The effect of paramagnetic manganese cations on ^{1}H MR spectroscopy of the brain

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Introduction

The paramagnetic properties of divalent manganese cations (Mn^{2+}) and their in vivo resemblance to calcium cations (Ca^{2+}) has led to their use in morphological [1] and neural pathway [2] imaging. Mn^{2+} is taken up through Ca^{2+}-channels during neural activity and subsequently transported anterograde along microtubules at a velocity equivalent to fast axonal transport thereby making the metal suitable for neural tract tracing [2]. Mn is an essential trace element found at low concentrations in the brain. Elevated levels of Mn are neurotoxic and influence a range of neurophysiologic and metabolic processes and chronic exposure to Mn may lead to neurodegeneration [3]. The administration of Mn to observe, for example, neural pathways may therefore influence those same pathways due to the high local concentrations of Mn required to provide MRI contrast. As a result, the use of ^{1}H MRS to obtain a metabolic profile of the brain may be influenced by both Mn-induced metabolic changes and the effect of the paramagnetic metal ion on the relaxation of the metabolites themselves if the Mn cations and metabolites are in the same cellular compartment. Consequently, this study has investigated the effect of Mn on ^{1}H MR spectroscopy using an in vivo Mn-enhanced optic tract imaging model [2] together with phantom experiments.

Materials and methods

Five male Sprague-Dawley rats (300-350g) were used. $MnCl_2$ (3µl, 50 mM) was injected into the vitreous body of the animal's left eye under general anaesthesia. 24 hours after intravitreal injection, animals were anaesthetized and placed into a stereotactic device. Images and ^{1}H MR spectra were acquired using a Varian 4.7T animal scanner together with a home built volume and surface coil. T1 maps were acquired using spin-echo inversion recovery with multiple TIs. Single voxel PRESS ^{1}H MRS was performed following shimming over a 4x4x6 mm volume covering the superior colliculi. Spectra were obtained from a single isotropic 2.5mm voxel from either the left or right superior colliculus within the shimmed volume using identical acquisition parameters with TR=4s, TE=17ms and NT=300. Longitudinal relaxivity measurements were performed on 25mM solutions of the 'metabolites'; N-acetylaspartate (NAA), creatine (Cre) and choline (Cho) (pH=7.4) containing from 0–50 µM $MnCl_2$. Metabolite T1 values were measured using a PRESS sequence with 10 different TIs ranging from 1 to 6 seconds.

Results and discussion

The T1 maps showed that the Mn-enhanced (mean T1=901±50 ms, n=5) and unenhanced regions (mean T1=1254±25 ms, n=5) of the superior colliculus provided adjacent ROIs with significantly different relaxation times making the model highly suitable for comparing the effects of Mn on ^{1}H MRS. Phantom longitudinal relaxivities were determined as: r1(NAA)=30.5, r1(Cho)=5.3, r1(Cre)=6.4 and $R1(H_2O)=12.0$ $s^{-1}mM^{-1}$. This indicates that NAA is more susceptible to the paramagnetic relaxation effects of Mn^{2+} cations compared to choline and creatine. This is in accord with the anionic nature of the NAA molecule and the increased interaction with positive cations compared to the other metabolites as similarly observed for negatively charged Gd-DTPA and positively charged choline [4]. The in vivo water relaxivity has previously been reported to be approximately 50 [5]. Using this value it is possible to estimate the concentration of Mn in the enhanced superior colliculus region using $1/T1_{(enhanced)} = 1/T1_{(unenhanced)} + r1[Mn^{2+}]$, which provides a value of around 15 µM. Consequently, if the Mn^{2+} cations were in the same cellular compartment as NAA then significant changes in the metabolite T1 values would be expected. Selection of spectroscopic acquisition parameters is therefore of importance in order to minimise relaxation effects on the apparent metabolite concentrations i.e. use of a proton density weighted spectroscopic sequence. Here we have used PRESS with a relatively short TE of 17ms and a TR=4s showing demonstrating that ^{1}H spectra may be acquired without the paramagnetic effects of Mn dramatically influencing ^{1}H MR spectral quality.

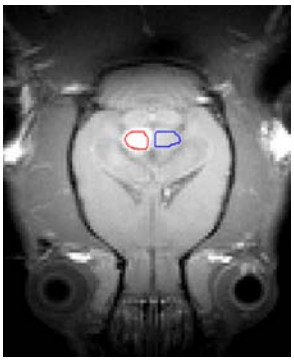

Figure 1: T1W image acquired 24 hours after intravitreal injection of 3 µl of 50 mM $MnCl_2$ into the rat's left eye. The enhanced region in the right superior colliculus and the unenhanced left superior colliculus provides two adjacent regions to compare the effects of Mn on ^{1}H MRS. The enhanced region possessed a mean T1 of 901±50 ms (n=5) whilst the contralateral region possessed a mean T1 of 1254±25 ms (n=5).

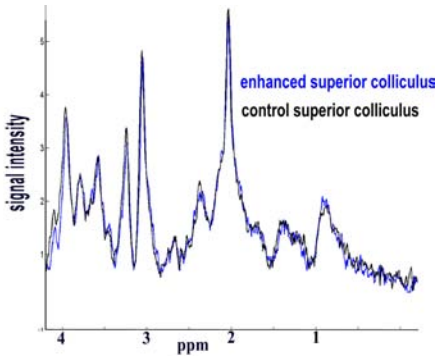

Figure 2: Typical proton MRS spectra acquired *in vivo* from adjacent 2.5 mm isotropic voxels in the (blue) Mn-enhanced and (black) adjacent, control and unenhanced superior colliculus. The effect of the Mn appeared negligible when TR=4s and TE=17ms suggesting that ^{1}H MRS may be used to obtain metabolic information that is not significantly influenced by the relaxation effects of the paramagnetic Mn^{2+} cations.

Conclusion

The large relaxivity measured for NAA suggests that if the metabolite and paramagnetic Mn^{2+} cations are within the same cellular compartment, significant relaxation effects may influence the apparent ^{1}H MRS metabolic profile obtained from brain tissue. This effect should be taken into account when performing spectroscopic investigations on brain regions with increased Mn concentrations.

References

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