Acute ischaemic stroke in rat imaged by $T_{1\rho}$ and $T_{2\rho}$ MRI using adiabatic pulses

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Introduction

$T_{1\rho}$ has been shown to visualize acute cerebral ischemia very shortly after cessation of cerebral blood flow below 20 ml / 100 g / min [1]. The extent of increase in the absolute $T_{1\rho}$ in the early moments of ischemia correlates with long-term histology outcome [2]. It has recently been demonstrated that rotating frame $T_{1\rho}$ and $T_{2\rho}$ relaxation measurements based on the adiabatic pulse sequences provide a tool to directly assess slow molecular motion with high sensitivity [3, 4]. We have shown that the intrinsic relaxation rate constant values are sensitive to fluctuations at the effective Larmor frequency (ω_{eff}) in the rotating frame, and this can be modulated differently during the adiabatic full passage (AFP) pulses with different modulation functions. Moreover, since the intrinsic relaxation rate constants at each exchanging site [A and B] are modulated during the course of AFP pulses, the relaxographic shutter-speed for the process ($\equiv \left| R_{1\rho A} - R_{1\rho B} \right|$) [5], and thus the exchange condition, is modulated. Here, this inherent property of adiabatic $T_{1\rho}$ and $T_{2\rho}$ measurements was utilized to investigate the tissue changes occurring during early moments of acute ischemic stroke.

Methods

Male Wistar rats (280 to 320g, n = 6) were anesthetized with 1 - 1.5 % isoflurane in 70/30 N_2O/O_2 for middle cerebral artery occlusion (MCAo) [6]. MRI experiments were performed in a horizontal 4.7 T magnet interfaced to a Varian Inova console during 90 minutes of MCAo and after reperfusion (MRI scans performed at 60, 90, 120 and 150 min from the onset of MCAo). The transversal imaging plane (thickness 1.5 mm) was positioned 4 mm from the surface of the brain. A quadrature half-volume coil was used in transmit/receive mode. Fast spin-echo (FSE) sequence readout (echo spacing 10 ms, TR 2.5 s, 64 x 128 pixels, FOV 2.56 x 2.56 cm^2) was used for the T_2, $T_{1\rho}$ and $T_{2\rho}$ measurements. D_{av} was quantified using a SE sequence incorporating four bipolar gradients along each axis with four b-values from 0 to 1370 s/mm^2 (TR 1.5 s, TE 55 ms, 64 x 128 pixels, FOV 2.56 x 2.56cm^2). The $T_{1\rho}$-maps were quantified using two techniques, first by five adiabatic on-resonance spin-lock pulses (Fig. 1a) ranging from 8 to 64 ms with a B_{1SL} = 0.8 G (conventional $T_{1\rho}$) and then by using AFP pulses with different hyperbolic secant modulation functions (HS1, HS4 and HS8) (Fig. 1c) [7]. Corresponding $T_{2\rho}$-maps were acquired using both rotary echo (Fig. 1b) and AFP-pulses with an adiabatic half passage in front and after the AFP train (Fig. 1d). T_2 was measured with analogous double spin echo preparation block consisting of AHP-AFP-AFP-reverseAHP before the same FSE sequence. Data were processed with Matlab software.

Results

D_{av} declined by >25 % in the ischaemic tissue by 60 minutes of MCAo (Table I) consistent with severe irreversible ischemia. Signal intensities acquired with all spin-lock MRI methods were elevated in the first observation point by 60 minutes of ischemia, when T_2 failed to show difference between ischemic and contralateral tissue. $T_{1\rho}$ acquired using HS8 pulses and conventional $T_{1\rho}$ showed the highest signal changes in the ischemic brain (Figs 2 and 3, Table I). $T_{1\rho}$ and $T_{2\rho}$ values measured using conventional techniques increased by 9 % and 5 %, respectively by 60 minutes of MCAo, continuing to increase over the entire observation time (Fig 3, Table I). Similarly, signals in images acquired using HS-pulses for $T_{1\rho}$ and $T_{2\rho}$ MRI showed increases by 4 - 7 % and 3 - 5 % respectively (Fig 2, Table I).

