Quantitative determination of Mn content in rat brain by fast T1 mapping

S. Tambalo[1], S. Fiorini[1], A. Daducci[1], F. Boschi[1], E. Nicolato[1], and P. Marzola[1]
[1]Morphological and Biomedical Sciences, University of Verona, Verona, Italy

Introduction

Manganese-Enhanced MRI (ME-MRI) is an emerging functional methodology based on differential distribution of Mn^{2+} between activated and non-activated brain areas in laboratory animals (1). Most of the paper reported in literature have used standard T1-weighted images to study Mn distribution into animals' brain; Mn accumulation in specific brain areas is measured by the enhancement of the signal intensity (calculated in comparison to the signal intensity before Mn administration or to other brain regions). However the concentration of Mn in rat brain can be evaluated quantitatively by using T1 mapping. In this work fast T1 mapping of rat brain was used in order to quantitatively determine the Mn concentration in different brain regions after i.p. injection of $MnCl_2$.

Materials and Methods

$MnCl_2$ was administered to eight weaned Wistar rats in the form of intraperitoneal (i.p.) injections. Three injections were performed over a seven days period (day 1, day 4 and day 7). A 90 mM solution of $MnCl_2$ in isotonic saline (0,9% NaCl in water) was injected at a dose of 0.2 mmol/Kg. The same volume of saline was injected into two control rats. MR images were acquired 24 h after the last injection. In a limited number of animals (n=2) the Mn dosage was increased to 0.4 mmol/kg, and the rate of clearance of Mn from brain was investigated up to 30 days after administration.

MR images were acquired at 4.7T using a Bruker Biospec Tomograph. Animals were anaesthetized by isoflurane. Images were acquired through a receiver-only surface coil optimized for rat brain. 3D-T1-w GRE images were acquired with the following parameters: TR=25 ms TE=4.2 ms, FOV=4x4x4 cm^3, MTX=256x128x128. 2D T1 maps were acquired using IR-SNAPSHOT FLASH sequence K-space segmented in 8 steps, with FOV=4x4cm^2, MTX=128x128, slice thickness=1mm, INV pulse shape=sech, TR=10 ms, TE=3.6 ms. Twenty-two slices were acquired to cover the whole rat brain.

Results

The segmented IR-FLASH sequence was preliminary tested by comparing the T1 values obtained by imaging to those obtained by using a classical spectroscopic IR sequence in 2% agarose gels containing different amounts of $MnCl_2$. Values determined by imaging were in good agreement with those obtained by spectroscopy (see Fig.1). On the same phantoms, Mn^{2+} relaxivity was determined by T1-maps (r_1=3.9 $mM^{-1}s^{-1}$, at 4.7T and 22°C). In Fig.3 we show T1-w images obtained in rat brain after 3 injections of $MnCl_2$. According to previously reported findings (2) Mn^{2+} enhancement is inhomogeneous: the pituitary gland undergoing the stronger enhancement (see arrow). In Tab. 1 we report the increase in the relaxation rates measured after three i.p. injections of $MnCl_2$. In the third column of Tab. 1 we report Mn^{2+} concentrations calculated according to the relaxivity measured in gel. Higher concentrations of Mn^{2+} are observed in the pituitary gland, in the striatum and in the olfactory bulb. Administration of an higher $MnCl_2$ dosage (0.4 mmol/kg with the same protocol as before) produced consistently higher values of ΔR1 and concentration: 0.079±0.003 mM in the Cortex. Such concentration decreased slowly with time, reaching 0.053±0.002, 0.021±0.002 and 0.002±0.002 mM at 7, 14 and 30 days after the last $MnCl_2$ injection, respectively.

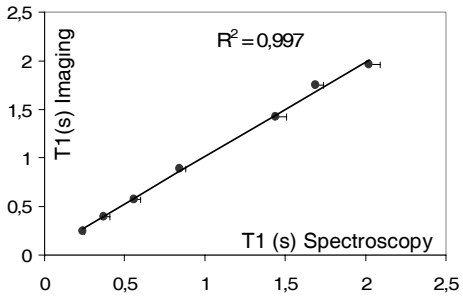

Fig.1 Correlation between T1 values measured by imaging and spectroscopy

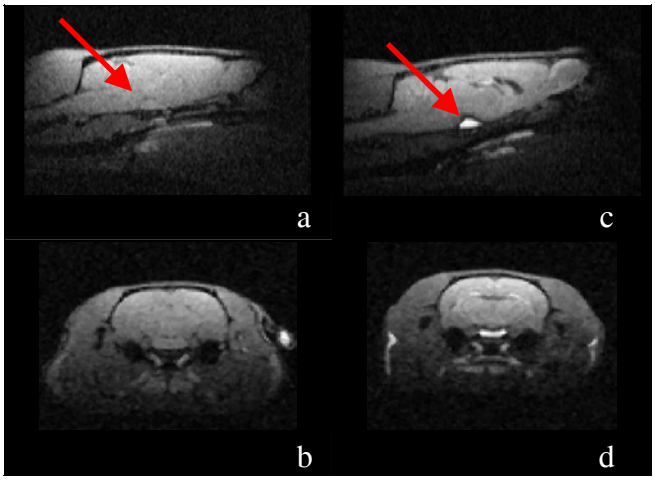

Fig.2: T1-w Images obtained before (a, b) and after (c, d) $MnCl_2$ i.p. administration

	ΔR1 (s^{-1})	C (mM)
Cerebellum	0.189±0.06	0.049±0.012
Olfactory bulb	0.339±0.01	0.087±0.004
Cortex	0.221±0.05	0.057±0.014
Pituitary Gland	1.467±0.15	0.377±0.038
Striatum	0.390±0.01	0.100±0.003
Hippocampus	0.183±0.07	0.047±0.017
Muscle	0.036±0.020	0.009±0.006

Table 1: Increase in the relaxation rates measured after three i.p. injections of $MnCl_2$

Conclusions

Quantitative concentration of Mn^{2+} in different brain areas was determined *in vivo* by fast T1 mapping in rats after i.p. administration of $MnCl_2$. Concentration values were obtained by assuming the same relaxivity in brain and agarose gel. Future work will be devoted to independently determine Mn concentration in brain in order to obtain a more realistic estimation of its relaxivity *in vivo*. The present work open the way to functional ME-MRI based on absolute measurement of Mn content, instead of Signal Intensity Enhancement, as a marker for activated brain areas.

References

(1) Yu et al., Nature Neuroscience 8:961-968 (2005).
(2) Hee Le et al., Magnetic Resonance in Medicine 53 :640-648 (2005)