Evaluating exchange processes in the human brain: magnetization transfer vs adiabatic rotating frame relaxation methods

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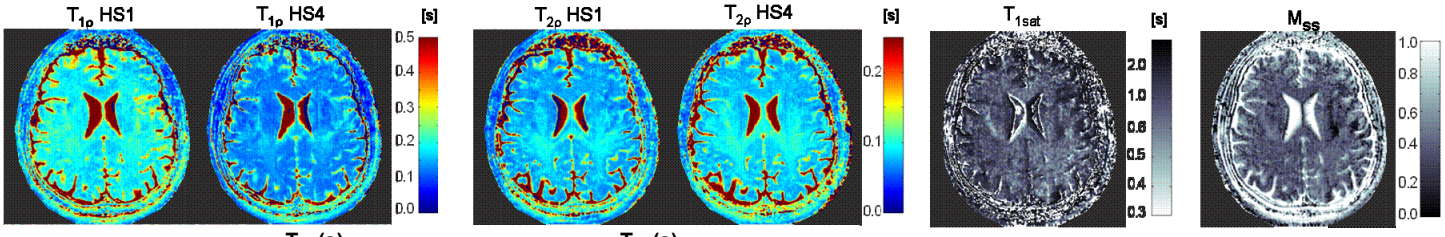
Introduction

Exchange processes of bulk water protons with the protons contained in the macromolecules of tissue can be investigated with magnetization transfer (MT) experiments, which rely on saturating the "solid" pool by placing a preparation pulse (typically a continuous-wave (CW) pulse) several kHz off-resonance from water [1]. Since the frequency of the off-resonance pulse does not have a major impact on the MT effect, the macromolecule pool is believed to generate a homogenously broadened line, and therefore the exchange process exploited by MT would occur between spin with identical chemical shift ($\delta\omega$=0, i.e. isochronous exchange - IE). By progressively incrementing the duration of the off-resonance pulse, the T_1 of water in presence of saturation (T_{1sat}) and the steady state magnetization (M_{ss}) can be estimated, and the exchange rate k_f can be extracted as $(1/T_{1sat})(1-M_{ss}/M_0)$. Investigation of exchange processes between spins with either identical or different chemical shifts ($\delta\omega\neq0$, anisochronous exchange - AE) can be exploited also by rotating frame longitudinal, $T_{1\rho}$, and transverse, $T_{2\rho}$, relaxations [2]. A typical method to measure $T_{1\rho}$ and $T_{2\rho}$ is the conventional spin-lock experiment, where a CW pulse is applied on-resonance or few hundred Hz off-resonance. Alternatively, rotating frame relaxation experiments can be performed during adiabatic pulses [3], during which the pulse frequency is swept typically over 1-3 kHz around the water resonance. These adiabatic methods have proven to be robust and artifact-free for *in vivo* applications, and offer the possibility to modulate MR contrast by using different pulse modulation functions [4]. Notably, by proper modeling of the relaxation processes, the simultaneous analysis of $T_{1\rho}$ and $T_{2\rho}$ during adiabatic pulses with different modulation functions allows the extraction of k_f for both IE and AE processes [5]. The present work aims at demonstrating different ranges of sensitivity to exchange processes of MT vs adiabatic relaxations experiments in the human brain at 4 T, relying on a quantitative analysis of the relaxation decays and on the formation of the steady state during MT.

Methods

Six healthy subjects were investigated on 4-T/90-cm Oxford magnet interfaced to Varian INOVA console. Images were acquired using fast spin echo readout, TR = 5 s, TE = 0.60 s, matrix 128 x 128, FOV = 20 cm x 20 cm, and slice-thickness = 3mm. In the adiabatic $T_{1\rho}$ configuration, a train of 4, 8, 12, or 16 HS1 or HS4 pulses was placed prior to the imaging readout, while in the adiabatic $T_{2\rho}$ configuration the train of adiabatic pulses was placed between two 4-ms adiabatic half passage pulses. RF peak power $\omega^1_{max}/(2\pi)$ of the adiabatic pulses was 0.88 kHz and 0.625 kHz for HS1 and HS4, respectively. Pulse length was 0.006 s, and the inversion bandwidth was ~1.6 kHz for both HS1 and HS4. For the MT experiment, a 6 kHz off-resonance CW-pulse, with incremental duration (0.2, 0.5, 0.8, 1.0, 1.2 s) and $\omega^1_{max}/(2\pi)$ = 0.2 kHz, was placed before the readout. All measurements resulted in similar RF power deposition. The theoretical formalism used to extract exchange parameters during adiabatic pulses have been described previously [5].

