Comparison of Magnetization Transfer Ratios in White Matter and Gray Matter of Neonatal, Juvenile, and Adult Rats

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Introduction

Magnetization Transfer (MT) imaging has been introduced as a potentially useful method for studying cerebral white matter injury. Relatively few studies have used MT to image hypoxic-ischemic injury in immature brain but there are indications that MT is a more sensitive method of early detection of ischemic injury following cerebral hypoxia/ischemia in infants [1] as well as in adult rats [2]. Detailed ontogenic changes and the evolution of MT following a cerebral hypoxic-ischemic insult can more readily be determined in animal models. The objective of the present study was to optimize the MT technique for its application in a well-established rat model of neonatal hypoxia-ischemia where we hypothesized that 1) MT would be sensitive to white and gray matter maturation and 2) MT would detect hypoxic-ischemic changes as indicated by a reduced magnetization transfer ratio (MTR).

Materials and Methods

MT imaging was performed in neonatal rats (n=3; 7-9 days of age), juvenile rats (n=3, 5 weeks of age), and adult rats (n=2). The neonatal rat had been subjected to cerebral hypoxia-ischemia as described previously [3]. In summary, under isoflurane anesthesia the right carotid artery was ligated and the pups were subsequently exposed to 8% oxygen for 70 minutes, with chamber temperature maintained at 35.5ºC. MT imaging was performed using a 9.4T/21cm MR imaging system with proton density-weighted spin echo single-slice and multislice acquisition, with MT saturation on and off. The imaging parameters were as follows: TR=3000ms (5000ms for 100 pulses), TE=15 ms, FOV=2.0^2 cm 72 hours; 2.5^2 cm 4 weeks; 3.2^2 cm adult, 256x128 matrix, 1.0mm slice thickness, and 1500 Hz frequency offset. The MT sequence dependence on the number of RF pulses (20, 40, 60, 80, and 100) was examined at 6μT; RF power and its dependence on RF power (2, 4, 6, 8, and 10μT) were examined using 60 pulses. A distilled water phantom was included in the FOV to estimate saturation. MTR was calculated as MTR= $(1-M_s/M_0) \times 100\%$, where M_s and M_0 were the signal intensities obtained with and without MT saturation, respectively. Differences in mean ROI's from regions of white matter of the external capsule and gray matter of the parietal cortex were compared using Student's two-tailed t-tests.

Results

Both white and gray matter MTR increased during maturation with the greatest changes occurring in white matter [Fig.1, Fig.2]. At the neonatal age, white matter exhibited significantly lower MTR than gray matter. Conversely, at the juvenile age, white matter exhibited a significantly higher MTR, and this difference was relatively constant with the application of additional pulses. MTR variations with number of pulses were similar between the juvenile and adult ages. A similar dependence of MTR on RF power was also observed for white vs. gray matter at the different ages. In the hypoxic-ischemic hemisphere of either neonatal or juvenile rats, white and gray matter MTR was substantially reduced ($p<0.05$). No differences in MTR where evident between the unaffected, contralateral hemisphere and control animals. MTR in multi-slice experiments had similar variations with pulse number and RF power except the MTR overall was greater than that in single-slice experiments.

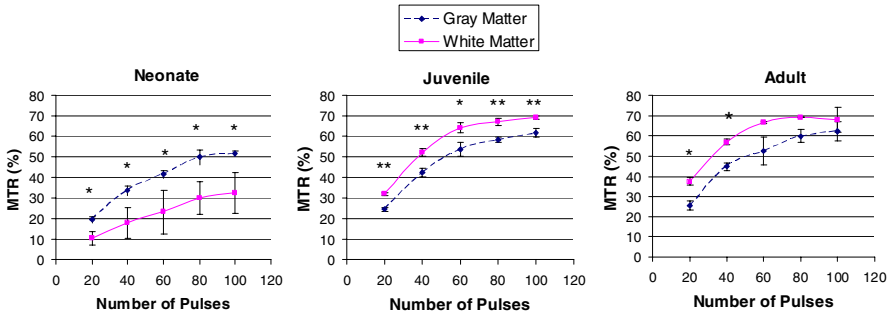

Fig. 1. MTR values in neonatal, juvenile, and adult rats using different numbers of pulses at a constant RF power of 6μT. Regions shown are the white matter (external capsule) and gray matter (parietal cortex) of the control hemisphere. *P<0.05 and **P<0.01.

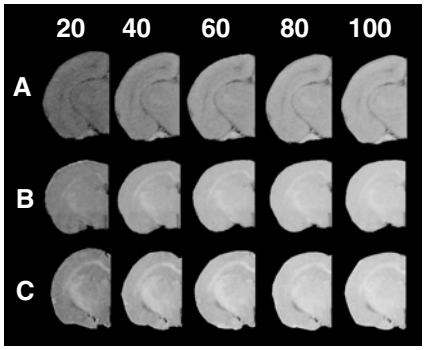

Fig. 2. MTR maps of neonatal (A), juvenile (B), and adult (C) rat brains. MTR shows maximal saturation between 60-80 pulses at RF power of 6μT.

Discussion and Conclusions

MT imaging was sensitive for detecting developmental changes occurring between the neonatal and juvenile ages, particularly in white matter. This reflects well the known increase in myelination and the sensitivity of MT imaging for detecting changes in white matter. Regarding optimization of the MT method, the MTR variation with the number of saturation pulses or RF power in single-slice experiments were similar irrespective of age (i.e., 60-80 pulses and 60 μT). The multi-slice experiment had a signal intensity reduction and thus increased MTR shown for each slice caused by additional MT effects from the 90° and 180° RF pulses applied to adjacent slices. The reduced MTR with hypoxia-ischemia may be due to both edema and loss of cellular structure. The results also support that MT imaging can be a useful method of detecting pathophysiological changes following HI, potentially allowing for early diagnosis and treatment for those infants affected by perinatal HI or cerebral palsy.

References

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