Age and Gender Related Changes of Human Brains using Magnetic Resonance Hybrid Diffusion Imaging

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Introduction

The q-space diffusion formulism first introduced by Callaghan [1] estimates the probability density function (PDF) of water diffusion. This approach is model-free and more generalized for describing complex brain tissues than diffusion tensor imaging (DTI) [2]. More recently, adaptations of this approach have been applied to human brains on clinical scanners, i.e. diffusion spectrum imaging (DSI) [3]. Several DTI studies have investigated the effects of aging on brain tissues [4-7]; however, only one study to date has examined the changes in q-space measures with age in children and young adults [8]. In this study, hybrid diffusion imaging (HYDI) [9] was used to estimate the diffusion PDF as well as DTI measures across 52 human brains over an age span of 18-72 years. Age and gender effects were investigated on both the PDF and DTI measures, including zero displacement probability (Po), mean squared displacement (MSD), fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (Da) and radial diffusivity (Dr).

Methods

HYDI was performed on 52 healthy volunteers (age: 39+/-14 years), 29 females (age: 43+/-14 years) and 23 males (age: 34+/-11 years), on a 3.0T GE-SIGNA scanner with an 8-channel head coil and ASSET parallel imaging. The HYDI encoding scheme is shown in Table 1. The DW pulse sequence was a SS-SE-EPI with cardiac gating. MR parameters were: δ/Δ=45/56ms, Δq_r=15.2mm^{-1}, q_{max}=76.0mm^{-1}, FOV_R=65µm, ΔR=6.6µm, voxel size=2x2mm^2, 30 slices with slice thickness=3mm, TE/TR=122/11700ms and a total scan-time of about 30 min. PDF measures including Po, a marker of restricted diffusion, and the MSD relating to the average diffusivity in a voxel were processed using the whole HYDI dataset. DTI measures (i.e. FA, MD, Da, Dr) were processed using the second shell of the HYDI scheme in Table 1. White matter (WM), gray matter (GM) and cerebrospinal fluid (CSF) were segmented by inputting Po to FMRIB's automated segmentation tool (FAST) after skull stripping using BET. WM/GM volume-ratio was defined as the whole-brain WM/GM voxel-count divided by the whole brain voxel-count. Shown in Figure 1, voxels with WM probability > 0.9999 or GM probability > 0.99 were selected for the following analyses. WM/GM contrast index was defined as the ratio of WM/GM difference to the average of WM/GM measures. The significance of age and gender effects was tested using linear regression analysis for both WM and GM. Lastly, a three dimensional ROI study was performed at the posterior limb of internal capsule and the splenium of corpus callosum.

Table 1. HYDI encoding scheme

HYDI Shell	Ne	b value (s/mm^2)
	1	0
1st	6	375
2nd	21	1500
3rd	24	3375
4th	24	6000
5th	50	9375
total	126	

Results and Discussion

The Po map in Figure 2 (a) shows the highest tissue contrast between WM and GM among all diffusion measures investigated in this study. This is consistent with the WM/GM contrast index study in Table 2. The FA and Dr measures also show relatively high contrast (Figure 2(d) and (g) and Table 2). Statistical p-values of age and gender effects on diffusion measures are listed in Table 3 and Table 4 for WM and GM, respectively. Numbers in bold fonts are p-values less than 0.05, which were considered statistically significant in this study. Overall the age-related changes of those diffusion measures that were found statistically significant are less than 3% per ten years. The absolute changes per ten years for WM Po, MD, Da and GM FA were 0.002, -8 x10^{-6}mm^2/s, -14 x10^{-6}mm^2/s and 0.007, respectively. These numbers were calculated from the estimated beta-parameters in the regression analysis. Only FA has significant gender related changes with 3% and 6% higher in male brains for WM and GM, respectively. Figure 3 illustrates that the WM volume-ratio appears to increase with age, whereas the GM volume-ratio decreases.

Conclusion

This is the first study to investigate the effects of age and gender on high b-value/q-space measures in middle-aged adults (18-72 years). Interestingly, there are small but significant changes in Po, FA, MD, Da over this age range as well as between men and women. A previous study of q-space measurements during development in childhood and very early adulthood, demonstrated an increase in Po and a decrease in MSD with age [8] although this trend was plateauing in early adulthood. Furthermore, using HYDI Po segmentation, WM volume-ratio increases while GM volume-ratio decreases with age.

References 1. Callaghan Clarendon Press 1991. 2. Assaf et al. MRM 2000;5:713-722. 3. Wedeen et al. MRM 2005;54:1377-1386. 4. Salat et al. ANNYAS 2005;1064:37-49. 5. Hsu et al. NeuroImage 2008;39:566-577. 6. Hugenschmidt et al. CerebCortex 2007:1-10. 7. Ardekani et al. MagnResonImaging 2007;25:154-167. 8. Bashat et al. NeuroImage 2007. 9. Wu NeuroImage 2007;36:617-629.

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Table 2. WM/GM Contrast index

	Po	MSD	FA	MD	Da	Dr
Mean	0.937	-0.179	0.790	-0.283	0.042	-0.603
SD	0.044	0.055	0.059	0.050	0.056	0.058

** the SD is one standard deviation across 52 subjects

Table 3. WM p-values

	Po	MSD	FA	MD	Da	Dr
Age	**< 10^{-4}**	0.527	0.707	**< 10^{-3}**	**< 10^{-4}**	0.126
Gender	0.198	0.133	**0.006**	0.074	0.617	0.103
intercept	0.104	577	0.580	463	817	287

** Unit of all diffusivities is10^{-6} mm^2/s

Table 4. GM p-values

	Po	MSD	FA	MD	Da	Dr
Age	0.128	0.072	**< 10^{-4}**	0.832	0.181	0.481
Gender	0.858	0.301	**0.008**	0.407	0.147	0.830
intercept	0.038	649	0.224	564	697	498

** Unit of all diffusivities is10^{-6} mm^2/s

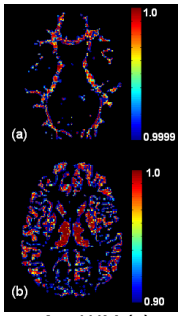

Figure 1. WM (a) and GM (b) probability maps.

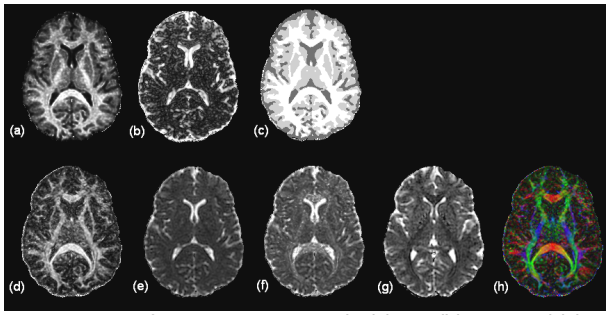

Figure 2. Maps of PDF measures are in (a) Po, (b) MSD. (c) is segmentation results of WM (white), GM (gray) and CSF (dark gray). Maps of DTI measures are in (d) FA, (e) MD, (f) Da, (g) Dr and (h) major eigenvector colormap.

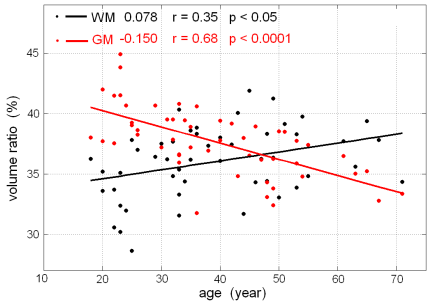

Figure 3. Regression analysis of WM and GM volume ratio vs. age.