Simultaneous Detection of Antioxidant Concentrations and Their T_2 Using Double Edited ^{1}H MRS

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Background

Oxidative stress is involved in the etiologies of cognitive decline and neurodegenerative disease (1). Since vitamin C (Asc) and glutathione (GSH) are the most concentrated chemical antioxidants in the human central nervous system (2), the recently demonstrated simultaneous quantitation of these compounds in the human brain in vivo via edited ^{1}H MRS (3) may represent a clinically relevant antioxidant profile. Because transverse relaxation rates (T_2) might differ between patients and controls via mechanisms such as iron accumulation, and therefore affect quantification of concentration, **the goal of this study** was to measure T_2 along with antioxidant concentrations in the human occipital cortex in vivo.

Methods

Asc and GSH resonances were detected at multiple echo times using DEW MEGA-PRESS edited ^{1}H MR spectroscopy at 4 T (3). T_2 were calculated by solving $SI=SI_0e^{-TE/T_2}$. Ideally, spectra would be measured over a broad range of TE. However, the minimum TE is limited by the long, selective pulses required for editing and the maximum TE is limited by signal loss to T_2 relaxation. Feasibility of measuring T_2 with clinically relevant measurement error at TE 102, 112, 122, 132, 142, and 152 ms was evaluated via Monte Carlo analysis. A 190 ms anticipated T_2 in vivo for Asc and GSH at 4 T was extrapolated from T_2 of similar compounds reported in the literature (4,5). Based on previously reported edited spectra measured at 4 T (3), summing over a reasonable sample size (22 human subjects) would result in a SNR of 10 for Asc. Signal strengths (SI) were measured via LCModel with simulated basis spectra (density matrix formalism), which accounted for J-modulation, so decrease in signal strength over time directly reflected T_2 relaxation. Asc and GSH concentrations were quantified in each subject from the sum of spectra measured at all TE to maximize sensitivity.

Results

Simulated spectra matched measured spectra for all metabolites in the basis set at all TE, as illustrated for Asc and GSH in fig. 1. Figs. 2 and 3 illustrate that the Asc and GSH resonances detected in vivo via summing spectra measured at all TE had similar intensity as those measured at 112 ms as originally optimized (3). The 162 and 77 ms T_2 calculated for Asc and GSH respectively in one subject using the signal intensities (SI) listed on fig. 3 were reasonable, although uncertainty was high. This uncertainty would be improved by averaging data from several subjects in practice. Monte-Carlo simulations predicted that the largest group-wise (n = 22) measurement error (bias + SD) in T_2 was 74 ms greater than the anticipated 190 ms, which would lead to a quantification error of only 18%.

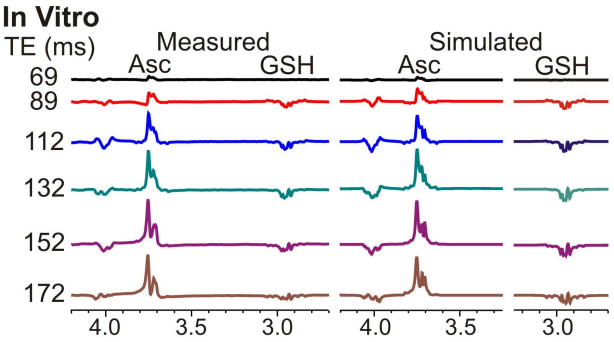

FIG 1. Asc and GSH resonances measured in vitro (37 C, pH 7.1) and simulated.

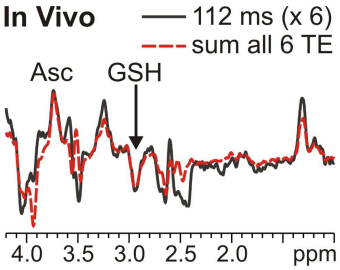

FIG 2. Human occipital cortex spectra measured with surface coil at 112 ms TE (27 mL VOI, NEX=294, TR = 4.5 s), and summed over all TE.

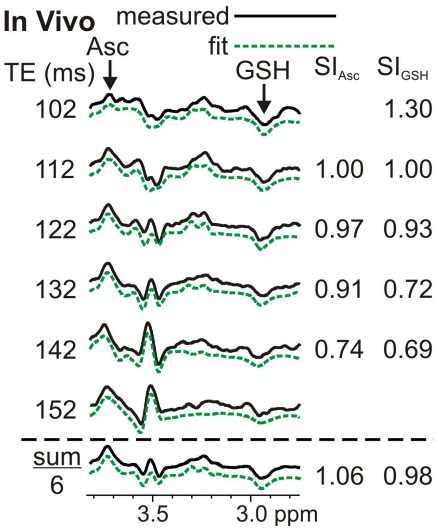

FIG 3. In vivo spectra measured at each TE as in fig. 2, sum over all TE (bottom), and results of LCModel fitting (fit) including measured signal intensity (SI).

Conclusions and Discussion

We conclude that T_2 can be estimated simultaneous with Asc and GSH concentrations in the human brain in vivo via DEW MEGA-PRESS spectra measured at multiple echo times. This protocol retains the same signal to noise as originally proposed for noninvasive detection of the antioxidant profile (3). Monte-Carlo analysis predicts that influence of T_2 on concentration can be measured within 18 % error via data pooled from a study-relevant sample size. As such, this methodology can be applied to test the hypothesis that variance in T_2 has negligible impact on concentration differences measured in patients versus controls.

References and Acknowledgments
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