Sensitivity and specificity to quantify changes in human brain glutathione and ascorbate concentrations using short echo-time ^{1}H MRS at 3 T and 7 T

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Target audience: Researchers who use ^{1}H NMR spectroscopy beyond NAA, creatine, choline and *myo*-inositol

Purpose: Glutathione (GSH) and ascorbate (Asc) are two important antioxidants that are concentrated in the human brain at ~1 µmol/g[1]. Their resonances are difficult to quantify due to low signal-to-noise and spectral overlap. The purpose of this study was to determine the accuracy and precision with which well-controlled changes in GSH and Asc signals can be detected in short echo time (T_E) human brain spectra acquired at 3 T and 7 T. Our ***hypothesis*** was that changes would be more readily picked up at higher field.

Methods: Five healthy subjects were examined at both 3 T and 7 T. Ultra-short T_E ^{1}H spectra were measured from an 8 ml VOI located in the posterior cingulate cortex using STEAM[2] (T_R= 4 s, T_E = 8 ms, 64 averages). A freshly made GSH phantom (10 mM) was measured analogously under physiological conditions. This phantom spectrum was accordingly line broadened and injected into the in vivo spectrum for each subject at a level of -100% to 100% of the GSH signal present in the baseline spectrum. All resulting spectra were analyzed with LCModel[3] using simulated basis spectra and a measured macromolecule spectrum. Analogous experiments were carried out for Asc. The two-tailed, unpaired student's t-test was used to compare concentrations measured from altered spectra relative to baseline.

Results: Figure 1 shows in vivo spectra after addition and subtraction of GSH signal. Change was more apparent at 3 T than 7 T. An increase in GSH concentration of ~35% and above (P < 0.05) could be detected at both 3 T and 7 T although the precision (i.e., CRLB) to measure GSH is better at 7 T. The accurate detection of a reduction in GSH signal was possible up to -30% at both 3 T and 7 T (P < 0.05 at 3 T, Figure 2A). Similarly, the change in Asc signal was detected at ~30% and beyond (P < 0.05) at 7 T (Figure 2B). A small increase of 11% was observed in GSH when Asc was increased to 100% at 7 T. Asc could not be reliably quantified at 3 T; it was either under- or over- estimated based on the % of Asc signal injected (Figure 2B).

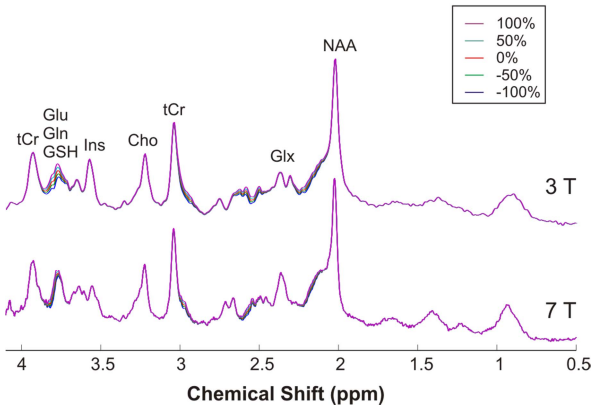

Figure 1: Example of in vivo spectra from the same subject at 3 T (top) and 7 T (bottom) after injecting different levels of phantom measured GSH signal.

Discussion: Attempting to quantify changes in antioxidants from short T_E spectra is innovative. Quantitation of weakly represented neurochemical concentrations from short T_E spectra without editing is attractive because several compounds can be detected at once and confounding by transverse relaxation is avoided. This study is unique because few others have assessed the accuracy and precision of such quantification. Large changes in Asc signal (although unlikely due to strong homeostatic mechanisms in the human brain[4]) would result in counter-fit changes in GSH signal at 7 T (Figure 2B). Paradoxically, large changes in Asc signal have negligible influence on GSH signal at 3 T, likely due to failure to resolve Asc at 3 T.

Conclusions: This study advanced knowledge on the accuracy with which weakly represented neurochemical resonances can be quantified from short T_E human brain spectra. It shows that an increase in GSH signal can be accurately measured at 3 T and 7 T, although a quantitative decrease in signal is difficult to detect below 30%, especially at 3 T. In addition, a B_0 field above 3 T is necessary to accurately quantify Asc signal using short T_E sequences. As such, we have increased our capability to choose the optimal pulse sequence and field strength to study hypotheses involving weakly represented neurochemicals.

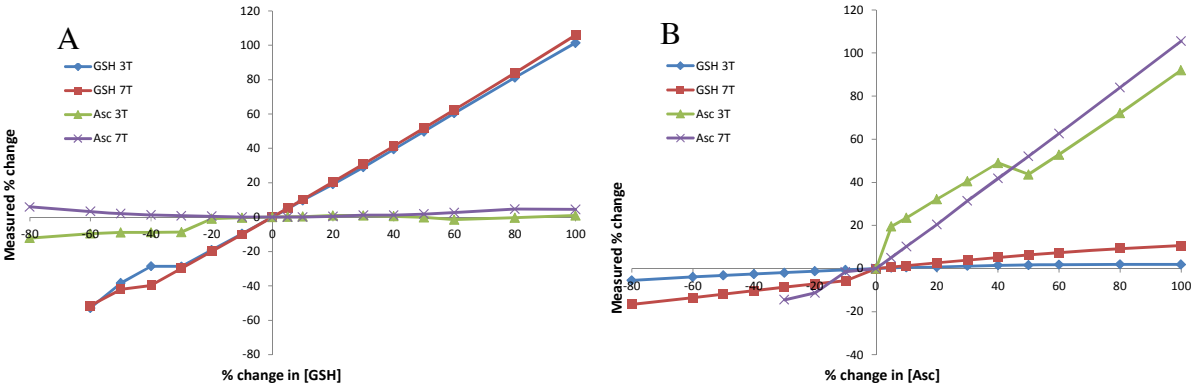

Figure 2: Mean change (5 participants) in [GSH] and [Asc] at 3 T and 7 T when phantom (A) GSH and (B) Asc signals were injected into in vivo spectra.

References: 1.Terpstra et al MRM 2006; 2. Emir et al NMR Biomed 2011; 3. Provencher MRM 1993; 4. Spector J Neurochem 2009.

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