Vitamin C concentration measured in the human brain in vivo using LCModel analysis of fully resolved 1H edited spectroscopy at 7 Tesla

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Introduction

Noninvasive detection of Vitamin C (ascorbate, Asc) in the human brain was recently demonstrated at 4 T using in vivo edited ^{1}H MRS (1). Editing efficiency was compromised therein in order to ensure exclusive detection of Asc. Due to increased frequency separation at higher magnetic field (B_0) the Asc resonance can be completely resolved and edited with full efficiency, which along with increasing sensitivity should lead to increased signal to noise per volume of interest and scan time. At 7 T, Asc can be detected without contributions from glycero-phosphocholine (GPC), which contributed a small resonance that was not fully resolved from Asc at 4 T. The goals of this study were to quantify Asc concentration in the human brain in vivo using LCModel analysis of edited spectra measured at 7 T from a smaller region of interest than previously reported, and to determine whether Asc measured at 4 T was quantified accurately despite contributions from GPC. Since Asc is one of the two most concentrated non-enzymatic antioxidants in the CNS, in vivo detection could be used to study how Asc is involved in protecting the brain from oxidative stress.

Methods

MEGA-PRESS editing (2) was optimized for detection of the 3.73 ppm resonance of Asc via J-coupling to the resonance at 4.01 ppm. The optimal TE (112 ms) determined previously (1) accommodated placement of an editing pulse (40-ms Gaussian inversion) at 4.01 ppm on every other scan without concern over partial excitation of overlapping resonances or coediting of GPC. Subtraction of spectra measured with the editing pulse "on" from those measured when the editing pulse was "off"-resonance resulted in the edited spectrum. Quantitation was calibrated in vitro and based on the Asc signal strength measured using LCModel versus the area under the 3.03 ppm Cr resonance in the sub-spectrum. An in vivo Cr concentration of 8.5 µmol/g was used as an internal reference. 8 normal volunteers (3 male, mean age 28 years) were scanned according to procedures approved by the institutional review board using a 7 T/ 90 cm magnet (Magnex), a Varian spectrometer, and a surface quadrature transceiver (3). Volumes of interest (8 cm^3) centered on the midsagittal plane in the occipital lobe were selected using multislice TURBOFLASH images. Shims were optimized using FASTMAP (4).

Results

A representative edited spectrum is illustrated in fig. 1. The small number of resonances coedited with Asc was limited to those anticipated, all of which were fully resolved from Asc. The fit residual indicates that LCModel successfully modeled the in vivo spectrum as a linear combination the basis spectra. The measured Asc concentration was 1.3 ± 0.2 µmol/g (mean ± SD, n=8) with an average CRLB of 7 % (range 5 – 9 %). Macromolecule resonances were not detected in an inversion recovery experiment at 7 T (not shown).

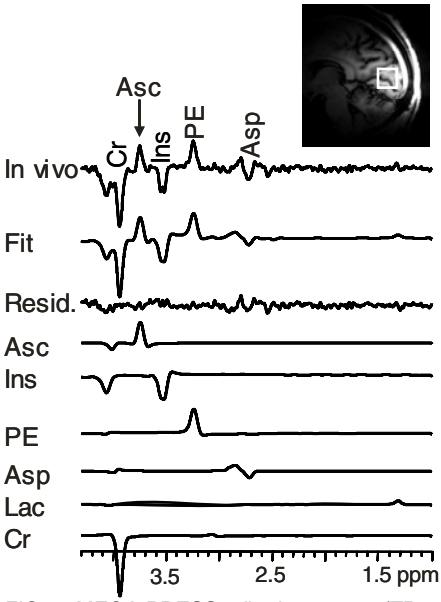

FIG. 1. MEGA-PRESS edited spectrum (TR = 5 s, NEX = 512) from the VOI outlined and LCModel analysis. The following coedited with Asc: myo-inositol (Ins), phosphoryl ethanolamine (PE), aspartate (Asp), lactate (Lac), and creatine (Cr).

Conclusions and Discussion

Asc concentration was measured at 7 T in the 8 cm^3 VOI with a smaller measurement error (CRLB = 7%) than previously reported (5) at 4 T in a 27 cm^3 VOI (9 %) in the same brain region. Increased editing specificity at higher field resulted in fewer coedited resonances. In particular, glycerolphosphorylcholine (GPC), which coedited with Asc at 4 T due to a coupling partner at 4.31 ppm, in the bandwidth of the editing pulse then placed at 4.13 ppm, no longer coedited at 7 T. The Asc concentration measured in the human occipital lobe in vivo at 7 T was the same as that measured at 4 T, 1.3 ± 0.3 µmol/g (mean ± SD, n=4) where a small GPC resonance partially overlapped the edited Asc resonance, but was separated using LCModel (5). Therefore, this study indicates that the Asc resonance edited at 4 T was quantified accurately despite contributions from GPC. The small discrepancies in LCModel analysis of the 7 T edited spectrum near Asp were likely due to slight miss-phasing of the Asp basis spectrum and unlikely to influence Asc quantitation.

Table 1 Summary of volumes of interest (VOI), mean Asc concentrations (µmol/g), mean CRLB, and signal to noise measured at 4 (TR = 4.5 s, NEX = 512) versus 7 Tesla.

B_0	VOI	[Asc]	SD	n	CRLB	S/N
4 T	27 cm^3	1.3	0.3	4	9 %	12
7 T	8 cm^3	1.3	0.2	8	7 %	10

References and Acknowledgments

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NIH R01NS038672 and P41RR008079
MIND institute, Whitaker and KECK foundations