Combined Effects of Albumin and Manganese on 1H Relaxation Rates of aCSF

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Introduction:

The use of manganese (Mn) as a contrast agent for neuro-anatomical and functional mapping has been studied in animal models for the last decade. More specifically, Mn contrast enhancement is directly proportional to the changes in relaxation rates in the brain tissue in these animal models (1,2,5). However, the binding of Mn to many proteins alters its relaxation(3,4). Changes in the environment, including temperature variability, animal behaviour and stress, affect different metabolic processes and the protein levels produced in brain and Cerebrospinal fluid (CSF) which could then affect the Mn contrast. The aim of this study is to investigate the relaxation rate of Mn in artificial CSF (aCSF), when different levels of protein are present.

Materials and Methods:

In Vitro T_1 and T_2 relaxation measurements were performed. Albumin (Bovine Alb, lyophilized powder >96%, Sigma) was chosen due to its large presence (67% composition) in CSF. Thirty five 0.5 ml samples were made with the following dilutions in aCSF; Albumin concentrations: 0, 0.9, 1.8, 2.7 and 4.05g% and Mn concentrations of 0.06, 0.1, 0.3, 0.6, 1.0, 1.5 and 3.0 mM (pH adjusted to 7.4, osmolarity 300).

Imaging was performed on a 800 mm 3T Magnex magnet with a Evo console (MR Solutions, UK), using a homebuilt coil (D=7mm). The samples were imaged at Day 0, 3, 6 and 9 after mixing using the same protocol: 1) T1-bulk measurements (SE-TR=10000ms, 20 TI-s train: 16-9000 ms 2) T2 bulk (SE-TR=2000ms, 25 TEs: 1-300 ms) Signal intensity were extracted from the data and relaxation rate values were calculated, with IDL software written in the CCBN lab using the Marquard Levenberg fitting method.

Results and Discussion: Relaxation rates of Mn Alb aCSF solutions vs the Albumin concentration were plotted for all days of imaging. No significant differences were found between values across time (example: Smpl29: Day0 to 9, LSF slope±SD: 0.000037± 0.0000019,R=0.99863). Figure 1 A) and B) show clear changes in 1/T1 and 1/T2 as Albumin concentration increases, confirming the hypothesis that Mn enhancement changes in aCSF in the brain when binding with the respective protein. Also Figure 1 C) 1/T1 vs Mn concentration is shown.1/T2 had a similar behaviour. The Mn doped aCSF (Alb=0) relaxes slower, and as protein is introduced into the mixtures and it's concentration increases, the Alb-Mn-aCSF solutions relax faster.

Conclusion: This is the first study that investigate the combined effects of Albumin and Manganese on 1H Relaxation Rates of aCSF. It demonstrates that Mn enhancement changes in aCSF in the brain when binding with the present proteins. Therefore, change in the environment, animal behaviour and stress will affect the final contrast.

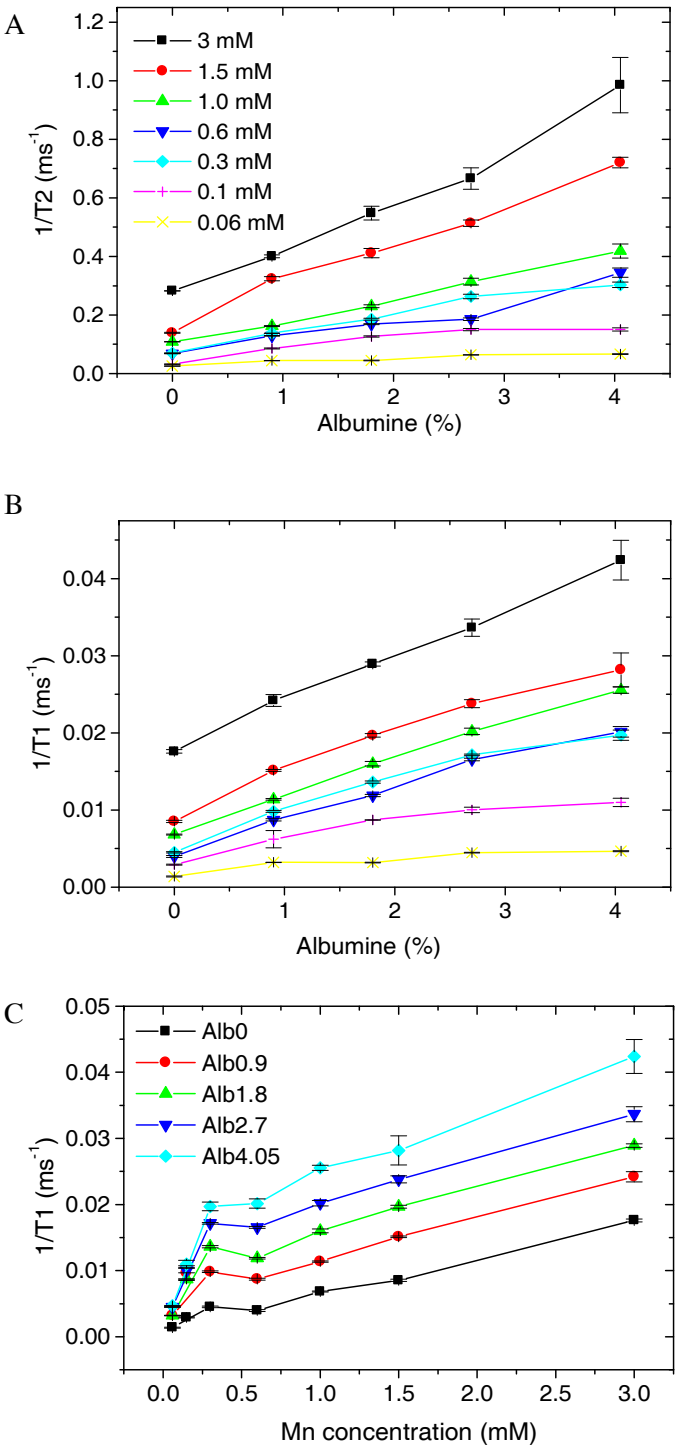

Figure 1. Relaxation Rates of samples in different albumin concentrations for Day 3 of imaging A) 1/T2 B) 1/T1 C) 1/T1 vs

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