Altered antioxidant profile in the healthy elderly occipital and posterior cingulate cortices measured via 7 T ^{1}H MRS

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Target Audience: aging, dementia and oxidative stress researchers, geriatricians, and MR spectroscopists

Purpose: Oxidative stress occurs at an early stage of age related cognitive decline[1]. Ascorbate (Asc, vitamin C) and glutathione (GSH) are key contributors to the antioxidant network. Prior ^{1}H MRS measurements of these antioxidant concentrations in the elderly[2] could have been confounded by transverse relaxation (T_2)[3]. Goals of this work were to utilize short echo time (T_E) ^{1}H MRS to overcome such confounding, and to study a brain region that is pertinent to the pathology of Alzheimer's disease (AD), i.e., the posterior cingulate cortex (PCC). Innovations were scanning at ultra-high field and focusing of multiple transmitters to optimize power. Our hypotheses were that GSH signal differences in the OCC would be less pronounced than when measured at long T_E and that Asc homeostasis[4] would be preserved.

Methods: Healthy volunteers (MOntreal Cognitive Assessment scores ≥ 25), 17 young (age 19-22, 5 subjects scanned 3 times) and 16 elderly (age 70 - 88, 6 subjects scanned 3 times), were studied using a 7-T, 90-cm horizontal bore magnet equipped with a Siemens console and body gradients. A home-built 16-element transmit-receive transmission line head array[5] was used and transmit phase of each channel was optimized via individual 1 kW CPC amplifiers[6]. *In vivo* ^{1}H NMR spectra were acquired from OCC and PCC volumes of interest (VOI = 8 cm^3, figure 1) using a STEAM sequence with VAPOR water suppression and outer volume suppression[7] (T_R = 5 s, T_E = 8 ms, NS = 64 for OCC, 128 for PCC). First- and second-order shims were adjusted using FASTMAP[8]. Metabolite concentrations were quantified using LCModel[9] with a simulated basis set (18 metabolites and experimental macromolecule spectra) and water corrected for tissue content as the internal reference[2]. Age groups were compared using a 2-tailed t-test without correction for multiple comparisons.

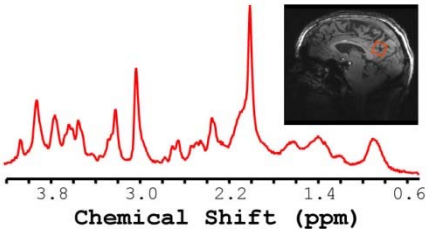

Figure 1. Representative PCC spectrum from an elderly subject.

Table 1. Mean ± SD [Asc]$_{brain}$ and [GSH]$_{brain}$ in the two brain VOIs.

VOI	Metabolite	Young	Elderly	*p*
OCC	Asc	1.5 ± 0.2	1.7 ± 0.2	0.005
	GSH	1.3 ± 0.1	1.1 ± 0.2	<0.001
PCC	Asc	1.3 ± 0.2	1.7 ± 0.2	<0.001
	GSH	1.39 ± 0.08	1.28 ± 0.09	0.002

Results: Figure 1 illustrates the high data quality achieved in this study. Table 1 shows that Asc concentration ([Asc]$_{brain}$) was higher and GSH concentration ([GSH]$_{brain}$) lower in elder subjects in both brain regions. The Asc difference in the PCC was the most significant (p = 1.8 x 10^{-5}). Figure 2 shows the test-retest data for Asc in the PCC by age group. Test-retest repeatability was smaller than between person variance. [Asc]$_{brain}$ were higher in a few elder subjects than any of the other subjects.

Discussion: The 17% lower OCC [GSH]$_{brain}$ in the elder cohort measured herein is smaller than previously measured with anticipated confounding by T_2, consistent with faster metabolite relaxation in elder subjects[3]. The higher [Asc]$_{brain}$ in the elders is analogously consistent. It is yet to be determined whether [Asc]$_{brain}$ can be quantified reliably using short-echo time spectroscopy at fields lower than 7 T.

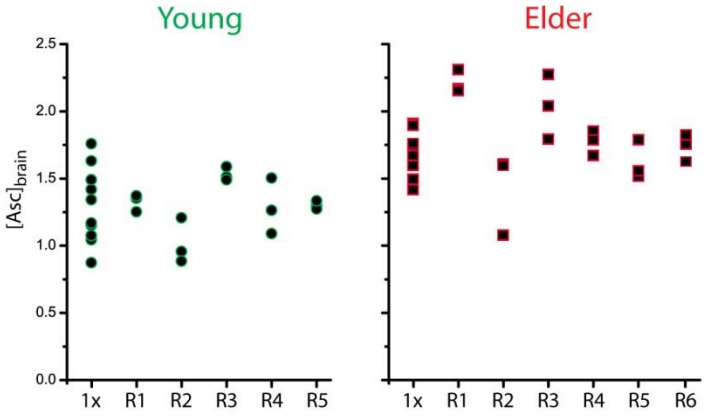

Figure 2. [Asc]$_{brain}$ in PCC of individual young and elderly subjects including retest values.

Conclusion: This unprecedented demonstration that [Asc]$_{brain}$ is generally higher in the elderly, as well as extraordinarily high in the PCC of some elder individuals has important implications for ongoing development of vitamin C based prevention and treatment of cognitive decline[10]. This study demonstrates utility of short-echo time ^{1}H MRS at ultra-high field to: investigate the mechanisms of cognitive decline, contribute a biomarker pertinent to cognitive decline, and monitor treatment response.

References: 1. MF Beal *et al.* Ann Neurol 2005, **2.** U Emir *et al.* NMR Biomed 2011, **3.** M Marjanska *et al.* PLoS One 2013, **4.** H Tsukaguchi *et al.* Nature 1999, **5.** G Adriany *et al.* MRM 2008, **6.** GJ Metzger *et al.* MRM 2008, **7.** I Tkac *et al.* MRM 2001, **8.** R Gruetter, I Tkac MRM 2000, **9.** SW Provencher MRM 1993, **10.** FE Harrison *et al.* Nutrients 2014.

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