

INDUCED T_1 , T_2^* AND PHASE CHANGES FOLLOWING MANGANESE SYSTEMIC ADMINISTRATION AT 14.1T

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Introduction: Manganese Enhanced MRI (MEMRI) has been increasingly used in animal neuroimaging thanks to its T_1 shortening properties and the fact that it can enter active voltage gated calcium channels [1]. With the higher magnetic field strengths, while the longitudinal and transverse relaxivity as a function of Mn^{2+} concentration, r_1 and r_2^* , remain virtually unchanged, the tissues R_1 and R_2^* tend to decrease and increase respectively. Furthermore, the susceptibility induced frequency shift varies linearly with the increase of the magnetic field. Mn^{2+} , due to its paramagnetism, can thus be exploited using phase imaging to further enhance neural architecture in animal models [2].

The aim of this study was to quantitatively evaluate the dynamic evolution of T_1 , T_2^* in different regions of the rat brain throughout a Mn^{2+} systemic administration, follow its uptake at 14.1T and access the impact on phase imaging.

Methods: All scans were performed on a 14.1 T/26 cm scanner (Varian/Magnex Scientific) using a home built quadrature surface coil as RF transceiver. T_1 mapping was obtained using a multi-slice inversion-recovery Look-Locker Segmented Echo Planar Imaging sequence [3] with 20 inversion times (50ms to 4050ms), TR/TE=24.5s/5.7ms, FA=20°, FOV=22*13mm², resolution =172*172*1000 μm^3 . For Nyquist ghost correction, a readout polarity reversal scheme was used [4] making the total acquisition time of 14mins. T_1 was calculated using a Nelder-Mead fitting algorithm. T_2^* maps were obtained using a multi-echo gradient echo multi slice sequence with 8 echo times (3.1 to 35.3ms), FA=60°, FOV=22*22mm², resolution = 115*115*1000 μm^3 and total acquisition time of 8mins. Respiration gating was used to avoid respiration induced artifacts (implying an effective TR~1s). Phase images were unwrapped and filtered by a 2D Gaussian highpass filter to remove large scale phase variations. T_1 -, T_2^* -weighted and phase images with in-plane resolutions of 33 μm were obtained using a gradient echo sequence with respiration gating (TR~1s), TE=5ms(T_1 -w)/16ms(T_2^* -w), FA=90°/6 averages (T_1 -w), FA=50°/11 averages (T_2^* -w), FOV=17*17mm², resolution = 33*33*400 μm^3 .

To measure the effect of Mn^{2+} on r_1 , r_2^* , χ at 14.1T, a phantom containing 9 different tubes with different Mn^{2+} concentration (from 5 μM to 500 μM) was used. Two adult rats (Sprague-Dawley) were scanned under 2% isoflurane anesthesia. T_1 , T_2^* and phase images were obtained prior and after intravenous Mn^{2+} administration (175mg/kg in 1 hour) every 45min for 16hours. High resolutions images were obtained on the same animal prior and 24h post Mn^{2+} systemic administration.

Results: As it can be seen in Figure 1, after Mn^{2+} systemic administration and throughout a period of 16h, a T_1 decrease of 4% and 8% and likewise a T_2^* decrease of 24% and 23% are observed in the cortex and hippocampus respectively while in the corpus callosum no significant decrease can be observed as expected from the absence of voltage gated calcium channels in this region. From the relaxivity r_1 and r_2^* established from the phantom data (7s⁻¹.mM⁻¹ and 213s⁻¹.mM⁻¹ respectively), the T_1/T_2^* measured in 4 different animals (see Table 1) and their variations (see Figure 1), it is possible to estimate an uptake of Mn^{2+} of 0.74/0.64 μM Mn in the cortex and 1.52/0.63 μM in the hippocampus.

After 24h post Mn^{2+} systemic administration, an enhancement in T_1 -weighted image is observed (see Figure 2). The T_2^* -W images despite the long echo time were found to also have a signal enhancement which might be explained by the high flip angle used making the T_1 weighting outweigh the T_2^* weighting. On the other hand, phase images show, in comparison to the pre Mn^{2+} , increased contrast of the hippocampus (CA1, CA2 and dentate gyrus) and cortical layers (see red arrows) which is in good agreement with the regions enhanced in the T_1 -weighted image.

Discussion : Look-Locker EPI and multi-echo GRE sequences provide fast parameter mapping acquisitions and thus the capacity to dynamically and quantitatively study the Mn^{2+} uptake in various regions of the *in vivo* rat brain after systemic administration but suffer from low SNR when compared to T_1 - or T_2^* -weighted images or phase images. Nevertheless, such quantitative data will allow revisiting whether “positive contrast” as given by T_1 -w or “negative contrast” as given by T_2^* -w offers improved contrast at 14.1T. From the preliminary data, phase imaging seems a potential candidate to explore MEMRI as the contrast observed in the phase images is improved not only by the uptake of Mn^{2+} (responsible for a local variation of susceptibility that increases the frequency shift) but also by the increased SNR due to the reduction in T_1 .

References & Acknowledgements: [1] Silva, A. et al., NMR in Biomed. 2004; [2] Marques J.P. et al., *Neuroimage* 2009 ; [3] Gowland, P. et al., *MRM*, 1993; [4] van der Zwaag, W., *JMRI*, 2009; This study was supported by Merck Serono, by CIBM of the UNIL, UNIGE, HUG, CHUV, EPFL and the Leenaards and Jeantet Foundations.

	Cortex	Hippocampus	WM
T_1 (s)	2.30±0.15	2.31±0.17	1.92±0.08
T_2^* (ms)	30.9±3.6	29.1±6.5	16.4±2.1

Table 1 T_1, T_2^* in the cortex, hippocampus and corpus callosum in the *in vivo* rat brain averaged over 3 animals.

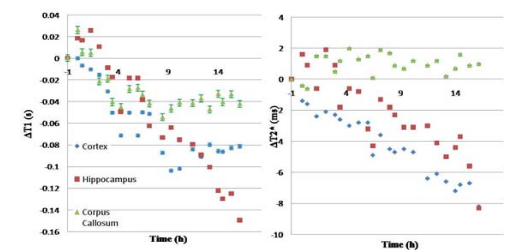


Figure 1. Plots showing the evolution of ΔT_1 , ΔT_2^* in the brain regions mentioned above following Mn^{2+} systemic administration and during 16h.

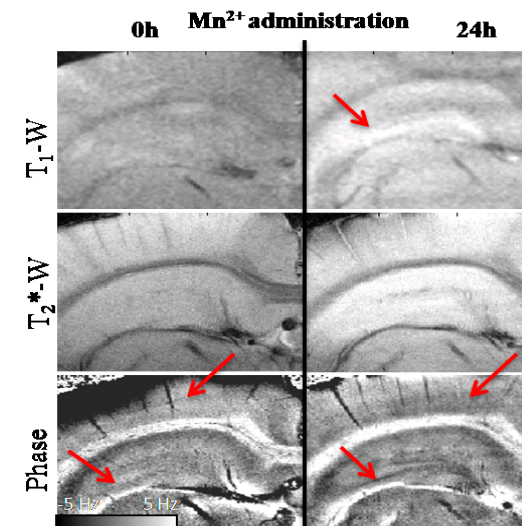


Figure 2. T_1 -W, T_2^* -W and Phase images are shown pre and 24h post Mn^{2+} administration.