Posterior Cingulate Metabolic Profile at Ultra-High Field Indicates Decreased Anti-Oxidative Capacity with Aging.

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Background: Metabolic profiles in the posterior cingulate have been found to be perturbed in many neurodegenerative diseases[1,2] and mental disorders[3]. There is also increasing interest in the functional role of the posterior cingulate in relation to the default mode network that shows alterations in those diseases and during development and aging. Ultra-High field spectroscopy has the potential to characterize neurotransmitter profiles due to improved spectral resolution. The aim of this study was, to use a newly suggested ^{1}H spectroscopy sequence optimization[4] for observation of coupled metabolites glutamate and glutamine at 7T, and to investigate changes that may occur during healthy aging.

Method: Eleven healthy subjects took part in the study (age range 19-72). All subjects underwent medical interview and cognitive testing using the revised Addenbrooke's cognitive examination which allowed elimination of subjects with mild cognitive impairment. Subjects underwent a scanning session including MPRAGE anatomical images for localisation followed by a water-suppressed ^{1}H spectral acquisition from the posterior cingulate (STEAM TE/TM/TR=74/78/3000ms, VOI=25x25x30mm^3, BW=3000Hz, No. samples = 2048). All MR measurements were acquired on a Philips Achieva 7T system. Six spectra were collected, each with 32 averages, and were phase-corrected and averaged together before spectral analysis in LCModel using water referencing. Total spectral acquisition time ~11mins. Metabolite concentrations were estimated in arbitrary absolute units and ratios relative to creatine and total metabolite signal (tot) to account for atrophy.

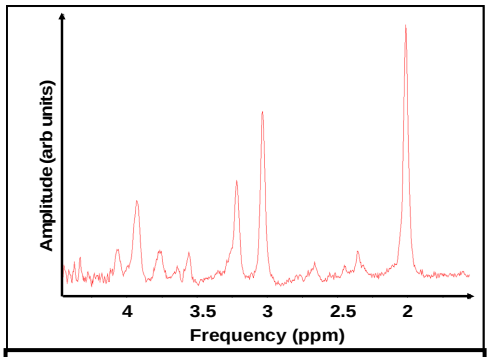

Figure 1: A typical acquired spectrum.

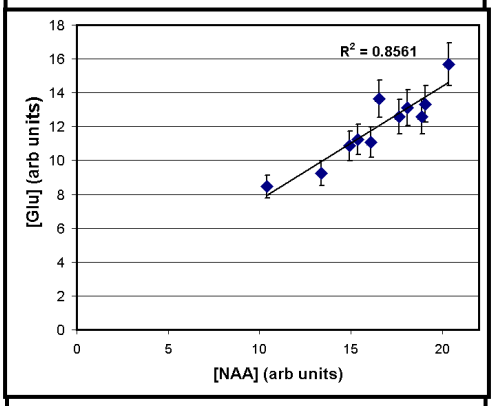

Figure 2: Correlation between NAA and Glu

Results and Discussion: Results from the new optimized sequence gave good results for N-acetyl aspartate (NAA), creatine (Cr), choline (Cho), guanidinoacetate (Gua), myo-inositol (mI) and glutamate (Glu) (Rao-Cramer bounds from LCModel <10%) in all subjects and line shapes for glutamate and glutamine tended towards the pseudo-singlets demonstrated in the literature[4]. Results from Asp were also relatively good (<20%), however results for glutamine were less reliable (mean±SD=35±15%) mainly due to shorter T_2 relaxation times at the higher field strength causing reduced signal to noise (SNR) at the longer echo times used.

In partial agreement with previous finding, absolute, but not relative NAA was found to decrease with age (P=0.04) suggesting a bias from uncorrected brain atrophy. Significant decreases were also found in levels of glutamate (p=0.01), and Glu/Cr, but not Glu/tot. Correlation of Glu with NAA (Fig. 2) was extremely high (p<0.001) supporting the notion that reduction of glutamate is mainly due to atrophy. The Glu/Cr decrease may indicate additional age-specific decline in agreement with previous findings from Kaiser et al[5] and Chang et al[6]. Cho/tot was found to be significantly increased with age (p=0.03) suggesting membrane dysfunction. Perhaps most interestingly, Tau/tot was significantly decreased (p=0.03) with age which was mirrored by increases in Gua/tot (p=0.08). In view of the suggestive anti-oxidative properties of Taurine[7] and inhibition of anti-oxidative properties by elevated levels of Gua[8] it is tempting to speculate that decreases in Tau and increases in Gua may reflect decreased ability of the aging brain to cope with oxidative stress. Future studies, and further analysis establishing tissue content of the voxel will need to be carried out to assess the exact cause of the metabolic changes.

A second limitation of this study is the possibility that changes in relaxation rates of the metabolites may have affected the results due to the chosen medium long echo times.

Conclusions: UHF MRS in normal aging confirmed previous findings of decreased concentrations of NAA and glutamate reflecting brain atrophy. Decreased glutamate/Cr with constant NAA/Cr points towards altered neuronal function. Most interestingly, decreased Tau and a tendency for increased levels of GUA is consistent with the expected decreased anti-oxidative capacity of the aging brain.

References: 1. Kizu, O. et al, *Neuroradiology* (2004), pp277 **2.** Godbolt, A. K. *Am.J. Neurology*, (2006) pp718. **3.** Shimizu, E. et al, *J. Psychiatric Research,* (2007), pp49 **4**. Yang, S. et al, Mag. Res. Med (2008), 59, pp236 **5.** Kaiser, L. G. et al *Neurobiol. Aging*, (2005) 26(5) pp665. **6.** Chang, L. et al, *Mag Reson. Imag.* (2008). **7.** Ward, R. et al, *Adv Exp Med Biol.* (2006);583 pp299 **8.** Poon, H. F. et al, Clin. Geriatr. Med (2004) 20(2) pp329.