Measurement of glutamate ADC in the monkey brain using an optimized diffusion-weighted STEAM sequence at 3T

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Introduction

Whereas diffusion-weighted (DW) MRI mostly provides information on tissue structure, diffusion-weighted MR spectroscopy could give an insight into brain metabolism by reflecting metabolite compartmentation. DW MR spectroscopy allows for measuring the apparent diffusion coefficient (ADC) of metabolites, determined by log-linear regression at rather low b values, mostly associated with the fast diffusion component. Among brain metabolites detectable by ^{1}H-NMR, glutamate is of major interest since it is the main excitatory neurotransmitter in mammal brain. However J-modulation makes it difficult to detect glutamate with diffusion-weighted sequences requiring long echo times. Up to now glutamate diffusion coefficient has only been measured in the rodent brain on high field animal systems [1]. Our purpose has been to measure glutamate ADC in the monkey brain on a whole-body 3 Tesla system. A first set of experiments was dedicated to the optimization of a diffusion-weighted sequence for glutamate detection. After this preliminary work, glutamate ADC was measured in the monkey brain using the optimized sequence.

Materials & Methods

TE and TM optimization. Based on literature ADC values [1] and on SNR measurements on our 3T system, a maximum *b* value of ~3000 s/mm² was chosen for the measurement of glutamate ADC (expected glutamate attenuation of ~25% for *b*~3000 s/mm²).

A diffusion-weighted STEAM sequence was implemented (Fig. 1), in which TE and TM are closely related to the gradient diffusion duration δ and the diffusion time Δ (δ~TE/2 and Δ~TM+TE/2). Therefore a given *b* value can be obtained by several possible combinations of TE and TM. Knowing the strong effect of TE and TM on glutamate magnetization, it was essential to choose a (TE,TM) combination maximizing glutamate signal. The evolution of glutamate magnetization during the STEAM sequence cannot be predicted easily, mostly due to the difficulty to accurately determine the T1 of glutamate protons in the monkey brain at 3 Tesla. Therefore the sequence optimization was performed experimentally by testing different (TE,TM) combinations all corresponding to b_{max}=3000 s/mm² at maximum gradient strength on our system. Spectra were acquired in the monkey brain for (TE,TM) values of (15ms,300ms), (18,180), (21/110), (24,70) and (27,50). Optimization experiments were conducted on 2 macaque monkeys (detailed experimental protocol described bellow). Signal intensity of glutamate was measured at 2.35ppm. As shown on Fig. 2, the optimal (TE,TM) combination for glutamate detection with *b*~3000 s/mm² was found to be (TE,TM)=(21ms,110ms), corresponding to δ=7.8ms and Δ=121ms.

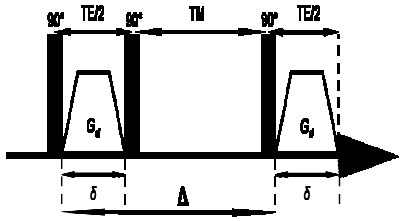

Fig. 1: STEAM excitation scheme with diffusion gradients Gd

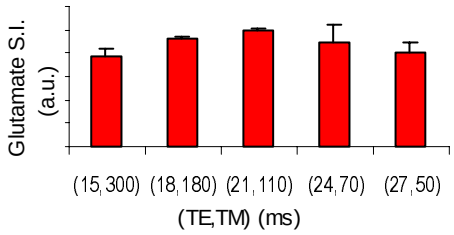

Fig 2. *Glutamate signal intensity measured for different (TE,TM) combinations all corresponding to bmax=3000s/mm²*

Diffusion experiments. Diffusion experiments were performed with the optimized STEAM sequence on our whole-body 3T system (Bruker, Ettlingen, Germany). Two macaque monkeys were anesthetized with i.v. propofol infusion. Each monkey was studied twice in separate experiments. A 3.9mL voxel was positioned in the center of the brain around the striatum. Diffusion-weighted spectra (TR=2.5s, 360 transients, BISTRO-type OVS, VAPOR water suppression) were acquired with 6 different *b* values obtained by varying *Gd* from 0 to 95% of Gd_{max} (Gd_{max} corresponding to b_{max}~3000 s/mm²). Spectra (Fig. 3) were analyzed with LCModel [2] using a basis-set including NAA, NAAG, glutamate, glutamine, lactate, myo-inositol, creatine, aspartate, taurine, succinate, choline and glucose. The basis-set was simulated under NMR-Sim 2.8 (Bruker, Ettlingen, Germany).

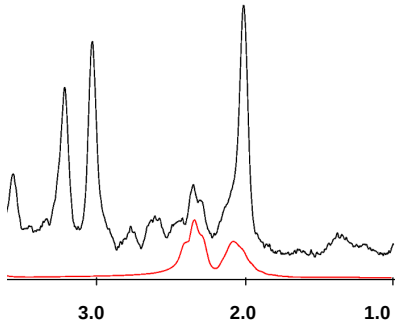

Fig 3. *Typical STEAM spectrum acquired for b=1123 s/mm² and glutamate contribution assessed by LCModel (in red)*

Results & Discussion

Fig. 3 shows a DW STEAM spectrum acquired in one monkey and glutamate contribution as derived from LCModel analysis. Glutamate ADC determined by log-linear fit (Fig. 4) was 0.18±0.01 µm²/ms for the first monkey (n=2) and 0.16±0.01 µm²/ms for the second one (n=2). Glutamate ADC as measured in our study is higher than values reported in the rat cortex (0.112±0.002 µm²/ms, [1]). This discrepancy may result from interspecies difference and/or regional brain difference (our monkey measurement were performed in a subcortical area).

This study demonstrates the ability to measure glutamate ADC in a 3.9mL voxel in the monkey brain using an optimized STEAM sequence on a whole body NMR system. Further development include measurements of regional differences in the brain (cortical vs. subcortical areas). This work should prove useful for exploring neurodegenerative processes where impairments in glutamate compartmentation is highly suspected.

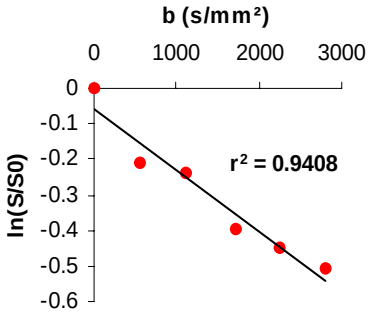

Fig 4. *Glutamate signal decay measured in one monkey*

References

[1] Pfeuffer et al., J. Cereb Blood Flow Metab, 20, 736, 2000
[2] Provencher, Magn Reson Med, 30, 672, 1993