Increased T_1 and decreased MTR detected in an excitotoxic lesion in rat brain in the absence of perfusion changes

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Introduction

Recent rodent studies performed at high magnetic fields (≥7T) have reported increases in T_1 relaxation as a consequence of reduced perfusion[1-3], which are not observed at lower field strengths. Rapid increases in T_1 in response to reduced cerebral perfusion have been found both in the presence[1,2] and absence[3] of reduced ADC. Similarly, we have recently demonstrated an increase in T_1 and decreases in ADC and MTR of tissue water that are a direct consequence of ET-1-mediated vasoconstriction[4]. In this study we investigate further T_1 relaxation changes in brain tissue with a model of excitotoxicity, which does not induce changes in cerebral perfusion.

Methods

Male Wistar rats (~220g) were anaesthetised with 2.0% isoflurane in 70%N_2O:30%O_2, and injected in the left striatum with 8μg of the excitotoxin N-methyl-D-aspartate (NMDA) in 1μl 0.1% BSA/saline (*n*=10). MRI was performed at 7T with a Varian Inova spectrometer. Animals were positioned in a quadrature birdcage coil and isoflurane was reduced to 1.7% (actively scavenged). In all cases, 1mm thick coronal images were acquired through the injection site. At all imaging time points, a series of EPI data was acquired for calculation of T_1 maps (Ti=0.025, 0.25, 0.5, 0.75, 2, 5s, TE=20ms), T_2 maps (TR=5s, TE=26, 36, 46, 56, 66, 76, 86ms), ADC trace maps (TR=5s, TE=45ms, δ/Δ=12/17ms, b=125,500,1000,1500smm^{-2}) and MTR maps (TR=5s, TE=26ms; ± saturation pulses –1500Hz from ^{1}H freq.). Images were acquired pre-injection and every 20min post-injection for 2h (n=3). In addition, some animals were imaged pre-injection and at 20min post-injection only (n=2) or pre-injection and at 2h post-injection only (n=2). In the other 3 animals, CBV maps were obtained from a time series of GE images (TR=20ms, TE=10ms) during bolus injection of contrast agent, and T_1-weighted images (TR=500ms, TE=20ms) were acquired 10 minutes later to ensure BBB integrity.

Results

The ADC of the injected striatum was significantly reduced compared to pre-injection values at all time-points post-NMDA injection, and also compared to the non-injected striatum (Fig. 1). The T_1 of the NMDA-injected striatum was significantly elevated compared to the non-injected striatum (Fig. 2), whilst the MTR (calculated as M_0-M_{SAT}/M_0, where M_{SAT} and M_0 are the signal amplitudes obtained with and without saturation, respectively) of the injected striatum was significantly decreased (Fig. 3). No significant changes in striatal T_2, CBV or BBB integrity were observed following NMDA injection.

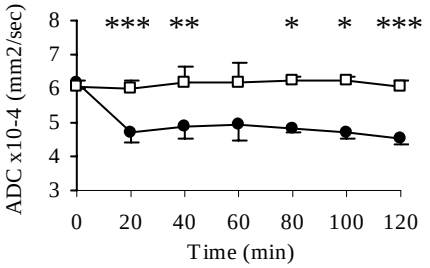

*Fig.1 ADC values for injected (●) vs. non-injected striatum (□). Values are mean ± SD. *P<0.05, **P<0.02, ***P<0.0001 left vs. right.*

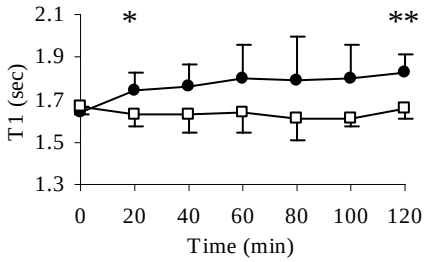

*Fig.2 T_1 values for injected (●) vs. non-injected striatum (□). Values are mean ± SD. *P<0.05, **P<0.02 left vs. right.*

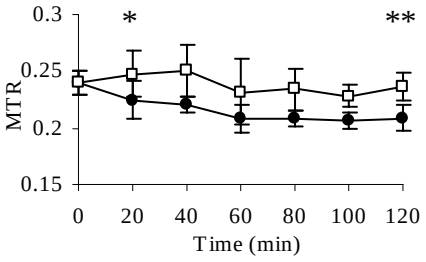

*Fig.3 MTR values for injected (●) vs. non-injected striatum (□). Values are mean ± SD. *P<0.05, **P<0.02 left vs. right.*

Discussion

NMDA is an excitotoxin which gives rise to cytotoxic oedema and, subsequently, neuronal cell death. The reduction in tissue ADC is in accord with previous studies demonstrating such effects of NMDA within the brain parenchyma. However, the effects of this excitotoxic injury on tissue T_1 and MTR have not previously been investigated. Here we demonstrate a significant elevation in T_1 and a significant reduction in MTR following NMDA injection in the absence of perfusion changes. These findings suggest that the increases in tissue T_1 that have been reported recently are not related to reduced perfusion *per se*, but to events that are common to models of reduced perfusion and excitotoxicity. Interestingly, an increase in T_1 and decrease in MTR have also recently been demonstrated in a model of spreading depression[5]. The increase in T_1 is unlikely to arise from increased tissue water, since no BBB breakdown or evidence of vasogenic oedema was observed. Rapid increases in $T_1\rho$, which is thought to reflect interactions between macromolecules and free water, have also been reported in models of cerebral ischaemia[6]. In addition, $1/T_1$ has been shown to be linearly related to protein concentration[2]. Thus, it is possible that the increased T_1 relaxation time observed in this study reflects either changes in the protein content of the tissue or alterations in tissue structure.

References

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