Towards pooling of neurochemical profiles obtained in the human brain at 3 T in a multi-site setting

Dinesh K Deelchand[1], Isaac M. Adanyeguh[2,3], Uzay E Emir[1,4], Tra-My Nguyen[2], Romain Valabregue[2,3], Pierre-Gilles Henry[1], Fanny Mochel[2,3], and Gülin Öz[1]

[1]Center for Magnetic Resonance Research, University of Minnesota, Minneapolis, MN, United States, [2]INSERM UMR S975, Brain and Spine Institute, Hospital La Salpêtrière, Paris, France, [3]University Pierre and Marie Curie, Paris, France, [4]FMRIB Centre, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, United Kingdom

Target audience: MR spectroscopists interested in metabolites beyond NAA, creatine and choline

Introduction: Proton MR spectroscopy (MRS) is a non-invasive tool that allows the measurement of a wide range of biochemical compounds in the brain in both health and disease. However, unlike structural MRI[1], it has not gained widespread acceptance as a routine clinical tool for diagnostic and prognostic purposes, partially due to the relatively large variation in metabolite concentrations or ratios reported from different sites using vendor-provided MRS sequences (PRESS and STEAM)[2-4]. Hence, there is a need to standardize robust MRS acquisition and analysis methods, as emphasized by a recent MRS Consensus effort[5]. The aim of this study was to examine the reproducibility of metabolite concentrations measured in two challenging brain regions using semi-LASER with identical experimental protocols and a widely available commercial 3 T platform at two different sites.

Methods: Two different cohorts of healthy volunteers matched for age- and BMI (N=24-33 per site) were studied on Siemens 3 T scanners located in Minneapolis (CMRR) and in Paris (ICM). The standard body coil was used for RF transmission and 32-channel head coil was used for signal reception. B_0 shimming was achieved with FAST(EST)MAP[6]. A modified semi-LASER sequence[7] (T_E = 28 ms, T_R = 5 s, 64 averages) was used to acquire spectra from the cerebellar vermis and pons. Spectra were processed in Matlab and quantified with LCModel[8] with water scaling option using simulated basis spectra in addition to experimentally measured macromolecule spectra. Metabolites that were quantified with Cramér-Rao lower bounds (CRLB) ≤ 50% from at least half of the spectra from a particular brain region were included in the neurochemical profile. In addition, if the correlation between two metabolites was high, their sum was reported. Metabolite concentrations were determined after correcting for T_2 relaxation times, tissue water content and CSF contributions (determined using the fully relaxed unsuppressed water signals acquired at different T_Es) in the selected VOI.

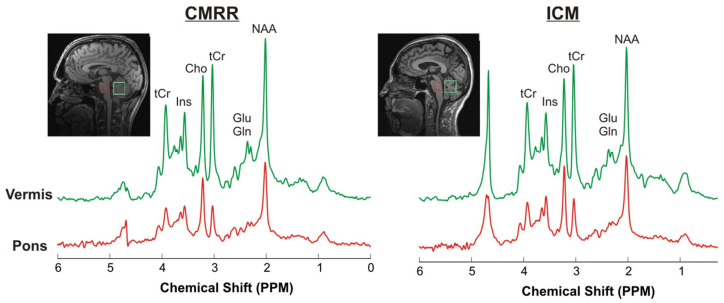

Fig. 1: Proton spectra (LB=1 Hz, GF=2.2Hz) obtained from the cerebellar vermis ($10 \times 25 \times 25$ mm^3) and pons ($16 \times 16 \times 16$ mm^3) in two different subjects at the two sites.

Results: Using semi-LASER with identical parameters and identical B_0 and B_1 calibration protocols, consistently high quality ^{1}H spectra with comparable peak SNR were obtained at both sites (Fig. 1). This in turn allowed to reliable quantification of 13 metabolites in the vermis and 10 in the pons compared to 3 to 5 metabolites in prior multi-site MRS trials using vendor-provided MRS sequences[9]. The neurochemical profiles were nearly identical at the two sites (Fig. 2), e.g., [tCr] in vermis was 11.1 ± 0.7 (SD) µmol/g (CMRR) and 10.8 ± 1.2 µmol/g (ICM), while [tCr] in pons was 5.4 ± 0.3 µmol/g (CMRR) and 5.5 ± 0.6 µmol/g (ICM). Similarly, no differences were observed in metabolite quantification precision (as determined by CRLB) between the sites (Fig. 2). Within each site, the between-subject coefficients of variance for singlet resonances and *myo*-inositol were substantially higher than their CRLBs, indicating precision to detect inter-individual differences in the healthy brain (data not shown).

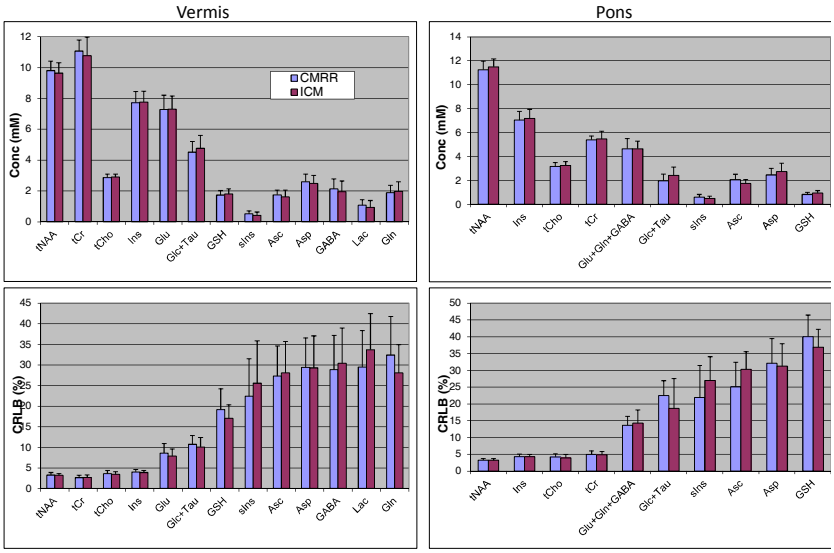

Fig. 2: Mean metabolite concentrations (in µmol/g) and CRLB (in %) measured in the cerebellar vermis (N = 24 at CMRR, N = 33 at ICM) and pons (N =16 at CMRR, N = 23 at ICM) at the two sites. Error bars represent inter-subject SD.

Conclusion: Highly reproducible neurochemical profiles can be obtained using widely available commercial 3 T hardware at different sites, provided that the same, optimized acquisition and analysis techniques are utilized at all sites. This will allow pooling of multi-site data in clinical studies, which is particularly critical for rare diseases.

References: 1. Hentschel et al. Int J Geriat Psychiatry 2005; 2. Komoroski et al. MRI 2004; 3. Jessen et al. Neurology 2009; 4. Keevil et al MRI 1998; 5. Oz et al. Radiology 2013 in press; 6. Gruetter & Tkac MRM 2000; 7. Oz & Tkac MRM 2011; 8. Provencher MRM 1993; 9. Vavasour et al . PISMRM 2010. *Supported by NIH grants R01 NS070815, P41 RR008079, P41 EB015894, P30 NS076408 and the Assistance Publique des Hôpitaux de Paris, ANR-10-IAIHU-06.*