Conclusions

These data show that every spin-lock technique used provided significant signal changes in acute phase of brain ischemia. Modulating the "shutter speed" of given MRI technique led to altered sensitivity to the ischaemia. This indicates that optimization of the spin-lock contrasts is possible by changing the amplitude modulation function in both adiabatic $T_{1\rho}$ and $T_{2\rho}$ approaches. A further option to modulate sensitivity of given MRI technique to ischemia includes the recent formalism for time-dependent $T_{1\rho}$ relaxation [3] encoded to the relevant spectral densities. $T_{1\rho}$ and $T_{2\rho}$ MRI provide complementary information to diffusion and T_2 MRI in the brain exposed to MCAo that may facilitate further characterization of tissue viability and damage progression also in clinical settings.

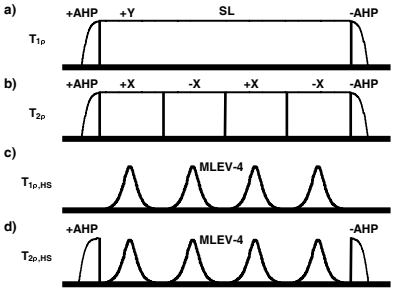

Fig.1: Preparation pulse sequences used in the study. Spin-lock (SL) time in each is 8ms. AHP = Adiabatic Half Passage.

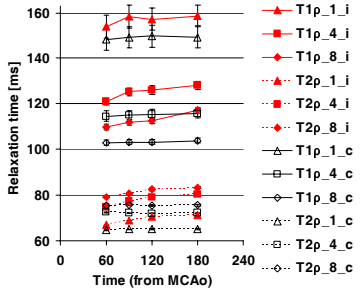

Fig.2: $T_{1\rho}$ and $T_{2\rho}$ relaxation time constants (mean ± SEM) as measured using the HS AFP pulses. In the legend numbers 1, 4 and 8 refer to HS pulses, i = ipsilateral and c = contralateral side.

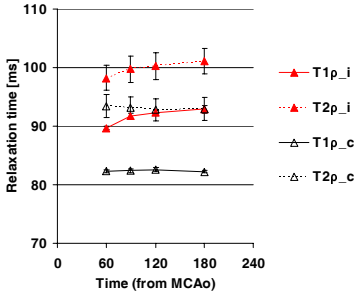

Fig.3: $T_{1\rho}$ and $T_{2\rho}$ relaxation time constants (mean ± SEM) as measured using conventional techniques. In the legend numbers 1, 4 and 8 refer to HS pulses, i = ipsilateral and c = contralateral side.

Table I: Relative differences of ipsilateral compared to contralateral values at time points indicated (mean ± SEM). Significance between ipsilateral and contralateral values was tested by Student's t-test (*P<0.05, **P<0.01). "c" refers to conventional techniques and numbers 1, 4 and 8 to HS pulses.

MCAo duration	ΔD_{av} [$*10^{-3}$ mm^2/s]	ΔT_2 [ms]	$\Delta T_{1\rho,c}$ [ms]	$\Delta T_{2\rho,c}$ [ms]	$\Delta T_{1\rho,1}$ [ms]	$\Delta T_{1\rho,4}$ [ms]	$\Delta T_{1\rho,8}$ [ms]	$\Delta T_{2\rho,1}$ [ms]	$\Delta T_{2\rho,4}$ [ms]	$\Delta T_{2\rho,8}$ [ms]
60min	-28.5 ± 0.9**	-0.2 ± 0.5	9.0 ± 0.4**	5.1 ± 0.2**	4.1 ± 0.8*	6.0 ± 0.9*	6.6 ± 0.2**	3.4 ± 0.4*	3.2 ± 0.4*	4.9 ± 0.3**
90min	-18.5 ± 1.8**	5.4 ± 0.5*	11.3 ± 0.7**	6.9 ± 0.4**	6.3 ± 0.6**	9.2 ± 0.7**	8.2 ± 0.4**	6.1 ± 0.2**	6.8 ± 0.2**	6.7 ± 0.2**
120min	-18.5 ± 1.1**	6.4 ± 0.5**	11.7 ± 0.6**	8.0 ± 0.6**	5.4 ± 0.5**	9.6 ± 0.7**	8.9 ± 0.4**	8.6 ± 0.2**	9.8 ± 0.6**	9.4 ± 0.4**
150min	-18.4 ± 1.1**	8.2 ± 0.5**	13.0 ± 0.7**	8.9 ± 0.5**	7.9 ± 0.6**	10.8 ± 0.5**	12.7 ± 0.5**	9.9 ± 0.4**	11.1 ± 0.4**	10.2 ± 0.5**

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