Age and Gender Related Changes in DTI Metrics in Deep Grey Matter of Normal Human Brain

D. Pal[1], A. Yadav[1], R. K. Rathore[2], C. M. Pandey[3], M. Kumar[1], R. Trivedi[1], and R. K. Gupta[1]

[1]Department of Radiodiagnosis, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India, [2]Department of Mathematics and Statistics, Indian Institute of Technology, Kanpur, India, [3]Department of Biostatistics, Sanjay Gandhi Post Graduate Institute of Medical Science, Lucknow, UP, India

Introduction: The human brain is unique in its protracted process of development, which continues until late in the fifth decade (1). Understanding human brain development is of great clinical importance, as many neurological and neurobehavioral disorders have their origin in early structural and functional cerebral maturation. T2 relaxation measure of extrapyramidal nuclei shows a decline with age and is suggested to be due to increasing iron concentration (2). However, there poor correlation between T2 value and actual iron concentration has been reported. Diffusion tenor imaging (DTI) has been used to quantify white matter changes over time and is known to predict white matter maturation (2). Age related changes in the white matter has been shown by using region of interest (ROI), voxel based analysis or quantitative fiber tracking. The cortical grey matter maturation in fetal and early postnatal period has also been extensively studied. A recent study has shown increased FA in the deep grey matter nuclei in adult controls and suggested it to be due to increased iron concentration in these regions with age (3). The purpose of the study was to quantify fractional anisotropy (FA) and mean diffusivity (MD) in basal ganglia to see the age related changes from new born to 52 years of age to see change in pattern relating to age and gender. To the best of our knowledge, this is the first study to describe the changes relating to age and gender in deep grey matter nuclei.

Materials and Methods: ***Subjects:*** Conventional MRI and DTI were performed on normal human brain with age group ranging from 10 days to 52 years. Healthy volunteers were recruited from the community who had come for routine brain screening with no neurological symptoms. In addition the healthy volunteers from the hospital staff were also excluded. Small babies formed the controls in project relating to hypoxic ischemic encephalopathy. The subjects were excluded if they were obese, or if they had a current or prior serious illness, or a medical history of diabetes, cardiovascular disease, or difficult to control hypertension. The final normal population (*N*= 125) consisted of 75 males and 50 females.

Imaging protocol: MRI data was acquired on a 1.5-T GE MRI scanner using quadrature transmit–receive head coil. The MRI protocol included T2, T1, T1 magnetization transfer (MT), T2-fluid attenuated inversion recovery (FLAIR), T2 gradient recalled echo sequence, and DTI. DTI was acquired by using a single-shot echo planar dual spin-echo sequence with ramp sampling. The b-factor was set to 0 and 1,000 s/mm^2; TR, 8 s; TE, 100 ms; and NEX, 8. In total, 32 to 36 axial sections (depending upon head size) were acquired with a slice thickness of 3 mm, no inter-slice gap, FOV of 240 mm. The diffusion tensor encoding used was a dodecahedral scheme with 10 uniformly distributed directions. The DTI data were processed using JAVA based software as described in detail elsewhere (4). The DTI-derived maps were displayed and overlaid on images with different contrasts to facilitate the region-of-interest (ROI) placement. The elliptical ROIs of size ranging from 2×2 to 5×5 pixels were placed on grey matter nuclei namely caudate nuclei, putamen and globus pallidus at the level of third ventricle on axial image.

Results: In this study we observed relationship between age and DTI metrics in deep grey nuclei of normal human brain. Cubic fit gave the best result in term of R^2 value (Table 1). An increasing trend in FA along with decreasing trend in MD in deep grey nuclei was observed as a function of age. FA values were found to be higher in males compared to females (Fig.1). However, no consistent pattern in MD values was observed in deep grey nuclei associated with gender (Fig.2).

