Noninvasive Quantification of Human Brain Antioxidant Concentrations via Double Edited ^{1}H MRS Throughout Intravenous Delivery of Vitamin C

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Introduction

Antioxidant defenses are involved in protecting against dementia and neurodegenerative disease. Vitamin C (ascorbate) and glutathione (GSH) are the two most concentrated chemical antioxidants in the human central nervous system [1]. While human brain region specific ascorbate concentration ([Asc]) changes have been measured post mortem as a function of age [2], studies in young rats suggest that brain Asc homeostasis is maintained [3] by transporters in the choroid plexus. A recent study used short TE STEAM at 3 T to report an increase in brain [Asc] induced by IV administration of Asc [4]. The goal of this project was to investigate temporal changes in brain Asc and GSH levels after IV administration of Asc using short TE STEAM and double editing with (DEW) MEGA-PRESS at 4 T.

Methods

Asc and GSH were resolved from overlapping resonances via DEW MEGA-PRESS in the human occipital lobe (27 cm^3 VOI) using a half-volume quadrature RF coil [5]. Concentrations were quantified using LCModel fitting and NAA (10 mM) as an internal reference [5]. To compare adequacy for resolution of Asc without editing [4], the neurochemical profile was also measured via LCModel analysis of ultra-short echo-time STEAM spectra [6]. Edited and STEAM spectra were measured from 10 subjects before, 1, 5, 10 and 24 hours after IV bolus delivery of 3 g vitamin C. Two control studies without Asc administration were completed.

Results

Serum [Asc] were on average 1 mg/dL, 11 mg/dL, 3 mg/dL, 2 mg/dL, and 1 mg/dL before and 1 h, 5 h, 10 h and 24 h after IV bolus. STEAM and DEW MEGA-PRESS spectra with the contribution of individual metabolites fit via LCModel analysis are shown in Fig. 1. [Asc] measured in the occipital lobe of 10 subjects before and after IV bolus of vitamin C are illustrated in Fig. 2. Measured concentrations are not consistent with a brain antioxidant response of altered [Asc] ≥ 8 % (95 % CI) at any time point ($p > 0.95$). However, in at least one subject (open red diamond, fig 2), [Asc] may have increased at the 10 hour time point. [GSH] was quantified with an average error (CRLB) of 7 % with editing and 9% with STEAM. No change in GSH concentration was measured with either method. Quantification of [Asc] using short TE STEAM was less precise (CRLB > 30%) than using DEW MEGA-PRESS (CRLB < 7%).

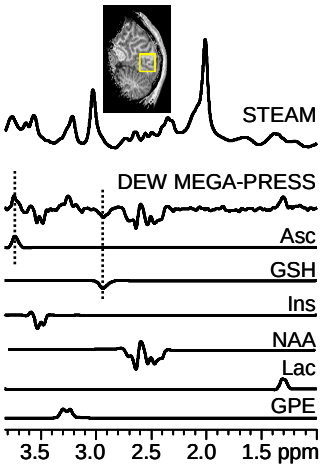

FIG 1. STEAM (NEX = 64, TE = 4 ms, TR = 4.5 s), and DEW MEGA-PRESS spectra (NEX = 576, TE ranging from 105 to 155 ms, TR = 4.5 s). Inset: VOI location in occipital lobe.

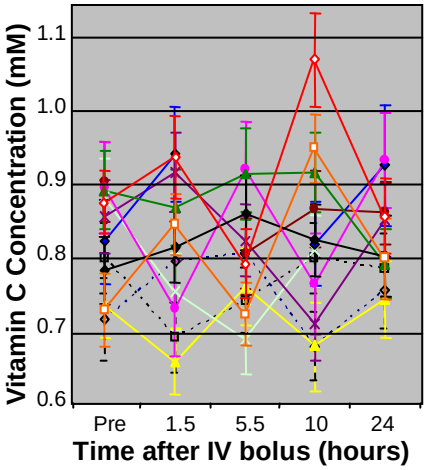

FIG 2. Asc concentrations before and after IV bolus of 3 g vitamin C in 10 humans (solid) and corresponding findings from 2 control studies (dashed). Error bars illustrate CRLB.

Conclusions and Discussion

Precision of Asc quantification in the human brain at 4 T was substantially higher using DEW MEGA-PRESS than short TE STEAM. With the increased selectivity achieved via spectral editing, changes in brain Asc levels on the order of 20% as reported previously [4] were not observed. Inter-individual variance in how brain [Asc] responds to vitamin C supplementation is consistent with hypotheses on individualized responses to antioxidant treatments [7]. High sensitivity of DEW MEGA-PRESS for the detection of Asc and GSH in the human brain at 4 T opens new possibilities for non-invasive monitoring antioxidant defenses against neurodegeneration.

References and Acknowledgments

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