MORE THAN MEETS THE EYE: AGE AND PATHOLOGY-RELATED MTR CHANGES IN VERY PRETERM BRAINS

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Introduction:

Magnetization transfer ratio (MTR) provides a semi-quantitative measure of myelination, a key maturational process of the CNS[1]. As such, MTR may enable the detection of disease not distinguishable on conventional MR imaging[2]. However, few studies have explored the use of MTR in evaluating CNS development in the paediatric population, with fewer still in preterm infants[1,3,4]. Our study compared MTR values of three different deep grey matter (GM) structures in the very preterm (<32 weeks GA) brain, presenting with various pathologies.

Methods:

Subjects: The study cohort included 44 preterm neonates born between 24 to 32 weeks gestational age (GA) (mean, $28^{6/7}$ weeks) and scanned between 26 to 34 weeks (mean, $30^{2/7}$ weeks). Informed, written consent was given by the infants' parents; the study was approved by the hospital's research ethics board. Infants were separated into four groups according to radiological findings on conventional MR scans: 26 normal (including 2 with non-specific basal ganglia hyperintensity), 8 white matter (WM) injury only, 3 Grade I germinal matrix haemorrhage (GMH) and WM-injury, and 7 Grade II GMH and WM-injury. All cases had normal-appearing deep GM. The GMHI+WM group was excluded due to insufficient sample size.

MR Acquisition: MR scans were performed on a 1.5T GE Signa Excite HD scanner (GE, Milwaukee, WI, USA) using an MR-compatible incubator and neonatal head coil (Advanced Imaging Research, Inc. Cleveland, USA). High resolution axial T_1- and T_2-weighted (T_1w and T_2w) volumes were acquired using 3D spoiled gradient recalled (SPGR) (TR/TE/FA=23ms/4ms/19º, BW=15.63kHz, FOV=12.8cm, matrix=128x128, 110 slices of 1 mm) and multi-slice 2D FRFSE (TR/TE/ETL=4000/145ms/19, BW=25kHZ, FOV=12.8cm, matrix=128x128, 90 slices of 1 mm). MT images were obtained with 1x1x1.5 mm voxel size and TR/TE/FA=27ms/4ms/10º by acquiring the sequence twice – once with an off-resonance MT saturation pulse and once without.

Image Processing: The Brain Extraction Tool (BET) was used to segment T_2w volumes into brain and non-brain[5]. Images were reviewed on a case-by-case basis and an inter-slice motion correction algorithm based on the MNI minctracc tool[6] was applied where needed. All images were corrected for intensity non-uniformity using the MNI N3 algorithm[7]. The anterior and posterior commissures (AC-PC line) and mid-sagittal plane were manually tagged on T_1w scans using Display software. These tag files were then used to align T_1w, T_2w and MT scans in a Talairach-based orientation with the origin at the AC. MTR images were obtained by computing the percent difference between scans with and without the off-resonance pulse. The thalami (left and right), basal ganglia (BG) (left and right) and pons (single volume) were manually segmented on T_1w scans for each subject and MTR values for these structures extracted.

Analysis: A paired t-test was conducted for each group (by pathology) comparing the left and right BG and thalami. To assess age-related changes in MTR values in the current cohort, a linear regression analysis was performed. A two-way between subjects analysis of variance (ANOVA) was conducted to determine if there were significant pathology-related differences in the relation between mean MTR values and age in each of the three brain regions segmented.

Results:

A paired Student's t-test confirmed that no significant differences ($p<0.05$) in mean MTR existed between the left and right BG and thalami. Therefore, left and right volumes were combined for analyses. Linear regression showed that mean MTR increased with GA in the BG and thalami (T) for both the normal (r=0.61 BG, 0.67 T) and WM-injury (r=0.85 BG, 0.80 T) groups. However, the correlation between mean MTR and GA for the BG and thalami was poor in the GMHII+WM group (r=0.03 BG, 0.01 T) (Fig. 1). No correlation between mean MTR and GA was seen in any of the groups for the pons. Two-way ANOVA confirmed that the increase in MTR with age was similar in the BG and thalami for the normal and WM-injury groups. Furthermore, pathology had a significant effect on MTR in the BG ($p<0.05$), with higher values seen in the normal group compared to the WM-injury group. The lack of correlation between MTR and age in the pons may be attributable to the earlier maturation of white matter tracts passing through this region of the brain. This is consistent with studies demonstrating myelination of the pons at ≤28 weeks GA, as well as the caudal-to-rostral nature of myelination in the developing CNS[8]. The poor correlation between MTR and age in the GMHII+WM group is consistent with a previous study where severe pathology had a strong effect on MR parameters that was not age-dependant[9].

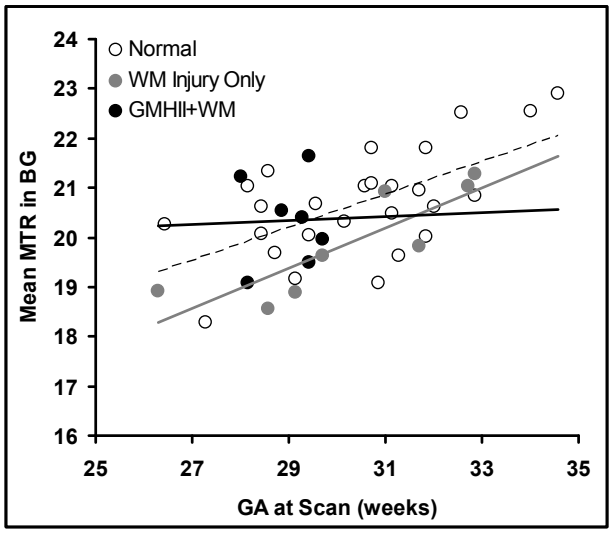

Fig. 1: Mean MTR versus GA at scan for basal ganglia of individual subjects.

Conclusions:

In normal preterm infants or those with some degree of WM-injury but normal appearing deep GM structures, MTR increased with GA in both the BG and thalami. This relation was not seen in the pons or in infants with more severe injury, presumably due to earlier WM maturation of the pons and injury-related developmental effects, respectively. In the BG, the normal group demonstrated consistently higher MTR values than the WM-injury group, indicating GM effects not detected on conventional MRI.

References: **1.** Xydis V et al. *Eur Radiol, 2006; 16: 215-220.* **2.** Rovira À & Adelaida L. *Eur J Radiol, 2008; 67: 409-414.* **3.** Engelbrecht V et al. *AJNR, 1998; 19: 1923-1929.* **4.** Van Buchem MA et al. *AJNR, 2001; 22:762-766.* **5.** Smith SM. *Hum Brain Mapp, 2002; 17:143-155.* **6.** Collins DL et al. *J Comput Assist Tomogr, 1994; 18:192-205.* **7.** Sled JG et al. *IEEE Trans Med Imaging, 1998; 17:87-97.* **8.** Counsell SJ et al. *AJNR, 2002; 23:872-881.* **9.** Nossin-Manor R et al. *Proc Intl Soc Mag Reson Med 17, 2009; 5669.*