Quantitation of vitamin C in short-echo STEAM spectra in vivo: Validation against edited spectroscopy in rat brain.

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Introduction

Non-invasive detection of vitamin C (ascorbate, Asc) in vivo using ^{1}H edited NMR spectroscopy was recently reported in human brain at 4T (1). The goal of this study was to determine if Asc concentration can be reliably quantified from ultra-short echo-time STEAM spectra using spectral deconvolution in spite of strong overlap with resonances of Glu and Gln. Therefore, in vivo STEAM and edited spectra were measured concurrently in rat in rat brain, where direct biochemical validation is possible.

Methods

All experiments were performed on a Varian INOVA/Magnex 9.4T spectrometer. The location of the volume of interest (VOI, 4 x 2 x 4 mm^3) was based on RARE images (Fig. 1). Shimming was performed using FASTMAP. Two spectroscopic techniques were used, ultra-short echo-time STEAM (2) and spectral editing (1). ^{1}H homonuclear difference editing for the C6H_2 protons of Asc (3.73 ppm) consisted of PRESS localization (TE = 160 ms) with frequency selective editing pulses applied alternately at 4.01 ppm (C5H Asc) during both echo periods (1). Since editing is highly selective at 9.4 T, myo-inositol was the only metabolite expected to co edit (Fig. 1, phantom, 20 mM Asc, 20 mM Ins, and 7 mM NAA). Quantification of Asc from edited spectra was based on relative intensities of edited Asc versus NAA in the sub spectrum and on corresponding phantom calibration. For metabolite quantification from STEAM spectra LCModel with Asc in the basis set was used. Spontaneously breathing rats were anesthetized by a gas mixture (O_2:N_2O = 1:1, 1.5% isoflurane).

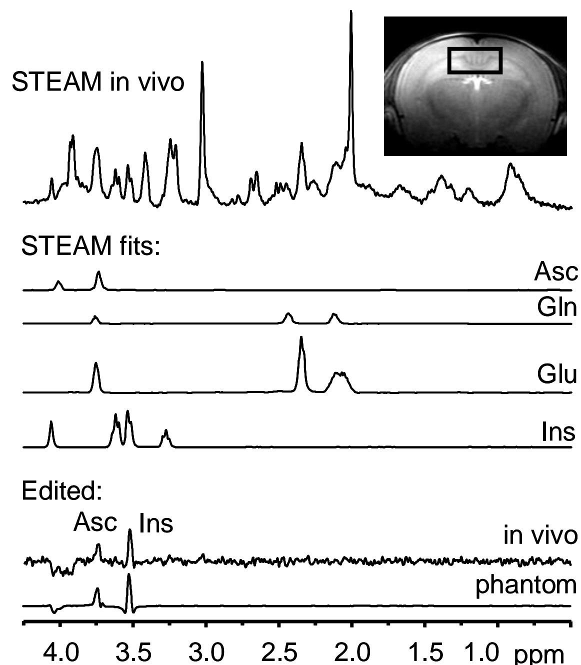

Fig. 1 In vivo STEAM spectrum (TR = 5 s, TE = 2 ms, NEX = 160) with LCModel fit of select metabolites, edited spectra (TR = 5 s, TE = 150 ms, NEX = 512), and image illustrating the VOI.

Results and Conclusion

Both STEAM and edited spectra were measured from the same VOI in 12 rats of variant age. The STEAM spectrum with selected metabolite spectra (LCModel fitting) along with an edited spectrum from the same VOI is illustrated in Fig 1, along with an edited spectrum from the phantom. Ascorbate concentrations measured using these two spectroscopic techniques were in excellent agreement. All data points were in close proximity to the unity line (fig. 2), which fit within the 95% confidence interval (R = 0.9). The Asc concentrations also agreed well with the results of biochemical assays (3). Ascorbate was quantified from STEAM spectra with low values of Cramer-Rao lower bounds (4% – 11%), which predict achievable precision between ± 0.1 and ± 0.2 μmol/g. The results of this study validate addition of Asc to the expanding list of neurochemicals that can be quantified simultaneously using ultra-short echo-time STEAM spectra, given high spectral quality and correct fitting.

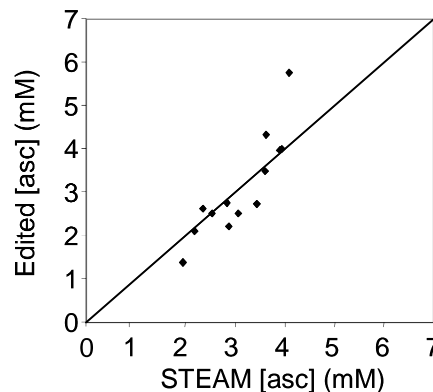

Fig. 2 Correlation between Asc concentrations quantified from edited spectra versus STEAM spectra in 12 rats (age 8 – 43 days).

References and Acknowledgments 1) Terpstra et al, Magn Reson Med, 51: 225, 2004. 2) Tkac et al, Magn Reson Med, 50: 24, 2003. 3) Rice ME, Trends Neurosci, 23: 209, 2000.
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