Metabolic Profiling of the Posterior Cingulate Gyrus in Healthy Adults: A ^{1}H MRS Study

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Introduction: The effects of aging on the human brain have been studied at both cellular and macroscopic levels (1-3). Marner et al observed a 45% decrease in myelinated fibers from ages 20 to 80 resulting from a 23% decrease in white matter volume (2). Pakkenberg et al observed a 10% decrease per decade of neocortical neurons over the age range of 20 to 90 years without changes to neuronal density, suggesting that the reduced number of neurons relates to reduced brain volume (1). Here, we employ short TE ^{1}H MR spectroscopy to investigate whether these reported findings are associated with changes in cerebral metabolite concentrations in the posterior cingulate gyrus among three groups: healthy young (HY), healthy middle-aged (HM), and healthy elderly (HE).

Methods: Data were collected from three healthy groups: young (5 men, 5 women, mean: 25.7 yrs, range: 20-31 yrs), middle-aged (6 men, 8 women, mean: 48.9 yrs, range: 40-51 yrs), and elderly (5 men, 6 women, mean: 63.9 yrs, range: 60-71 yrs). The spectroscopic examination included STEAM (VOI~6cm^3, TR/TM/TE = 5000/10/10 ms, 112 excitations, 2500 Hz spectral width, and 2048 complex points), a water reference experiment for phase correction, a progressive TR T_2 experiment (4) for compartmental analysis. All data were collected in the posterior cingulate gyrus using a 1.5 T Siemens Magnetom Sonata MRI system. LCModel was used for metabolite quantification (5).

Results: Metabolite concentrations, both in absolute terms (tNAA, Glx, tCr, tCho, and mI) and ratios (tNAA/tCr, Glx/tCr, tCho/tCr, and mI/tCr), were analyzed using a two-way ANOVA with gender and age group as factors. In terms of absolute concentrations, tCho (p=0.003, 87% power) was the only metabolite that exhibited any significant differences, but only as a factor of age group (Fig 1a). Post hoc comparisons showed that [tCho] was different between HE and HM as well as HE and HY. Although an age-dependent concentration increase was visible in both genders, the overall effect was driven by changes in men. For ratios (Fig 1b), tCho/tCr (p=0.011, 71% power) and tNAA/tCr (p=0.009, 73% power) exhibited significant differences for age and gender, respectively. Post hoc comparisons indicate that the gender differences were driven by a larger ratio of tNAA/tCr in women, compared to men, in the HY. The age-dependent decrease in tCho/tCr was driven by differences between HY and HE.

Discussion: While an age-related increase in choline concentration is a fairly consistent finding in ^{1}H-MRS, the neurobiological and neuropsychological significance of this increase is currently unknown. Cohen et al showed that uptake of ingested choline across the blood brain barrier decreases significantly with age (6) which suggests that the elderly brain is saturated with free choline. Because free choline is a substrate for the neurotransmitter acetylcholine (ACh), perhaps elevated tCho concentrations are indicative of decreased enzymatic activity, reduced metabolic demand for ACh, or neurodegeneration. Finally, this data suggests that the best method for characterizing the metabolic profile of healthy adults is absolute quantitation as opposed to metabolite ratios which show a decreased choline effect.

References: (1) Pakkenberg B et al. J Comp Neurol 1997; 384(2):312-20. (2) Marner L et al. J Comp Neurol 2003; 462(2):144-52. (3) Bozzali M et al. Magn Reson Imaging 2008; 26:1065-70. (4) Knight-Scott J et al, J Magn Reson 2005; 173:169-74. (5) Provencher S, Magn Reson Med 1993; 30:672-9. (6) Cohen et al, JAMA 1995; 274(11):902-7.

Figure 1. HY ( ), HM ( ), and HE ( ) metabolite concentrations (a) and metabolite ratios (b). In terms of metabolite concentrations, HE has a significantly larger concentration of tCho (p=0.003) than HM (t=2.607) and HY (t=3.748). For metabolite ratios, tCho/tCr differences between age groups was significant between HY and HE (p=0.011).