Feasibility of regional glutathione measurement in healthy older individuals using ^{1}H MEGA-PRESS MRS

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Introduction

Glutathione (GSH) is an important antioxidant which may protect against inflammation-induced oxidative stress and is therefore of great interest in age-related neurodegenerative disorders such as dementia, with its up-regulation thought to provide additional protection against neuronal damage. The purpose of this ongoing study is to investigate the interpretability and feasibility of glutathione measures in certain brain regions involved in cognition and mental flexibility – precuneus, anterior cingulate cortex (ACC), dorsolateral prefrontal cortex (DLPFC) and hippocampus – in clinically acceptable measurement times (<10 minutes per region) within a healthy older population.

Methods

GSH was measured in seven healthy older volunteers (average age 64.5 years; range, 60-72 years; 4 males), using a ^{1}H Mescher-Garwood point-resolved spectroscopy (MEGA-PRESS) sequence[1-3] at 3T (GEHealthcare, MR750 Discovery, TR = 2000ms, TE = 131ms, 128 ON and 128 OFF acquisitions), in the precuneus (35 x 25 x 20mm^3), ACC (30 x 25 x 20mm^3) DLPFC (32 x 16 x 20mm^3) and hippocampus (35 x 20 x 20mm^3). LCModel was used for metabolite quantification, reported as ratios and water-scaled values – correcting for GM/WM ratios and CSF contribution[4] after segmentation in SPM12. Cramér-Rao lower bounds (CRLB) and SNR were used to assess spectral quality[5] with exclusion if both CRLB>30% and SNR< 3. T-tests were carried out in SPSS.

Results

The results of preliminary analysis found the precuneus to be the most reliable area for GSH measurements, with CRLB 13-26%, and an SNR of 3-5 in the edited spectra. For the ACC, CRLB were between 15-30% for six of the participants with SNRs of 3-4, with one participant having a CRLB of 49% and SNR of 2. Quality of DLPFC spectra varied substantially between the six participants (CRLB 12-58%, SNR 0-4)= 0 and was unacceptable for the hippocampus in 4 participants (SNR < 3, CRLB >50%). Thus, only the precuneus, ACC and DLPFC were further analysed, limited to participants with acceptable quality. Regional estimates of GSH (absolute and relative to Cr) were within the expected range (*Figure 1*), and did not show significant regional differences (paired t-tests, p>0.05), or age effect when compared to our reported findings in young children[2], (p>0.05).

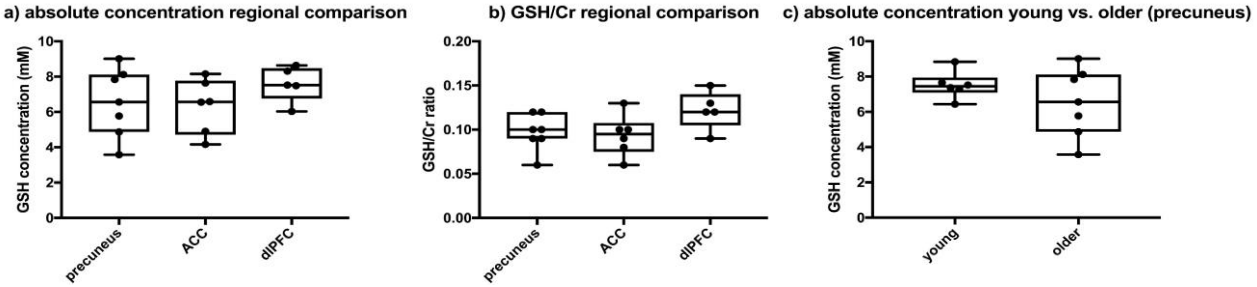

Figure 1: a) comparison of absolute GSH concentration estimates derived from clinical practical acquisition protocol in the precuneus, ACC and DLPFC; b) comparison of GSH/Cr ratios in the precuneus, ACC and DLPFC; c) Comparison of GSH in the precuneus of young[2] and older participants.

Discussion

The main finding of this preliminary analysis is that it is possible to estimate GSH levels in acceptable measurement times in the precuneus and ACC in most healthy older participants. In some participants, DLPFC measures were feasible, but larger voxel sizes should be trialled. We did not achieve satisfactory GSH estimates in the hippocampus. Future work will consider further the impact of age-related atrophy upon the spectral quality and SNR, optimisation of DLPFC and hippocampus, and explore the effects of health interventions.

Conclusion

We demonstrated that GSH measurement in older individuals is feasible in two out of the four tested brain regions, however our preliminary data do not support major regional differences.

References

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