

SINGLE VOXEL 1H SPECTROSCOPY IN THE HUMAN HIPPOCAMPUS AT 3 T USING LASER: A REPRODUCIBILITY STUDY.

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Introduction

Scan to scan reproducibility is a challenging issue, especially in the deep brain regions such as hippocampus where lower SNR and poor magnetic field homogeneity can lead to larger uncertainties in metabolite quantification. Furthermore, the reproducibility of voxel placement on repeat scans adds to these uncertainties. Few studies have investigated ¹H-MRS reproducibility in the hippocampus [1-4] either at low magnetic field strength [1-3] or with few subjects [1,4]. Relatively large volumes of interest were used in most of these studies, resulting in partial volume effects [2-4]. In this study, we looked at the reproducibility of the spectroscopic measurements in the hippocampus at 3 tesla using localization by adiabatic selective refocusing (LASER) sequence [5]. We performed our measurements in the volume of 2.4 mL to minimize partial volume effects.

Methods

10 healthy subjects (27.8 ± 3.7 years: 6 males, 4 females) were scanned during three different sessions on consecutive days at the same time of the day using a 3 T Siemens TIM Trio using a LASER sequence [5] with VAPOR water suppression [6]. All scans were performed using body coil excitation and 12-channel receive phased-array head coil. High-resolution three-dimensional T₁-weighted images were acquired for localization and repositioning of the spectroscopic voxel which was rotated and placed along the long axis of the left hippocampus to cover its body and most of its tail portion (Fig. 1). Rigorous guidelines were established to guarantee optimal voxel repositioning from one session to another. All first- and second-order shim terms were automatically adjusted using FAST(EST)MAP [7]. During each session, 3 acquisitions with 256 water-suppressed averages (T_E = 65 ms, T_R = 3 s) and 4 water-unsuppressed averages (T_E = 65 ms, T_R = 15 s) were obtained without voxel repositioning.

In vivo spectra were analyzed using LCModel with a simulated basis set which included 19 metabolites. Quantification of the *in vivo* metabolite signals was based on the unsuppressed water signal as an internal reference taking into consideration T₁ and T₂ relaxation of water and partial volume of white matter, gray matter and CSF in the voxel of interest. For each subject, mean concentrations, standard deviations (SD) and coefficients of variation (SD/mean) over the 9 measurements (3 measurements × 3 sessions) were calculated. The means of the coefficients of variation for ten subjects were estimated for each metabolite (Table 1).

Results and Discussion

Good quality spectra (SNR = 10 ± 0.9; water linewidth = 4.5 ± 0.3 Hz) were obtained from all the subjects (Fig.2). Excellent fits for five metabolites with mean Cramer-Rao lower bounds under 5% for *N*-acetylaspartate and *N*-acetylaspartylglutamate (tNAA), choline containing compounds (tCho), creatine and phosphocreatine (tCr) and myo-inositol (Ins), and under 14% for glutamate and glutamine (Glx), were obtained with LCModel, showing the feasibility of obtaining a reliable neurochemical profile of the human hippocampus by ¹H-MRS in a small volume at 3 T. Individuals differed significantly in the reproducibility (Table 1) of these metabolite values, thus confirming the need to estimate intra-individual reproducibility from a large sample of subjects. In this study, mean coefficients of variation were 5%, 8%, 7%, 10% and 22% for tNAA, tCr, tCho, Ins and Glx respectively, demonstrating that highly reproducible concentrations can be obtained from spectroscopic acquisitions at 3 T in a small VOI encompassing the hippocampus. Our results can be used to assess the changes that can be confidently detected over time in a group of patients. They can also be used to determine the sample size needed to detect a predefined amount of change in a metabolite concentration. For example, detecting a 5% change in tNAA in the hippocampus with our protocol would require a minimum of 10 subjects whereas the same 5% change in Ins would require at least 34 subjects to be detected (cf. *Sensitivity* formula in [8]).

Table 1. Mean ± SD and range over the ten subjects of coefficients of variation (CV) for the five main metabolites reliably detected.

CV	tNAA	tCr	tCho	Ins	Glx
mean ± SD	5%±2%	8%±2%	7%±3%	10%±3%	22%± 9%
min.	3%	6%	4%	5%	11%
max.	9%	12%	13%	15%	40%

References : 1. T. Hammen *et al. NMR Biomed* 18: 195 (2005), 2. J. Geurts *et al. J Magn Reson Imag* 20: 366 (2004), 3. C. Choi *et al. Magn Reson Med* 41: 204 (1999), 4. T. Venkatraman *et al. NMR Biomed* 19: 484 (2006), 5. M. Garwood *et al. J Magn Reson* 153: 155 (2001), 6. I. Tkáč *et al. Magn Reson Med* 41: 649 (1999), 7. R. Gruetter *et al. Magn Reson Med* 43 : 319 (2000), 8. W. Brooks *et al. Magn Reson Med* 41: 193 (1999)

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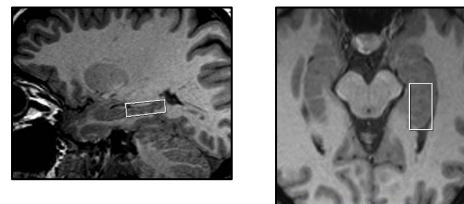


Fig. 1. Location and size of the voxel used in this study. VOI = 12 × 8 × 25 mm³

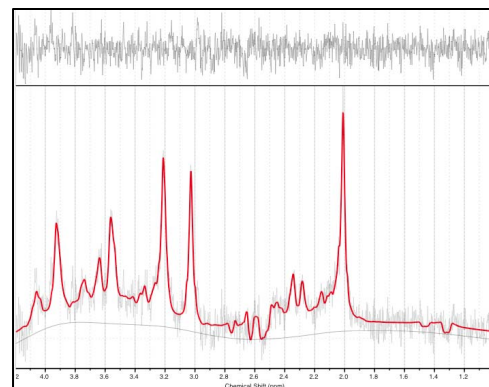


Fig. 2. Representative metabolite spectrum acquired using a LASER sequence (T_E = 65 ms, T_R = 3 s, N_{EX} = 256) from a 2.4-mL voxel in the left hippocampus and fitted with LCModel.