Results and discussion



$T_{1\rho}$ (s) | | | $T_{2\rho}$ (s) | |

	WM	GM	WM	GM
HS1	0.201 ± 0.015	0.234 ± 0.081	0.093 ± 0.07	0.071 ± 0.08
HS4	0.149 ± 0.013	0.156 ± 0.089	0.099 ± 0.06	0.078 ± 0.07

MT

	WM	GM
T_{1sat} (s)	0.72 ± 0.12	1.87 ± 0.2
M_{ss}	0.41± 0.06	0.40 ± 0.10

The figure shows representative adiabatic $T_{1\rho}$ and $T_{2\rho}$ maps, and T_{1sat} and M_{ss} maps from the same volunteer. The table reports the values of the above parameters for white matter and gray matter (SD deviation within subjects were ~10%). As expected, HS1 vs HS4 pulses generate different relaxations, with the difference being larger for $T_{1\rho}$ compared to $T_{2\rho}$ (35%-50% vs <10%, see tables). The estimated k_f of IE mechanisms in adiabatic $T_{1\rho}$ was 18 and 15 s^{-1} for white and grey matter, respectively. (Model of IE assumes two exchanging pools A and B of bound and free water, with P_A=0.2, $\tau_{cA} \sim 5\cdot10^{-9}$ s, $\tau_{cB} \sim 7\cdot10^{-11}$ s [5]). The contribution of AE mechanisms to $T_{2\rho}$ relaxations was 40-50%; the estimated intrinsic AE parameters were $k_f=12\cdot10^3$ s^{-1}, and $P_AP_B\Delta\omega^2=6\cdot10^3$ and $1.2\cdot10^3$ $(rad/s)^2$ for white and gray matter, respectively. The estimated k_f of IE from MT was in the slow exchange regime, i.e. 0.8 and 0.5 s^{-1} for the white and grey matter, respectively, in agreement with literature values [6]. Notably, these latter k_f values do not generate contrast in $T_{1,2\rho}$ of HS1 vs HS4, and overall have a minor contribution to both $T_{1\rho}$ and $T_{2\rho}$ relaxations (~10-15% and 5%, respectively). These results imply that the so-called MT effect is negligible during rotating frame relaxation measurements employing frequency swept pulses, similarly to what Balaban et al. predicted for the conventional spin-lock experiment [1]. Notably, while the MT effect arises from the proton exchange occurring between water and macromolecules, rotating frame relaxation measurements are mainly sensitive to exchange in the intermediate regime between water protons characterized by fast and slow tumbling, with the proton pool in slow dynamics likely reflecting the hydration shell of water surrounding proteins and ions.

Conclusion. Results demonstrate that rotating frame relaxation measurements (employing either CW or adiabatic pulses) and MT measurements are sensitive to exchange processes characterized by dynamics significantly different from each other and likely reflecting different physical processes, thus generating complimentary information to characterize the tissue.

References: [1] Balaban and Ceckler, Magnetic resonance quarterly 1992;8:116. [2] Abergel and Palmer, Concepts Magn Reson A 2003;19A(2):134. [3] Garwood and DelaBarre, JMR 2001;153:155. [4] Mangia et al. Magn Reson Imaging 2009;27:1074 [5] Michaeli et al. Curr Anal Chem 2008;4:8. [6] Yarnikh Magn Reson Med 2002;47:929 **Acknowledgments**: BTRR - P41 RR008079, P30 NS057091, R01NS061866 and R21NS059813.