

Reproducibility of metabolite measurements in patients with schizophrenia at 7T

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Target audience

Clinicians and scientists interested in studying metabolite and neurotransmitter concentrations in patients with schizophrenia using MRS.

Purpose

Knowledge of the reproducibility of metabolite measurements made using MRS in patients is essential for assessing the reliability of changes that may occur during the course of the disease and/or in response to treatment. Metabolites involved in the glutamatergic and GABAergic systems that are believed to play a role in pathophysiology of schizophrenia (SZ) may be more accurately determined at 7T than at lower field strengths. The purpose of this study was to assess the reproducibility of metabolite measurements made using the semi-LASER (sLASER) and STEAM pulse sequences in four different brain regions at 7 Tesla in patients with SZ.

Methods

After obtaining written consent under local IRB approval, 10 patients with stable, chronic SZ (7 males, 3 females, mean age: 39.2(12.4) years) were scanned twice, within a week, using a 7T scanner (Philips 'Achieva', Best, Netherlands) equipped with a 32-channel head coil (Nova Medical, Orlando, FL, nominal maximum $B_1 = 15 \mu T$). Spectra were acquired using a STEAM sequence (TR/TE/TM=3000/14/33 ms), and sLASER sequence (TE/TR: 29/3000 ms). VAPOR water suppressed spectra (64 averages) as well as unsuppressed spectra (16 averages) were collected from each of the following regions: anterior cingulate cortex (ACC; 30x20x20 mm³), left centrum semiovale (CSO; 40x20x15 mm³), left dorsolateral prefrontal cortex (DLPFC; 25x20x20 mm³), and bilateral thalamus (Thal, 20x30x15 mm³). Signal-to-noise ratio and linewidth were measured using in-house software. Spectra were analyzed using the LCModel⁴ using water as an internal reference. Basis set for LCModel was simulated in VESPA⁵. Metabolite concentrations are reported in institutional units (i.u). Reproducibility was assessed via coefficients of variation (CV).

Results

Figure 1 shows typical spectra from the ACC using STEAM and sLASER sequences. Results show higher SNR (NAA) of the sLASER sequence (avg SNR 60.7±19.3) than STEAM sequence (avg SNR 38.2±12.0) as expected, with similar linewidths. Figures 2 and 3 show average Cramer-Rao Lower Bounds (CRLB) and average CV, from 4 brain regions, of the metabolite concentrations measured during visits 1 and 2 for both pulse sequences. Figure 2 shows metabolite measurements made with higher precision with sLASER than with STEAM for most metabolites except GABA, GPC and GSH. However, of the metabolites shown in Figure 3, most metabolites except Cr, Gln and mI, show higher reproducibility with STEAM sequence as reflected by the CV. NAAG was measured with CRLB<10% and CV<10% in the CSO and with lower measurement precision and reproducibility in the cortical gray matter regions.

Discussion

Interestingly, the STEAM sequence shows higher reproducibility for metabolites that are of particular interest in SZ, for instance GABA, Glu, Gln, GSH, NAAG and Glx compared to measurements made with sLASER. This is inspite of the higher SNR and generally lower CRLB of the spectra acquired with sLASER sequence. The reasons for this are still being investigated. The 7T STEAM protocol allowed reproducible measurement of most metabolites with CRLB <10% for metabolites with high concentrations as well as CRLB<20% for metabolites with lower concentrations such as GABA, Gln and GSH.

References: 1. Lisman, et al. Trends Neurosci2008; 2. Coyle et al. Ann NY Acad Sci 2003; 3. Wassef et al. J clin Psychopharmacol2003; 4. Provencher, S.W; *MRM*. 1993; 30:672-679, 5.Sohar Vespa-Simulation Web Site.

<http://scion.duhs.duke.edu/vespa/simulation>

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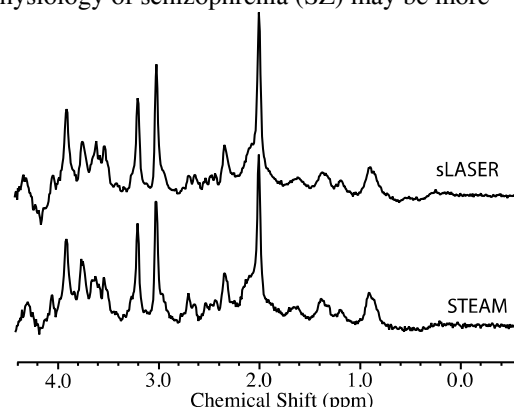


Figure 1. ACC spectra sLASER (TE=32 ms) and STEAM (TE/TM=14/33).

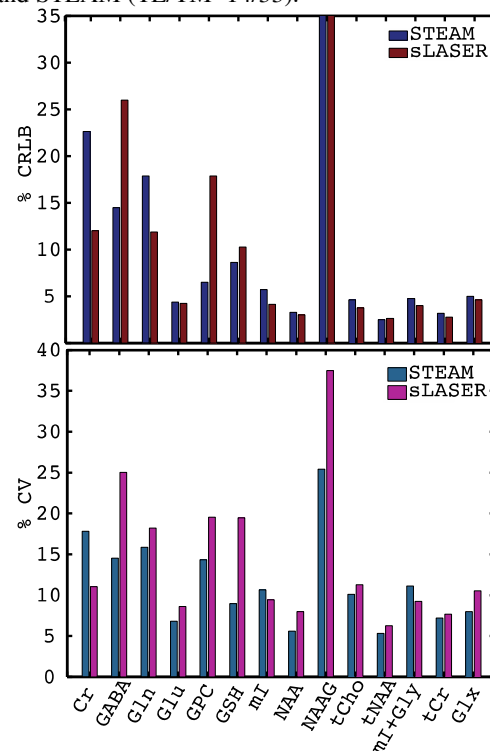


Figure 2(top) and 3(bottom). Average CRLB and CV of metabolite measurements made using STEAM and sLASER sequence from 4 regions