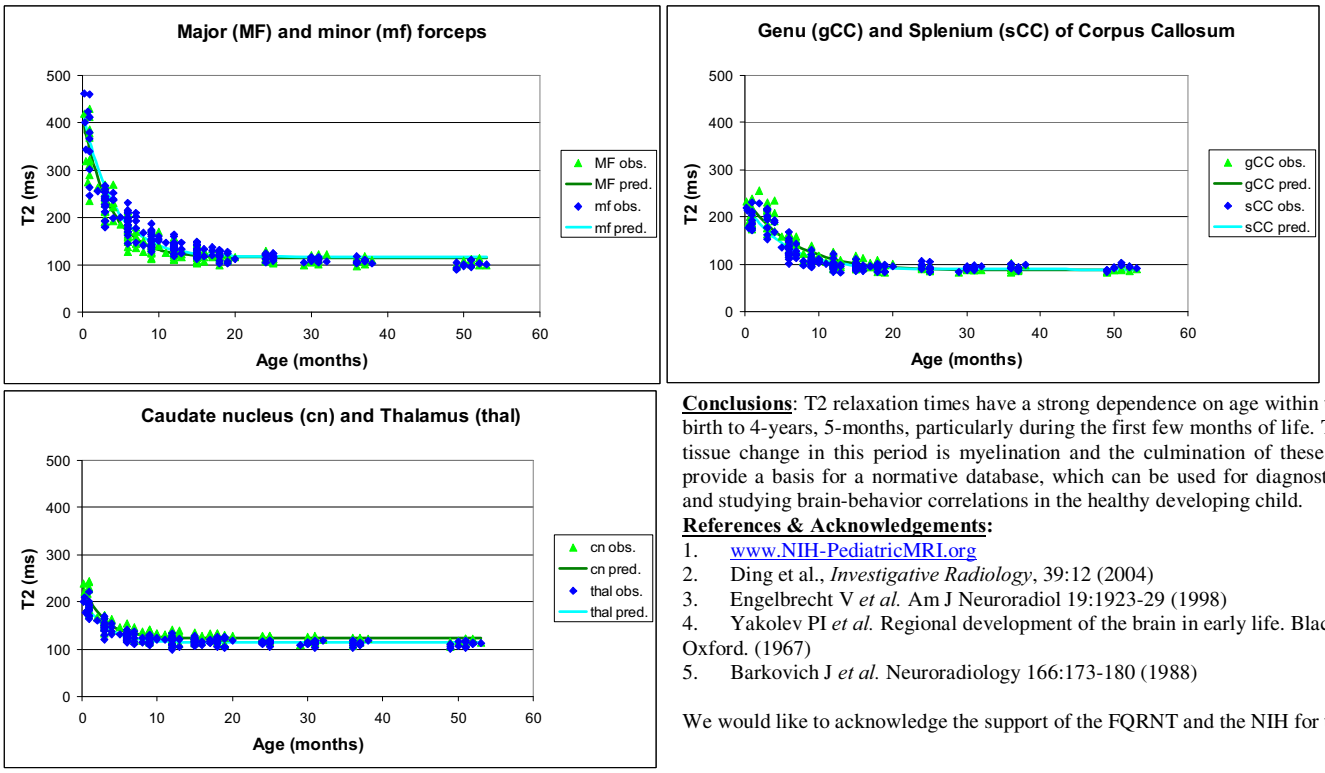

Figure1. Mono-exponential model of T2 decay with age in 6 ROIs

Conclusions: T2 relaxation times have a strong dependence on age within the range of birth to 4-years, 5-months, particularly during the first few months of life. The primary tissue change in this period is myelination and the culmination of these results can provide a basis for a normative database, which can be used for diagnostic purposes and studying brain-behavior correlations in the healthy developing child.

References & Acknowledgements:

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