Mapping Human Cerebral Water Compartments Based on Simultaneously Acquired T_1 and T_2 Data – Evidence of Dysmyelination in Phenylketonuria

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Introduction

Separate cerebral water compartments lead to multiple relaxation time components, mostly measured as T_2-dispersion. Relatively little is known about the water component in myelin layers that has short T_1 and T_2 relaxation times [1-3]. Relaxometry based on an inversion recovery (IR) multiple-echo sequence was used to characterize and map four brain compartments: tissue water in gray (GM) and white matter (WM), CSF, and water in myelin layers. In vivo measurement of myelin water content can provide a quantitative measure of myelin loss or abnormal formation and maintenance of myelin in demyelinating or dysmyelinating diseases. The method was tested on patients suffering from phenylketonuria (PKU) with known WM abnormalities, tentatively attributed to dysmyelination.

Method

Subjects: Twenty-two measurements on seven volunteers and four PKU patients were performed. Repeated measurements on volunteers were performed either at a different slice or at a different point in time. In patients, the slice was acquired including the known T_2-hyperintensities and repeated scans were performed at the same slice position. Methods: An IR fast-spin-echo sequence was modified to yield 32 images, each acquired with an individual TE (11ms spacing). The sequence was repeated with 5 different recovery times TI (10-2010ms). Thus, for each pixel 180 intensity values with different combinations of TE and TI were obtained. Imaging time for one slice (matrix: 512 ×16) was ~5min. Processing: The data were fitted to yield M_0, T_1, and T_2 of all four compartments in each pixel. For the presented results, T_1, T_2 were fixed for WM and GM and constrained for the myelin component and CSF.

Results

Figure 1 shows images of the different compartments for two slices. Images of WM, GM and CSF are well separated. The images of the myelin component show intense signals only in areas with high WM content. Overall, a content of 14.2±2.4% myelin component (% of WM) was found for control subjects (Fig. 2). Repeated scans at different slice positions and different points in time showed similar results (Fig. 2, the average difference in myelin component between repeated scans was 1.3% (% of WM)). For PKU subjects a significantly lower myelin component of 10.8±1.5% was found ($p<0.0002$ for all measurements, $p<0.02$ after averaging repeated scans). As for controls, repeated scans on two patients yielded similar results (Fig. 2). An additional finding was that the number of voxels with predominantly white matter (WM > 4×GM and 4×CSF) was significantly lower in PKU patients than in controls ($p<0.0001$), while the head size was not different.

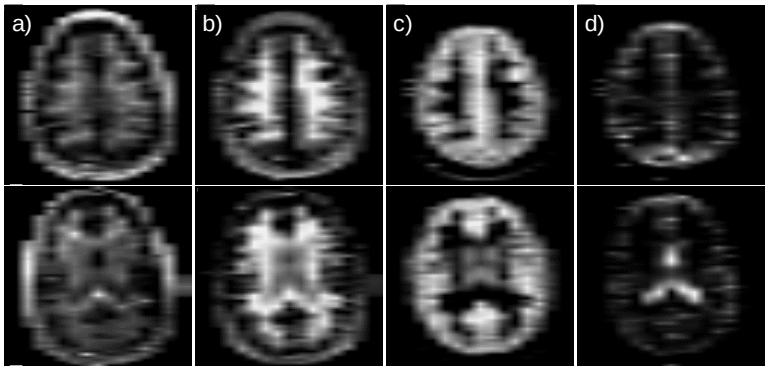

Figure 1: Images of the four compartments in two slices. Top row: slice above ventricle; Bottom row: slice including ventricles. a) Water in myelin layers, b) WM, c) GM, d) CSF

Discussion

Fitting of simultaneously acquired T_1- and T_2-data yielded consistent brain components. The method appears robust (low intrasubject variations for the myelin water content from multiple voxels; see Fig. 2 for standard deviations for individual scans) and suitable to characterize focal or diffuse cerebral abnormalities in pathology, even though component sizes or relaxation times may be systematically influenced by the enforced prior knowledge constraints. Myelin water distribution was found to correlate with white matter distribution, confirming previous results [1,2]. The average myelin component of 14.2% (relative to WM) matches literature values [1-3]. The results on PKU patients confirm the concept of dysmyelination as cause of the known MRI abnormalities.

References:

1. MacKay, et al. Magn. Reson. Med. 31: 673 (1994)
1. Whittall, et al. Magn. Reson. Med. 37: 34 (1997)
2. Kreis, et al. Proc. Soc. Magn. Reson. Med. 11: 1963 (1992)

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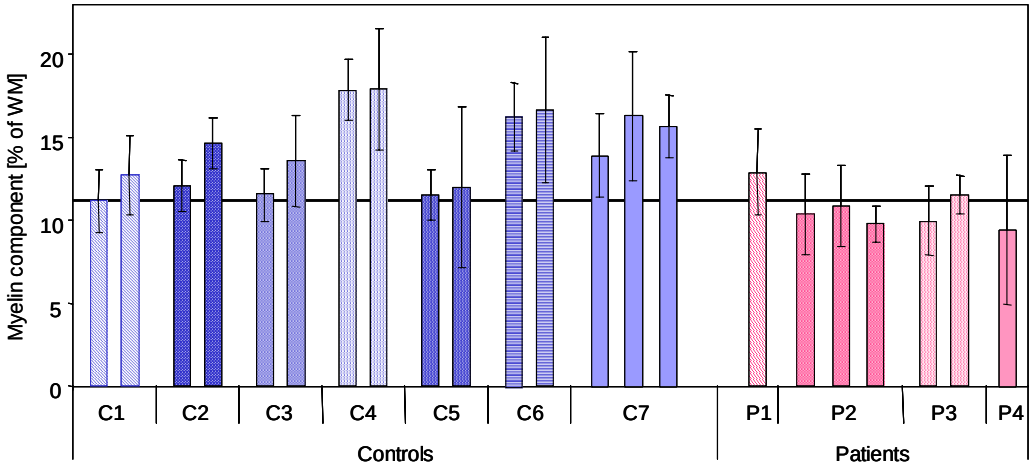

Figure 2: Short component contribution in WM (in % of WM, ± 1sd) for controls (C1-C7) and PKU patients (P1-P4). Repeated scans are shown with identical pattern. The solid line demonstrates the lowest value obtained for controls.