

Simultaneous Quantitation of T_2 and Concentration of vitamin C and GSH in the Human Brain In Vivo Using Multiple Echo Time Double Editing With MEGA-PRESS at 4 and 7 T

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Introduction

Noninvasive methodology for quantifying antioxidant concentrations in human tissue would be useful to study diseases that are known to involve oxidative stress. Vitamin C (ascorbate) and glutathione (GSH), the two most concentrated chemical antioxidants in the CNS can be detected using double editing with (DEW) MEGA-PRESS (1). For quantitation from spectra at the long TE characteristic of edited spectroscopy, influence of T_2 on resonance intensity is typically assumed constant across study populations. However, the following method for simultaneously measuring antioxidant concentrations and T_2 was developed to increase the certainty with which differences in antioxidant signals can be attributed to changes in concentration.

Methods

Although editing efficiency is optimal at one TE due to J-coupling, appreciable signal can be detected at sub-optimal TE. DEW MEGA-PRESS spectra (1) were measured at 4 (TR = 4.5 s) and 7 (TR = 5 s) Tesla from solutions of ascorbate (Asc) and GSH. Appreciable resonances were observed at several TE at both field strengths. DEW MEGA-PRESS spectra identified as such were measured in the human occipital cortex (4 and 7 T) using a surface coil. At 4 T, spectra were measured at several TE (NEX = 96 per TE) in 22 subjects. At each TE, spectra were summed over all subjects. To account for resonance intensity changes arising from J-modulation, Asc and GSH resonances were normalized to spectra simulated using density matrix formalism and apodized to mimic in vivo line widths. T_2 were calculated from normalized areas under the edited Asc and GSH resonances according to $A = A_0 e^{-TE/T_2}$. To study the impact of co-edited resonances from PC, GPC, Ins and NAA on integrated peak areas, contributions from these compounds were simulated.

Results

Fig. 1 illustrates that at 4 T, appreciable Asc and GSH resonances can be detected at several TE in the human brain. Simulated and measured solution spectra matched. Fig. 2 plots the normalized areas under the Asc and GSH resonances in the spectrum summed over 22 subjects at 4 T and T_2 fits. Table 1 reports corresponding T_2 . Confidence in the short GSH T_2 is substantiated by the small GSH resonance at 152 ms TE in vivo (fig. 1). Confidence in the T_2 measured for Asc was low, as expected given the poor fit (fig. 2). Simulated spectra evidenced contamination of the Asc resonance by co-edited PC, GPC, and Ins at physiologic concentrations, putatively compromising the T_2 measurement. Fig. 3 illustrates that at 7 T, appreciable Asc and GSH resonances can be detected at several TE in solution and in the human brain.

Discussion

To our knowledge, this is the first time the T_2 of GSH has been reported and edited GSH detected at > 4 T. The GSH T_2 was measured with practicable certainty in the human brain at 4 T. Detrimental influence of co-edited resonances on the Asc resonances measured at 4 T motivated attempts to fit via LCModel. Unfortunately, absence of macromolecule basis spectra and inconsistency in the spline baseline were problematic. Plausibility for measurement of Asc T_2 at 7 T is likely due to: minimal co-editing via increased spectral dispersion, shorter TE via shorter editing pulses and sensitivity gains.

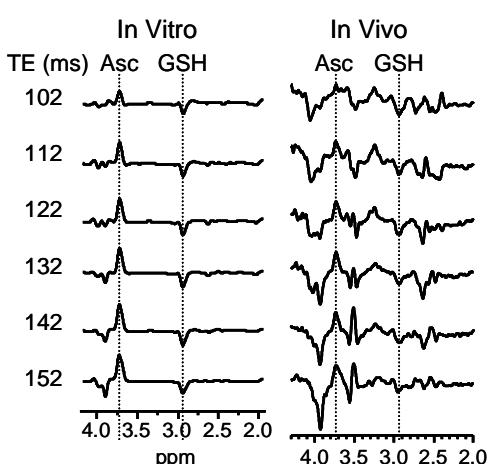


FIG. 1 DEW MEGA-PRESS edited spectra measured at 4 T. VOI = 27 mL.

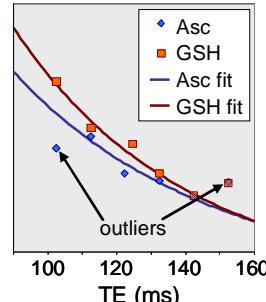


FIG. 2 Areas under resonances and T_2 fits.

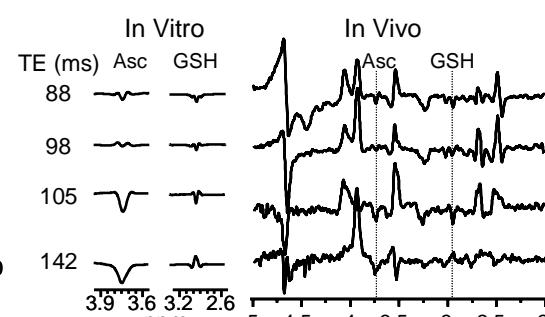


FIG. 3 DEW MEGA-PRESS edited spectra at 7 T. VOI = 8 mL, NEX = 256.

Table 1. T_2 (ms) and confidence intervals

T_2	low 95% CI	high 95% CI
Asc	57	32
GSH	50	41

Ref. 1) Terpstra et al. *Magn Reson Med* 56:1192 2006.

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