In-vivo insights into magnetization exchange in human white matter structures

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Introduction

Myelin water signal from human brain has previously been measured *in vivo*[1]. The myelin water fraction (MWF, the proportion of water trapped in the myelin bilayers) is quantitatively correlated to histological staining for myelin in central nervous system tissue[2] and hence is considered an *in vivo* measure of myelin content. Current *in vivo* measurement of MWF relies upon the assumption that individual water molecules do not move between the myelin water and the intra/extra-cellular (I/E) water pools on the measurement timescale. If water does indeed move (or exchange) between compartments on this time scale, then the measured MWF may not accurately represent the amount of myelin water present.

To simulate the MR characteristics of white matter, a previously established four pool model[3-4] including myelin tissue, myelin water, I/E water, and non-myelin tissue has been applied. In this model, there are three unknown cross relaxation times (T_{cr}). Here, we present an analytical approach to measuring cross relaxation times between myelin tissue and myelin water (T^{mw}_{cr}), myelin water and I/E water (T^{D}_{cr}), and I/E water and non-myelin tissue (T^{ie}_{cr}) in five different white matter structures from healthy human brain *in vivo.*

Methods

MR Experiments

Fifty-seven normal volunteers (37 male, 20 female) underwent MR examinations. All experiments were done on a 1.5T GE Signa scanner. A single transverse slice through the base of the genu and splenium of the corpus callosum was scanned. In addition to localizers, the MR examination included 5 experiments for each volunteer. The first 4 experiments employed a combined magnetization transfer (MT) – T_2 relaxation sequence consisting of a preparatory 19ms sinc MT pulse (2000Hz off resonance) followed by delay times of either (a) 0, 33, 66,, 100ms, (b) 66, 100, 200, 300ms or (c) 300, 450, 600, 750ms. Then a 90° slice selective pulse was applied, followed by 48 rectangular composite 180° pulses. The final experiment was a 90° slice selective pulse followed by 48 rectangular composite 180° pulses. Sequence parameters were: TR=3800ms, TE=10ms, FOV=22cm, matrix size = 64x64, slice thickness=5mm, 2 averages.

Data Analysis

Regions of interest were drawn for five white matter structures (genu (GU) and splenium (SP) of the corpus callosum, posterior internal capsules (IC), minor forceps (MN), and major forceps (MJ)). The T_2 decay curve at each delay time for each white matter structure was fitted using a non-negative least squares (NNLS) algorithm in order to obtain the T_2 distribution[5]. MWF was defined as the signal with T_2 below 50ms relative to the total signal in the T_2 distribution. The I/E water fraction was calculated by integrating the T_2 distribution between 50ms and 200ms and dividing it by the total signal in the T_2 distribution. The myelin water signal, I/E water signal, and total signal from each structure were separately averaged over all subjects. The mathematical differential equations (Bloch equations) that govern the dynamics of water signal in each of these 4 pools were solved analytically and signals from the five white matter structures were fitted by varying the T_{cr} times. T_1s used in this study were 830ms, 250ms, 1250ms, and 830ms for myelin tissue, myelin water, I/E water, and non-myelin tissue respectively.

Result

Figure 1 shows the myelin water and I/E water signals as a function of delay time averaged over all five white matter structures along with the fitted curve from the analytical solution to the four pool model. The signals from the myelin water pool (fig. 1a) and I/E water pool (fig. 1b) clearly show the existence of magnetization exchange processes between these two water pools. The cross relaxation times between each two adjacent pools for each of the five white matter structures are shown in Table 1. The T^{mw}_{cr}'s and T^{ie}_{cr}'s were found to be on the same order of magnitude for all of the examined white matter structures. The T^{D}_{cr}'s for all 5 structures were significantly higher than their corresponding T^{mw}_{cr} and T^{ie}_{cr}.

Table 1. Cross relaxation times corresponding to each examined white matter structure.

	GU	IC	MN	MJ	SP
T^{mw}_{cr} (ms)	184	116	137	210	95
T^{D}_{cr} (ms)	1267	793	1325	641	1140
T^{ie}_{cr} (ms)	142	86	291	112	257

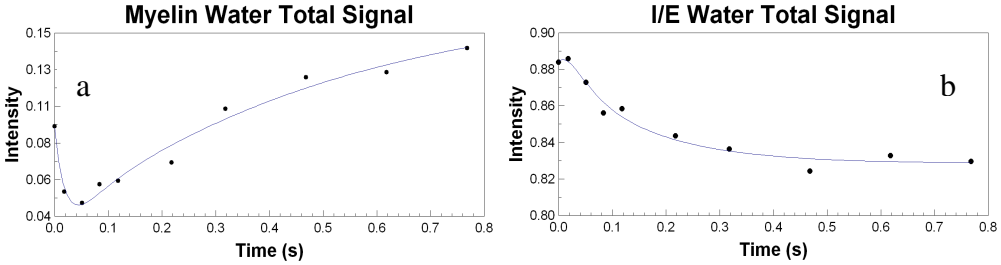

Figure1. (**a**) Myelin water signal and (**b**) I/E water signal collected at delay times from zero to 750 ms after the MT pulse averaged over all five structures.

Conclusions

Our findings clearly prove the role of exchange in transferring magnetization between all four mobile (aqueous) and non-aqueous pools.

The measured exchange rate between the I/E water pool and the non-myelin non-aqueous tissue pool was fairly close to the exchange rate between myelin water pool and myelin tissue pool, indicating that these two relaxation mechanisms are equally important in transferring the magnetization from aqueous pools to non-aqueous pools. The cross relaxation times between myelin water and I/E water obtained in this study were much longer than the typical T_2 values of white matter structures and hence the calculated cross relaxation correction for the MWF of these water pools is minimal.

References:

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