^{1}H MR Spectroscopic Assessment of Age-Related Changes in Young and Middle-Aged Women

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Introduction: Studies of cerebral brain aging often focus on the obvious and easily measurable differences between young (< 30 years) and elderly adults (> 65 years). Recent studies in gene expression suggest that mid-life aging processes exhibit greater diversity and heterogeneity than is seen in the elderly (1). Given that middle-age cognitive status is a more likely predictive discriminator of age-related normal and pathological cognitive processes, neurochemical markers collected during this stage of life would have a great utility in understanding the aging process. To date, few studies have specifically examined the middle-life aging processes. Particularly absent is information on women and the effects of age-dependent hormonal changes. As part of a pilot study, we used ^{1}H-MRS to examine the age-related neurochemical and relaxometric differences between healthy young (HY) and healthy middle-aged (HM) women.

Method: All participants were healthy women: 7 middle-aged (mean: 48.9 yrs, range: 41-52 yrs) and 5 young (mean: 25.6 yrs, range: 22 -29 yrs). Ingestion of food or fluids was prohibited for the 12 hours prior to the spectroscopic examination. In addition, all participants were examined between day 7 and day 21 of their menstrual cycle – between the late follicular phase and early luteal phase - to minimize water retention effects. The spectroscopic examination included a STEAM experiment (VOI~6cm^3, TR/TM/TE = 5000/10/10 ms, 112 excitations, 2500Hz spectral width, and 819.2 acquisition window), a water reference experiment for phase correction, and a progressive TR T_2 experiment (2) for compartmental analysis. All data were collected along the midline of the posterior cingulate gyrus using a 1.5 T Siemens Magnetom Sonata MRI system. QUEST was used to identify the metabolite resonances and the macromolecule background (3). Concentrations were reported in millimoles per kilogram of tissue water (4).

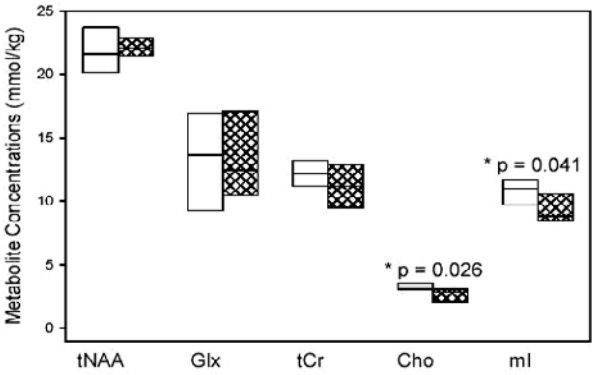

Figure 1. HM☐ and HY▩ metabolite concentrations as calculated using QUEST. HM women have significantly ($p < 0.05$) greater concentrations of Cho and mI than HY women.

Results and Discussion: Of the five major metabolites compared (total N-acetylaspartate (tNAA), glutamate+glutamine (Glx), creatine+phosphocreatine (tCr), choline containg compounds (Cho), and myo-Inositol (mI)), Cho and mI were both significantly greater in HM (mean increases of 24% and 17%, respectively) than in HY women (Figs 1 & 2). These increases are consistent with previous findings by Chang et al. (5) and with a hypothesis of normal atrophic cerebral aging: age-dependent breakdown of cell membranes (increased Cho) accompanied by gliosis (increased mI). Additional support for these aging effects is provided by a consistent trend of decreasing relaxometry parameters with aging (Table 1). The reductions in the tissue water T_1 and T_2 values are consistent with reduced water content, and the decrease in the local tissue fraction (f_2) supports the hypothesis of age-related atrophy. While the changes are small, the combination of water relaxometry and metabolite concentrations gives a detailed description of the effects of age-related, atrophic metabolic changes.

Table 1. Average Changes

	HM	HY
T_{1_tis}	935.49 ± 3.6%	961.08 ± 4.5%
T_{2_tis}	72.01 ± 3.4%	73.4 ± 1.7%
f_2	91.3% ± 1.9%	92.3% ± 3.1%
[Cho]	3.31 ± 9.4%	2.67 ± 20.4%
[mI]	10.98 ± 9.8%	9.41 ± 12.9%

References

(1) Lu T et al. *Nature* 2004;429:883-91. (2) Knight-Scott J et al. *Magn Reson Imag* 2005;23:871-6. (3) Ratiney H et al. *MAGMA* 2004;16:284-96. (4) Knight-Scott J et al. *Magn Reson Imag* 2003;21:787-97. (5) Change L et al. *Life Sciences* 1996;58:2049-56.

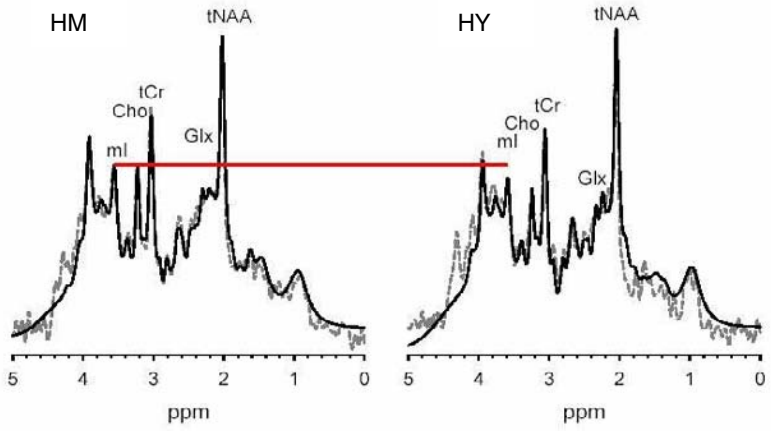

Figure 2. Representative spectra (— —) and fits (——) from a HM (left) participant and HY (right) participant collected from the posterior cingulate. The line across the two spectra highlights the obvious increase in Cho and mI in the HM spectra versus the HY spectra.