Molecular MRI detection of the brain development in normal children with magnetization transfer (MT) and amide proton transfer (APT) imaging

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TARGET AUDIENCE: Scientists and clinicians who are interested in the applications of MT and APT imaging to the brain development.

PURPOSE

Conventional MT imaging (quantified by an MR ratio, MTR) is sensitive to a semi-solid macromolecular phase in tissue (1,2), while APT imaging is a chemical exchange saturation transfer (CEST)-based approach by which endogenous mobile proteins and peptides can be detected (3,4). The aim of our work was to explore the brain development in the pediatric population using MT and APT imaging.

METHODS

Thirty children (16 males, 14 females, age range: 5 months to 16 years) without brain abnormalities were imaged on a 3Tesla Philips MR system. MR imaging data (saturation time = 800 ms; saturation power = 2 μT) were acquired using multiple frequency offsets, 15.6 ppm (2 kHz) for MT and -6 to 6 ppm (interval 0.25~1.0 ppm) for APT, in three transverse slices of the head, including pons, basal ganglia and centrum semiovale (CS). MTR at 15.6 ppm and MTR_{asym}(3.5ppm) were calculated in 10 ROIs: pons, middle cerebellar peduncle (MCP), genu of corpus callosum (GOCC), splenium of corpus callosum (SOCC), frontal white matter (FWM), occipital white matter (OWM), head of caudate nucleus (HOCN), putamen, thalamus and CS. All subjects were divided into five age groups: 0–1; 1–3; 3–6; 6–12; 12–16 years old. Age-related changes of MTR and MTR_{asym}(3.5ppm) were evaluated by an non-linear regression analysis. Correlations between MTR and MTR_{asym}(3.5ppm) in these sites were assessed with Pearson's correlation procedures. Gender differences were evaluated with a Mann-Whitney test. Statistical significance was accepted at $p < 0.05$.

RESULTS AND DISCUSSION

Tables 1 and 2 summarize MTR and MTR_{asym}(3.5ppm) of all ROIs for age Groups 1–5. MTR increased exponentially with age in the all brain regions ($y = a - b \exp(-x/c)$; Fig. 1), while MTR_{asym}(3.5ppm) declined exponentially with age in several brain regions ($y = a + b \exp(-x/c)$; Fig. 2), with the most significant change appeared within the first 2 years. Notably, there were significant negative correlations between MTR and MTR_{asym}(3.5ppm) in the GOCC ($r = -0.54$), SOCC ($r = -0.45$), FWM ($r = -0.60$), OWM ($r = -0.27$), putamen ($r = -0.32$) and thalamus ($r = -0.27$). There were no statistically significant differences in MTR or MTR_{asym}(3.5ppm) between males and females for all brain areas. The facts that MTR increased exponentially with age and MTR_{asym}(3.5ppm) decreased exponentially with age may mainly be associated with the myelination progress in the brain development, reflecting the interchange between the semi-solid and mobile macromolecular phases in tissue.

CONCLUSION

Our preliminary study has clearly shown that MTR and MTR_{asym}(3.5ppm) are two promising, complementary imaging biomarkers by which to monitor changes at the molecular level in the developing brain, presumably the myelination progress.

REFERENCES

(1) van Buchem et al. AJNR 2001;22:762. (2) Vassilios Xydis et al. Eur Radiol 2006;16:215. (3) Zhou et al. Nat Med 2003;9:1085. (4) Jones et al. MRM. 2006;56:585.

