Unearthing tiny signals in 1H NMR spectra from the human brain: Measurement of Vitamin C and phosphomono and -diesters in vivo.

M. Terpstra[1], P-G. Henry[1], R. Gruetter[1]

[1]Center for Magnetic Resonance Research, University of Minnesota, Minneapolis, MN, United States

Introduction: Vitamin C (ascorbate) is an important antioxidant and nutrient that was recently detected in the human brain in vivo (1). In addition, since they appear to be resolved and coedited with Vitamin C, GPC and GPE may be quantified separately from PC and PE respectively. Hitherto these compounds have only been resolved in ^{31}P NMR spectra in vivo. Lac also coedited. The goal of this study was to quantify all the resonances appearing in the spectrum edited for Vitamin C using LCModel.

Methods: ^{1}H MRS MEGA-PRESS difference editing (2) with 40 ms Gaussian (40 Hz band width) editing pulses applied at 4.13 ppm and an optimized TE of 112 ms was utilized to edit for the ascorbate (Asc) C6 protons at 3.7 ppm based on the coupling to the C5 protons at 4.0 ppm (1). Metabolite assignment (3) was verified and concentrations were quantified relative to coedited aspartyl NAA (assumed 10 mM) using LCModel analysis of edited spectra (2) between 3.82 and 1.0 ppm. Basis spectra were measured from pure metabolite solutions at physiologic pH and temperature. The metabolite-nulled experiment provided a basis spectrum for macromolecules. The basis spectrum for GPE was simulated by shifting the measured GPC resonance (3.67 ppm) to the reported (4) chemical shift of GPE (3.29 ppm), assuming similar coupling. Frequency referencing was based on lactate and NAA. To assess the validity of adding GPC and GPE to the basis set, LCModel analysis was first performed without these compounds in the basis set. Then GPC and GPE were added.

Results and Discussion: LCModel analysis with all compounds (including GPC and GPE) in the basis set from one representative in vivo edited spectrum provided an excellent reproduction of the in vivo spectral pattern (Fig. 1). Without GPC in the basis set, the fit residual near 3.7 ppm revealed a lack of completeness in the basis set that was remedied upon addition of GPC (not shown). Similarly, when GPE was not fitted, the fit residual in the vicinity of 3.3 ppm deteriorated (not shown). The metabolite concentrations quantified with LCModel are summarized in table 1. When GPC was added to the basis set, the SD of PC stayed the same, indicating sufficient spectral resolution to provide an accurate measurement of PC and GPC separately. Similarly, PE and GPE appear to be separable. In conclusion, vitamin C can be quantified with a precision of 10% (average CRLB) with the method described and simultaneously measured with 7 additional compounds.

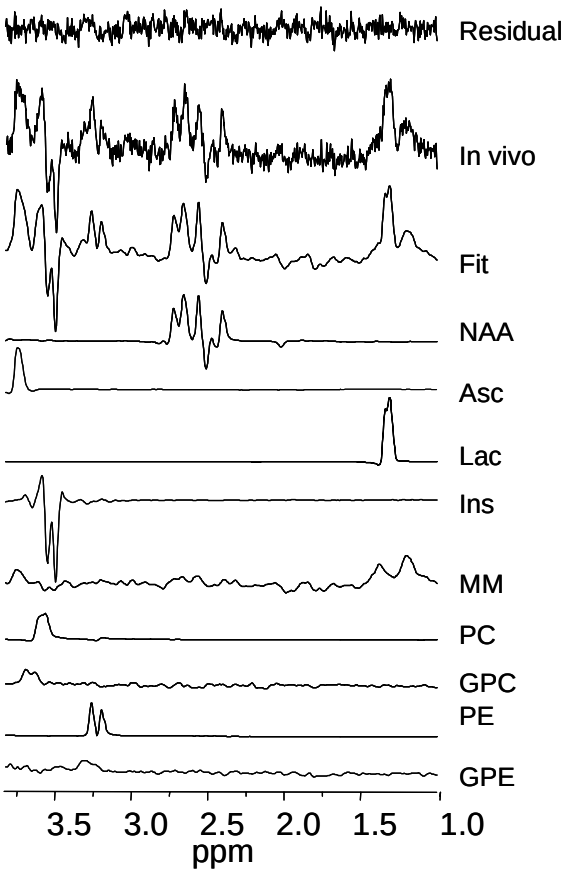

Figure 1: LCModel analysis of representative in vivo spectrum.

Table 1: Average (n=4) metabolite concentrations (mM) and Cramer-Rao Lower Bounds in parenthesis (CRLB, %) measured using LCModel analysis of edited ^{1}H NMR spectra in vivo. Relative to coedited NAA aspartyl resonance, assumed 10 mM.

Metabolite ±SD (CRLB)	***Asc***	***Lac***	***Ins***	***PC***	***PE***	***MM***	***GPC***	***GPE***
Without GPC or GPE	1.2±0.3 (10)	0.8±0.1 (6)	6.3±1.0 (6)	2.3±0.2 (16)	2.6±0.5 (10)	0.68±0.03 (12)		
With GPC And GPE	1.3±0.3 (9)	0.8±0.1 (5)	6.0±1.2 (6)	2.8±0.2 (12)	2.3±0.6 (11)	0.71±0.03 (9)	1.6±0.2 (18)	1.1±0.3 (22)

References and Acknowledgments: 1) Terpstra et al, *MRM* (in press). 2) Terpstra et al, MRM 2003 50:19. 3) Govindaraju et al, NMR Biomed 2000 13:129. 4) Willker et al, J. Magn. Res. Anal. 1996 2:21. NIH R01NS038672, NCRR BTRP P41RR008079