Double Edited NMR Spectroscoy for Detection of an Antioxidant Profile in the Human Brain In Vivo

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Introduction

Edited spectroscopy is useful for separating overlapping resonances (1). Although co-edited resonances are often retained, the edited experiment is typically designed for resolution of a single target resonance. The goal of this study was to deliberately add a second target resonance, i.e. reduced glutathione (GSH) to ^{1}H spectra originally edited for vitamin C (ascorbate, Asc) (2). Double editing, a versatile new technique was designed to measure the two most concentrated non-enzymatic antioxidants in the human brain in the same amount of time previously required to measure one, resulting in an antioxidant profile that could be used to assess oxidative stress non-invasively.

Methods

*D*ouble *E*diting *W*ith (DEW) MEGA-PRESS was accomplished by refocusing modulation of the Asc resonance at 3.73 ppm via a 40 ms Gaussian editing pulse applied near the offset (4.13 ppm) of a coupling partner for Asc on every other scan, as previously described (2) except the reference scans previously acquired in absence of the editing pulse were replaced by scans in which modulation of the GSH resonance at 2.95 ppm was refocused via application of an editing pulse applied at 4.56 ppm (the offset of a coupling partner for GSH). The double edited spectrum was the result of subtracting the Asc refocused spectrum from the GSH refocused spectrum. Pure reference spectra (editing pulse off) were also measured for validation purposes. All experiments used a 4T/ 90 cm magnet (Oxford), a Varian spectrometer, and a surface quadrature transceiver (3). Four normal volunteers (1 male, mean age 23 years) were scanned according to procedures approved by the Institutional Review Board. Volumes of interest (27 cm^3) centered on the midsagittal plane in the occipital lobe were selected using multislice RARE images. Shims were optimized using FASTMAP (4).

Results

Double edited (TE = 112 ms, TR = 4.5 s, NEX = 512) spectra measured in vivo and in vitro (35.5 mM Asc, 13.5 mM GSH, 35.5 mM NAA) are shown in Fig. 1 along with corresponding single edited and subspectra. The Asc and GSH double edited spectrum measured in a human brain in vivo contains a resonance from GSH (2.95 ppm) in addition to all resonances expected from Asc editing as previously described (2) and as illustrated in the single edited Asc spectrum in vivo. The single edited in vivo GSH spectrum does not retain co-edited resonances with offsets in the vicinity of the edited Asc resonance, nor does the single edited in vivo Asc spectrum exhibit co-edited resonances with offsets in the vicinity of the edited GSH resonance, ensuring resolved detection of both antioxidants in vivo. The double-edited spectra are clearly equivalent to the sum of the respective single-edited spectra. The remarkable repeatability of resonances detected using DEW-PRESS in vivo (fig. 2) further supports the assignment of GSH and Asc resonances.

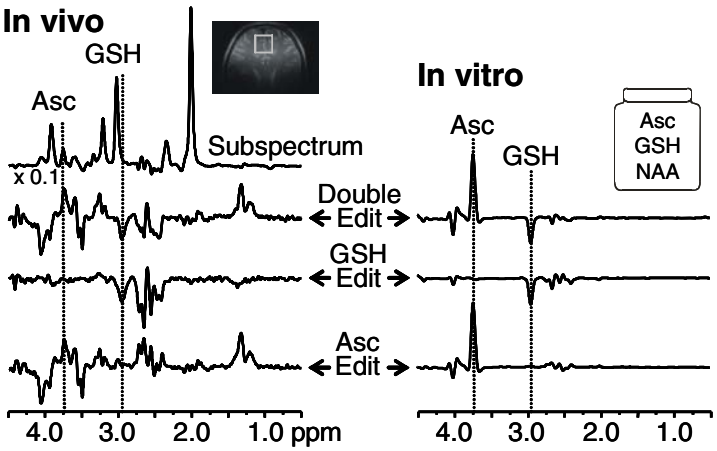

FIG. 1. Spectra measured in vivo from the volume of interest illustrated (left) and from phantom solution (right). For Double edit, 40 ms Gaussian editing pulses were applied at 4.13 and 2.95 ppm alternately. GSH Edit and Asc Edit were measured using typical on/off protocols as previously described, whereby co-edited resonances were also identified (2,5).

Discussion

The GSH resonance measured at 112 ms TE is approximately 75% as intense as that measured at 68 ms, the TE utilized previously for GSH editing in vivo (5). The overall sensitivity was judged equivalent to single editing. Utility of DEW for arbitrary compounds will depend upon editing efficiencies at a mutual echo time, as well as overlap among edited and coedited resonances. Double editing can also be used to edit other compounds and accomplished using double banded pulses. As such, it can be extended for editing *M*ultiple coupling systems simultaneously (MEW) and adapted for editing modalities other than MEGA, such as multiple quantum filtering (MEW-MQF, (6)) or heteronuclear multiple editing (MEW-POCE).

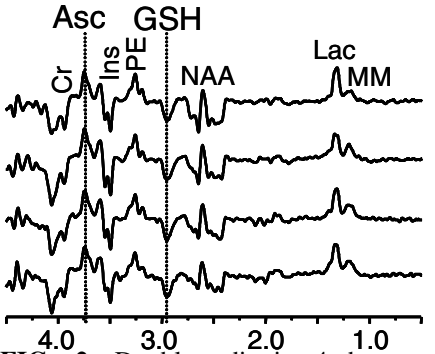

FIG. 2. Double edit in 4 humans (TE/TR = 112/4500 ms, NEX= 512).

References and Acknowledgments 1) Gadian, Oxford U Press, 1995. 2) Terpstra et al, Magn Reson Med, 51: 225, 2004. 3) Adriany et al, Magn Reson Med, 125: 178, 1997. 4) Gruetter et al, Magn Reson Med, 43: 319, 2000. 5) Terpstra et al, Magn Reson Med, 50: 19, 2003. 6) Lei et al, J Magn Reson, 143: 95, 2000. Financial sponsors: NIH R01NS038672 and P41RR008079, MIND institute, Whitaker and KECK foundations.