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Limits of Mn detection in vivo: Spatial segregation of relaxation behavior

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Introduction: MEMRI is a powerful tool for studying the structure, functional connectivity and activation of the central nervous system [1,2,3]. Quantitative analysis of signal intensity is used to monitor manganese (Mn) transport and tissue concentration, with a linear relationship typically being used to translate signal intensity into Mn concentration. However, it is known that the environment and molecular form may affect the magnetic properties of Mn in tissue [4,5]. For instance, little is known about the specific properties of Mn in tissue such as the cellular uptake and distribution as well as whether the detection limit of Mn changes in different brain regions. The aim of this study was to measure the relaxation features of Mn in different brain regions and reveal possible compartmentalization effects after focal injections of MnCl in the prefrontal cortex (PFC). Importantly, we show that relaxation behavior is brain region-specific, which, in fact, affects quantification in axonal transport rates and the estimated Mn concentration.

Materials and Methods: The longitudinal relaxation behavior in vitro (Mn phantom) and in vivo was examined using a progressive saturation (PS) sequence at 11.7T. Female C57Bl6 mice (n=2) were anesthetized and stereotactically injected with 5 nL 600 mM $MnCl_2$ in the PFC. Approx. 20 hrs after injection anatomical information was collected using a 3D RARE sequence and PS images were acquired for ten coronal slices with a thickness of 0.5 mm, each spaced 0.5 mm apart. The SR imaging was performed with the following parameters: Averages=1, FOV=1.28x1.28cm, matrix=64x64, 20 TRs between 200 ms and 10 s, TE=5.5 ms. T_1 maps were calculated using ImageJ. After MR measurements the animal was sacrificed, the brain quickly removed (~30 s) and placed in a brain matrix on dry ice. Coronal slices of 1 mm were cut and placed on glass slides on dry ice. Pictures were taken and cortical and striatal tissues dissected using a microscope. The samples were digested in 70% HNO_3 at 80°C, resuspended in 2% HNO_3 and Mn content was determined using ICP-MS, assuming 80% water content. Mn relaxation times in vitro were measured using the same PS sequence on a Mn phantom (aqueous solution). The slope of the relation between the relaxation rate ($1/T_1$) and Mn concentration is the relaxivity, r_1: $R_1=r_1[Mn]+R_1[0]$

Results: Signal intensity changes as a result of Mn presence are clearly observed in the MR reference scan and the corresponding T_1 maps (fig. 1). T_1 values were extracted from regions corresponding to the dissected tissue. The relaxation rates increased linearly with the corresponding Mn concentrations in the phantom (fig. 2A), cortex (fig. 2B) and striatum (fig. 2C). However, the slope is different in each case. The relaxivity was 4.6 $s^{-1}mM^{-1}$ in the phantom, 1.6 $s^{-1}mM^{-1}$ for the cortex and 0.8 $s^{-1}mM^{-1}$ for striatum. We measured a baseline concentration of Mn in mouse brain of 15 μM, which was used as an offset ($R_1[0]$) for the in vivo relaxivity plots. Notably, the measured relaxation rates show a linear relation with the concentrations, indicating that there is no quenching of the MR signal due to Mn compartmentalization. Note that in studies at lower field strengths, [6] found r_1 to be 6.8 $s^{-1}mM^{-1}$ for rat brain at 7 T and at 4.7 T [7] found an r_1 of 0.66 $s^{-1}mM^{-1}$ for rat striatum and 2.06 $s^{-1}mM^{-1}$ for rat cerebellum as well as a phantom r_1 of 8.4 $s^{-1}mM^{-1}$. Additionally, [8] reported earlier 4.7 $s^{-1}mM^{-1}$ for rat cortex at 11.7T. Comparison between data obtained using different field strength and species is problematic, however, the same relaxivity was observed in the mouse striatum as well as an increased r_1-value *in vitro* compared to *in vivo* values.

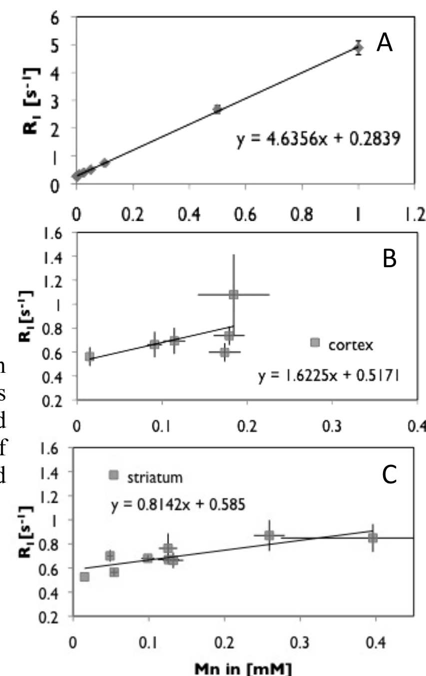

Fig. 2: Relaxation rates versus Mn concentration [mM] in water (A) and in vivo in the cortex (B) and striatum (C).

Conclusions: We show that the MEMRI signal intensity and T1 mapping correlates with Mn concentration as measured with ICP-MS and that Mn relaxation efficiency remains constant (thus indicating that quantification is not impaired by compartmentalization effects) throughout the cortex and striatum upon injection in the PFC. However, the data also show that longitudinal relaxation properties of Mn are brain tissue-specific, a feature that should be considered when quantifying Mn concentration and axonal transport rates in the brain.

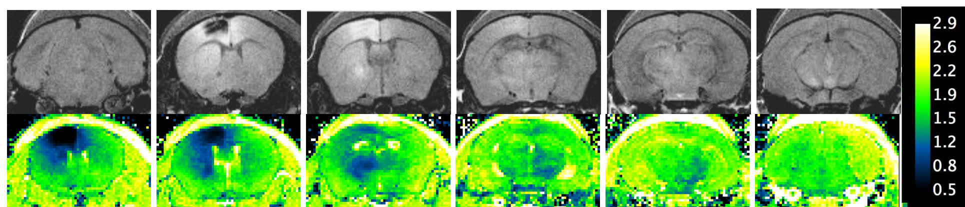

Fig. 1: Anatomical reference images after injection in the PFC (upper panel) and the corresponding T_1 maps (lower panel). Calibration bar indicates T_1 [s].

References: [1] T. Watanabe, *NMR in Biomed,* 17(2004)554-568 [2] R. Pautler, *MRM*, 40 (1998) 740-48 407 [3] Y. Lin, *MRM*, 38 (1997) 378-388 [4] Y. Kang, *Investigative Radiology*, 19(1984)399 [5]J. Gore, *IEEE Eng in Med and Biol,* 3 (1985)39-42 [6] N. Bock, *Brain Res*, 1198(2008)160-70 [7] N. Zhang, *ISMRM proc*, 2006 [8] K. Chuang, *MRM*, 61 (2009) 1528-1532