Improving the Detectability of Manganese Enhanced MRI by Fast T1 Mapping

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Introduction

There is growing interest in using MRI to detect manganese ion (Mn^{2+}) to trace neural pathways in vivo (1 – 4). It has been reported that Mn^{2+} can across at least 3-5 synapses thus opening the possibility to use manganese enhanced MRI (MEMRI) track tracing to visualize functional neural networks (1, 2, 4). A shortcoming is that regions far from the site of application of Mn^{2+} are difficult to detect. One possible reason is that when Mn^{2+} is transported along axons the concentration will gradually be diluted to a point that can not be identified in commonly used T1-weighted (T1W) images. Although T1 contrast can be optimized by TR and/or flip angle, it is difficult to span a broad range of Mn^{2+} concentrations with one set of imaging conditions. Therefore a direct measurement of T1 should be more sensitive than T1W images in detecting a broad range of concentrations including very low concentrations of Mn^{2+}. Since traditional T1 mapping methods are time consuming and impractical for high resolution 3D imaging, we implemented a fast T1 mapping sequence based on the Look and Locker approach (5). This fast T1 mapping sequence was compared with spin-echo T1W imaging in tracing connections in the olfactory pathway of the rat.

Methods

$MnCl_2$ was directly injected into the olfactory bulbs of male, Sprague-Dawley rats (200 – 250 g). Rats were anesthetized with 3% isoflurane and positioned in a stereotaxic frame. The site of injection in the bulb was determined by reference to a rat brain atlas (6). 50 nL of 100 mM $MnCl_2$ was injected using a 0.5uL Hamilton syringe. MRI was performed before and 36h after $MnCl_2$ injection.

MRI experiments were performed in a horizontal 11.7T/31 cm magnet (Magnex Scientific, Ltd., Abingdon, UK), interfaced to a Bruker Avance MRI console (Billerica, MA). A 30 mm transmit/receive surface coil was used. T1W images were obtained using a 3D fast spin echo (TR/TE=300/10 ms, 200 μm isotropic resolution). T1 mapping images were acquired by a 2D multi-slice Look-Locker sequence with 20 points sampled along the inversion recovery (TR=10s/TE=3ms/FA=25°, in-plane resolution = 200 μm, slice thickness = 0.5 mm, gap = 0.1 mm). To further speedup the image acquisition in the T1 mapping, multiple k-lines were acquired by multiple excitations at each time point. Centric-order phase encoding was used to reduce artifacts from different T1 weighting. The accuracy of the T1 mapping was compared with 2D spin-echo modified fast inversion recovery (MFIR) on $MnCl_2$ doped phantoms.

T1 maps were calculated in two steps. First, a 3-parameter non-linear curve fit was used to find the initial longitudinal magnetization, M_0, steady-state longitudinal magnetization, M_{eq}, and the apparent time constant T1*. Then the relation between M_0, M_{eq}, T1*, inversion delay, and multi-excitation was solved to determine the T1.

Results

The T1 values obtained by the Look-Locker method agreed well with those by the MFIR up to 4-fold acceleration. In phantoms, T1 changes associated with $MnCl_2$ concentrations as low as 5 μM could be measured. 36 h after injection into the bulb, signal enhancements in T1W images were observed in the olfactory bulb (OB), piriform cortex (Pir), anterior olfactory nucleus and ventral orbital cortex, but not the acumens nucleus (Acb), entorhinal cortex (Ent) or amygdala (Amy) (Fig. 1). In the T1 maps, significant T1 reduction ($p < 0.05$, paired t-test, n=5) can be seen in all the above mentioned areas. Averaged T1 changes ranged from 500 ms (in OB) to less than 100 ms (in Amy and Ent) (Fig. 2).

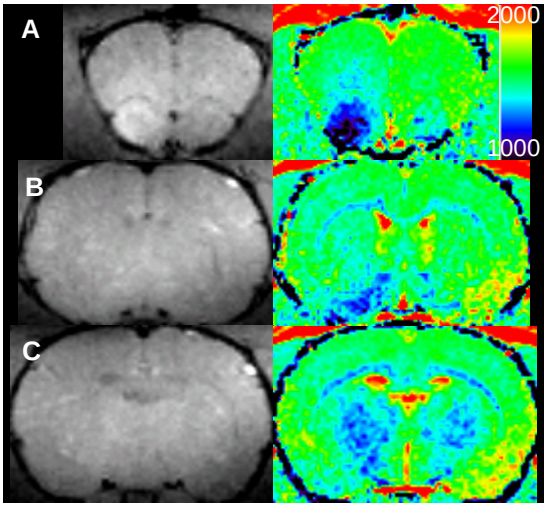

Fig. 1 T1W images (left) and T1 maps show (a) piriform cortex, (b) putamen, (c) amygdala.

Discussion

It is shown that T1 mapping can reliably detect T1 reduction of less than 100 ms, which can not be seen in T1W imaging for the parameters selected. If the relaxivity of Mn^{2+} in the tissue were similar to that in water, 100 ms T1 change would correspond to 5μM Mn^{2+}. Since tissue relaxivity is expected to be higher (7), it is likely that lower concentrations are being detected. Thus a more thorough extent of the transported Mn^{2+} can be observed. In addition, with multiple k-lines acquisition strategies, 3D T1 mapping can be obtained in reasonable time. One pitfall of the Look-Locker approach is that due to the use of gradient-echo acquisition it can suffer from susceptibility artifacts, especially at high fields and in regions close to amygdala and ventral part of hippocampus.

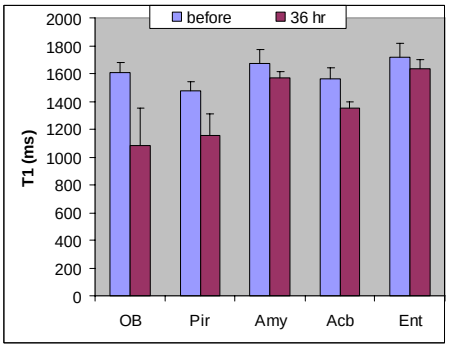

Fig. 2 T1 before and 36h after $MnCl_2$ injection into the OB.

Reference

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