Table 1. MTR at 15.6 ppm in all ROIs for age groups (mean ± sd)

ROI	0-1y (n=3)	1-3y (n=5)	3-6y (n=5)	6-12y (n=11)	12-16y(n=6)	R^2
pons	31.6±1.9	35.1±2.1	35.2±1.1	36.9±1.3	37.5±1.2	0.6*
MCP	31.1±0.9	33.7±1.2	34.6±1.5	36.6±2.1	36.6.±1.4	0.5*
GOCC	29.3±4.4	36.7±2.2	38.3±3.5	38.8±1.5	38.3±1.4	0.7*
SOCC	33.9±6.7	38.8±1.1	39.9±2.1	38.7±1.9	38.4±1.5	0.5*
FWM	24.1±3.4	30.3±1.9	32.5±2.5	33.1±1.5	33.7±1.4	0.8*
OWM	26.4±2.8	29.9±01.0	31.4±1.1	30.8±1.5	30.6±1.3	0.5*
HOCN	24.5±1.1	26.1±1.0	27.4±1.6	27.2±1.2	27.1±0.8	0.2*
putamen	26.3±2.1	28.0±1.7	28.7±1.3	28.3±1.3	28.0±0.5	0.1*
thalamus	29.3±0.6	30.1±0.8	31.9±1.8	31.7±1.3	32.4±1.3	0.3*
CS	27.8±2.8	31.8±1.0	33.3±1.6	32.7±1.9	32.6±1.9	0.5*

Table 2. MTR_{asym}(3.5ppm) in all ROIs for age groups (mean ± sd)

ROI	0-1y (n=3)	1-3y (n=5)	3-6y (n=5)	6-12y (n=11)	12-16y(n=6)	R^2
pons	0.8±0.3	0.6±0.3	0.8±0.4	0.8±0.2	0.9±0.3	X
MCP	0.5±0.2	0.4±0.3	0.2±0.4	0.5±0.3	0.5±0.3	X
GOCC	0.1±0.8	-0.3±0.2	-0.4±0.7	-0.4±0.4	-0.5±0.5	0.2
SOCC	0.1±0.6	-0.1±0.1	-0.3±0.3	-0.1±0.4	0.1±0.2	X
FWM	0.2±0.6	-0.8±0.2	-0.7±0.3	-0.6±0.3	-0.6±0.1	0.5*
OWM	0.1±0.4	-0.3±0.2	-0.4±0.4	-0.4±0.3	-0.4±0.2	0.3*
HOCN	1.1±0.2	0.8±0.4	0.6±0.6	0.8±0.2	0.9±0.1	0.1
putamen	1.2±0.7	0.6±0.5	0.6±0.4	0.8±0.1	0.8±0.1	0.2*
thalamus	0.7±0.1	0.8±0.2	0.7±0.4	0.7±0.2	0.8±0.1	X
CS	0.1±0.6	-0.2±0.3	-0.4±0.2	-0.5±0.3	0-.4±0.2	0.4*

X represents no significant correlation.* represents $P < 0.01$.

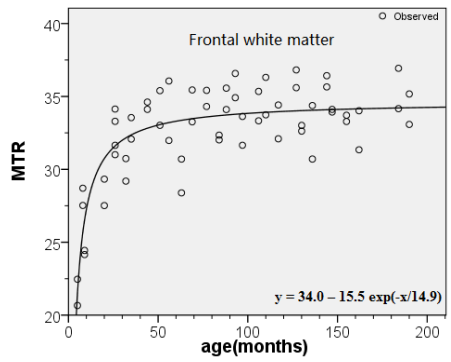

Fig. 1. Age-related changes of the MTR within FWM

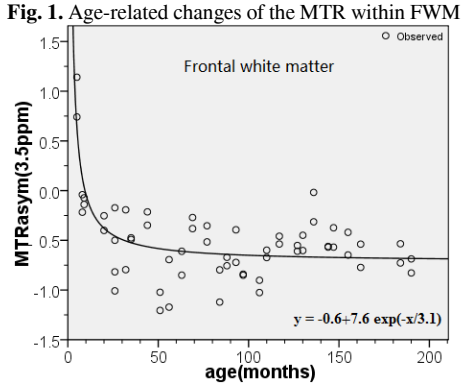

Fig. 2. Age-related changes of the MTR_{asym}(3.5ppm) within FWM