	Parameter	Region	b_o	B_1(E-04)	B_2(E-07)	B_3(E-10)	R^2
FA	All	Caudate nuclies	.0800	2.0	-5.0	-4.7	.821
		Putamen	.0685	2.0	-5.0	-3.7	.693
		Globus pallidus	.0872	1.0	-4.0	-4.1	.696
	Female	Caudate nuclie	.0779	2.0	-5.0	-4.3	.779
		Putamen	.0677	2.0	-4.0	-2.7	.534
		Globus pallidus	.0876	1.0	-4.0	-4.1	.659
	Male	Caudate nuclie	.0873	1.0	-2.0	-2.7	.841
		Putamen	.0716	2.0	-4.0	-3.3	.699
		Globus pallidus	.0856	2.0	-5.0	-5.4	.641
MD	All	Caudate nuclie	.6557	-.07	-2.0	3.9	.800
		Putamen	.6840	-.02	-2.0	4.8	.925
		Globus pallidus	.0856	2.0	-5.0	5.4	.641
	Female	Caudate nuclie	.7424	-.07	1.1	-5.0	.797
		Putamen	.6840	-02	-2.0	4.8	.925
		Globus pallidus	.6888	.028	-5.0	3.4	.901
	Male	Caudate nuclie	.7424	-.07	1.1	-5.0	.797
		Putamen	.6839	-.01	-3.0	-3.0	.731
		Globus pallidus	.6865	-1.0	4.7	-8.0	.816

Table 1 Relationship of FA and MD with age in deep grey matter of the normal human brain using cubic regression model.

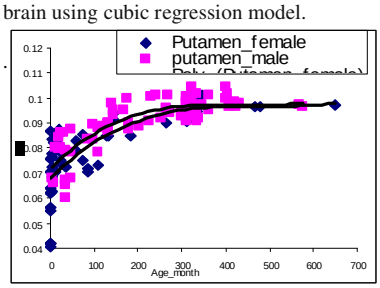

Fig. 1

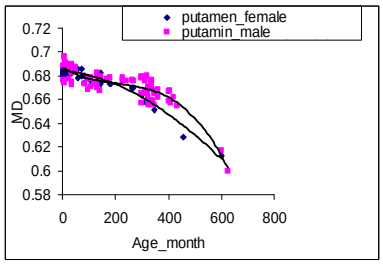

Fig. 2

Discussion: We observed increased pattern of FA values long with decreased MD values as a function of age in deep grey nuclei. It has been suggested that changes in DTI indices is due to decreased brain water content and increased structural complexities due to the normal course of development. For the white matter, these change are attributed to the ongoing myelination of white matter tracts but for grey matters it is because of decrease in water content and increase in iron deposition(3). A recent study in adult population has shown significant positive correlation between field dependent relaxation rate increase (FDRI) and FA, where FDRI is considered as marker of ferritin (3). In another imaging study in has reported that FDRI increase with age in normal human brain (2). It is known that with advancing age there is an increased deposition of iron in basal ganglia which gets more pronounced in Parkinson's disease and striatnigral degeneration. It has been also reported that increased FA in brain tumors is due to deposition of intercellular iron (4). The FA values in males are slightly higher than females which may be because of lower brain iron levels in women (5). During the course of development, we have observed decreased in MD values with increase in age, it is partly may be due to decreased brain water content (6). Structures that hinder water motion become more densely packed, increasing restriction to motion, as if the brain becomes more viscous as its water content decreases. Other factors that influence MD include increased binding of water to macromolecules such as myelin, reducing free water content, and the formation of new structural barriers to water diffusion such as dendritic arborization, axonal ramification, synaptogenesis, and glial proliferation within grey matter as well as progressive myelination within white matter (7). The current study demonstrates the variation in age related FA and MD values in deep grey nuclei of normal human brain should greatly improve our understanding of age related changes in healthy volunteers and it may be helpful in early diagnosis of neurodegenerative pathologies

Fig. 1 Variation of FA with age in males and females

Fig. 2 Variation of MD with age in males and females.

References:

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