

Concentration Changes of Vitamin C and GSH in the Human Brain as function of age

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Background

Vitamin C (Asc) and glutathione (GSH) are the most concentrated chemical antioxidants in the central nervous system. These antioxidant concentrations may reflect the pathogenesis of progressive neurodegenerative disorders, such as Alzheimer's and Parkinson's disease, as well as cognitive decline. Post-mortem and animal data indicate a 10 % [Asc] decrease per decade of age (1, 2). Double editing with (DEW) MEGA PRESS at high field has enabled noninvasive detection of these compounds in the human brain (3). Given the measurement error of DEW MEGA PRESS, a 25 % decrease in [Asc] may be measurable in young versus older subjects. This abstract presents preliminary findings on [Asc] and [GSH] as a function of age.

Methods

Six individuals were recruited for this study. The subjects were dichotomized into a younger group of 3 subjects (age 18 to 22 years) and an older group of 3 subjects (age 70+ years). Asc and GSH resonances were detected via DEW MEGA-PRESS (3) edited 1H MR spectroscopy at 4 T (TR 4.5 s and NEX =512) with a half volume quadrature rf coil. Echo time (TE) was optimized to minimize contamination from coedited PC, GPC, Ins and NAA. Optimal TE was based on density matrix simulations. Edited and coedited resonances were apodized to mimic *in vivo* linewidths and compared at physiologic concentrations. Signal strengths were quantified in each subject from the edited spectra via LCModel (3).

Result

Fig 1 illustrates that at 4T, PC, GPC, Ins and NAA contamination on Asc and GSH varies with TE, with minimal contamination occurring at 122 ms. Simulations accuracy was verified via solution spectra. Fig 2 and 3 show selected VOI in the visual cortex and detected Asc and GSH from a young and older subject. Average concentrations across the subjects for each group are summarized in Table 1. [Asc] in the older group is higher than in the younger group ($p<0.05$). The smaller [GSH] in the older group is not statistically significant ($p>0.05$).

Discussion

Asc concentrations measured in these six subjects are not consistent with the previously reported 25 % decrease in [Asc] [1]. However, several factors may introduce bias. First, NAA concentration may decrease with age [4]. Quantification utilized a constant [NAA] in this study. Correcting for the highest reported NAA decrease with age leads to a non-significant [Asc] increase ($p>0.05$). Second, LCModel fitting may introduce bias on measured [Asc]. Consistent apparent broadening of edited Asc resonance in elder subjects obstructs the baseline near 3.8 ppm such that the spline baseline fit by LCModel may be systematically biased. Confidence in findings may increase with increasing sample size and optimization of quantification methodology.

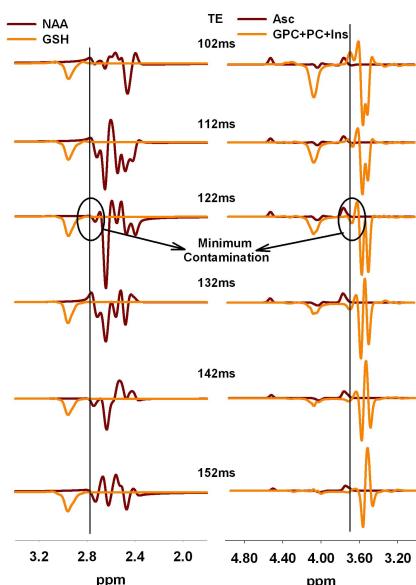


FIG 1. Simulation of contamination by PC, GPC, Ins and NAA on Asc and GSH.

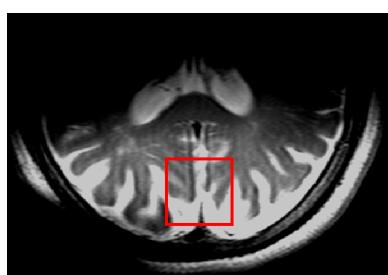


FIG 2. VOI of 27 mL overlayed on the transverse image.

Table 1. Average (n=3) antioxidant concentrations (mM) relative to 10mM NAA.

	young	old	p value
Asc	0.72±0.06	0.97±0.12	0.03
GSH	0.53±0.04	0.41±0.1	0.1

Supported by NIH: NIA R21AG029582, P30 NS057091, BTRR P41RR008079, and NCRR M01-RR00400.

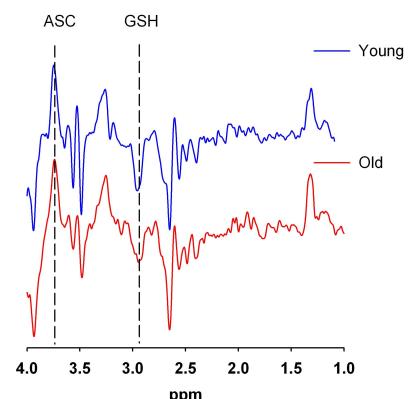


FIG 3. DEW MEGA-PRESS edited spectra at 4 T. VOI = 27mL, NEX =512, TE=122ms.

References

- 1) Schaus, Amer J Clin Nutr 5:39-41, 1957.
- 2) Hughes et al. Nutr Res 15: 755-766, 1971
- 3) Terpstra et al. Magn Reson Med 56:1192-2006.
- 4) Maudsley et al. ISMRM, 2009.