Hybrid Diffusion Imaging (HYDI) of Mild Traumatic Brain Injury (MTBI)

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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]. Many DTI studies have been used to detect white matter (WM) changes in mild traumatic brain injury (MTBI), [4,5]; however, to our knowledge no studies have examined changes in q-space measures in MTBI. In this study, hybrid diffusion imaging (HYDI) [6] was used to estimate the diffusion measures in individuals with MTBI as well as age and gender matched normal controls. Both 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), were investigated in whole brain WM, as well as the genu, splenium and body of the corpus callosum.

Methods

HYDI was performed in four individuals with MTBI and two healthy volunteers on a Philips 3.0T Achieva TX scanner with an 8-channel head coil and SENSE parallel imaging. The MTBI participants were diagnosed using ACRM criteria and were recruited from a Level 1 Trauma Center Emergency Department. All MTBI individuals were scanned approximately one month after injury and two underwent repeat scanning ~1 year later. All two controls were also scanned twice 1 year apart. All subjects were male. The HYDI encoding scheme is shown in Table 1. The DW pulse sequence was a SS-SE-EPI sequence. MR parameters were: δ/Δ=46/58.4ms, Δq_r=11.56mm^{-1}, q_{max}=57.8mm^{-1}, FOV_R=86.5µm, ΔR=6.5µm, voxel size=2x2mm^2, 40 slices with slice thickness=3mm, TE/TR=117/7550ms, SENSE factor=2 and a total scan-time of about 24 min. The FOV_R describes the scope of the neuronal microstructure that is "seen" under these diffusion parameters and ΔR describes the resolution, i.e. the resolvable neuronal diameter. 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 first and second shell (i.e. 27 directions) of the HYDI scheme in Table 1. Whole brain WM was segmented by inputting Po to FMRIB's automated segmentation tool (FAST) after skull stripping using BET. Three-dimensional ROIs including the genu (CCg), the splenium (CCs) and the body (CCb) of the corpus callosum were drawn on a combined image of FA map and segmented brain map using FSL View software. Histograms of diffusion measures of WM and ROIs were compared between MTBI and control participants at both time points. Due to known effects of age on white matter parameters, data was analyzed separately for younger age group (2 MTBI, 1 control, mean age = 20 y/o) and older participants (2 MTBI, 1 control, mean age = 50 y/o).

Table 1. HYDI encoding scheme

HYDI Shell	Ne	b value (s/mm^2)
0	1	0
1st	6	250
2nd	21	1000
3rd	24	2250
4th	30	4000
5th	61	6500
total	143	

Ne: number of encoding direction

Results and Discussion

Inspection of the histograms (Figures 1 & 2) suggests that the largest between group differences were found in Po in the genu of corpus callosum of the older age group and in the splenium of the corpus callosum in both age groups (Table 2). FA differed between groups (lower in MTBI) only in the genu of the corpus callosum of the older age group. Other diffusion measures did not show visible separations in histograms (Table 2). The whole brain WM and the body of corpus callosum did not show obvious separation of histograms in either age group (Fig. 2). Imaging at one year showed few differences. Overall these preliminary results are consistent with the hypothesis that Po may be more sensitive to the subtle effects of MTBI on white matter, particularly in the corpus callosum. Lower Po values (Fig. 1 (a)) in MTBI may reflect destruction of microstructural boundaries resulting in lower restriction of water molecules. It is also of note that age at time of injury may impact results. Table 2 shows that the splenium is affected for both age groups whereas only the genu was affected in the older age group.

Conclusion

HYDI approach is a convenient way to yield both PDF measures and DTI measures using one dataset. It has been used on normal aging study and the animal model of brain dysmyelination [7,8]. This study suggests that the PDF measure, Po, may be more sensitive than DTI measures in MTBI. It appears that some anatomical locations are more vulnerable (e.g. CCs) and that age may impact vulnerability patterns. This is a pilot study of HYDI in TBI. However, the results are encouraging and a continuing study that involves more subjects is underway.

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. Bigler amd Bazarian Neurology 2010;74:626-627. 5. Belanger et al. J Neuropsychiatry Clin Neurosci 2007;19(1):5-20. 6. Wu and Alexander NeuroImage 2007;36:617-629. 7. Wu et al. NeuroImage 2011;54:1840-1853. 8 Wu et al. NeuroImage 2011;58:829-837.

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Table 2: Visible separation in histograms

	Age group	Po	FA	Others
CCg	1	-	-	-
	2	+	+	-
CCb	1	-	-	-
	2	-	-	-
CCs	1	+	-	-
	2	+	-	-
Whole brain WM	1	-	-	-
	2	-	-	-

Age group: 1: ~20 year old; 2: ~50 year old
"+" denotes obvious separation of histograms between MTBI and controls.
"-" denotes no obvious separation.
Others: other diffusion measures.

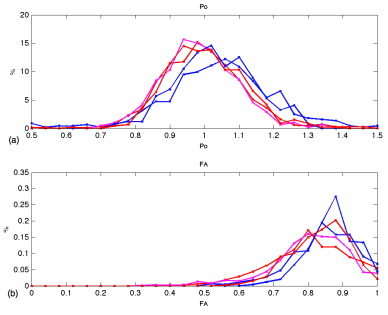

Fig. 1 Histograms of Po and FA in the splenium of the corpus callosum (CCs) for the older age group.
Blue lines: the control subject scanned twice.
Red lines: one MTBI subject scanned twice.
Pink line: the other MTBI subject scanned once.

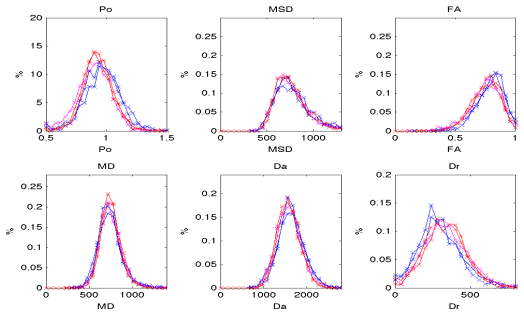

Fig. 2 Histograms of PDF and DTI measures in the body of the corpus callosum for the older age group. The unit of all diffusivity measures is mm^2/s.
Blue lines: the control subject scanned twice
Red lines: one of the MTBI subjects scanned twice
Pink line: the other MTBI subject scanned once.