Relationship between Body Fat Composition and Concentrations of Brain N-Acetyl-Aspartate and Choline Compounds in Middle-Aged Adults

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Introduction: Recent epidemiological studies have demonstrated that being overweight in midlife is associated with greater chances of developing late life dementia, especially in women [1-3], but that being overweight was related to reduced cognitive performance in men only [4]. Further, a neuroimaging study showed that higher generalized brain atrophy in a cohort of males and females in their 50's was associated with higher BMI that spanned a continuum from normal weight to obesity [5]. In the retrospective study presented here, we tested a cohort of healthy controls in their 40's for relationships between BMI and regional brain volumes as well as common regional brain metabolite concentrations.

Methods: We used MR data from 50 healthy, middle aged (41.7 ± 8.5) individuals (17 females), who served as controls in a study on the effects of HIV and chronic alcohol consumption on the brain and were free of any medical conditions [6]. BMI was obtained by self-report and ranged between 18.7 and 36.8 kg/m^2, spanning a range from normal weight to obesity. T1-weighted 3D MPRAGE images were acquired at 1.5T and segmented into matter (GM), white matter (WM), and cerebrospinal fluid (CSF) for the major lobes bilaterally. Spectroscopic data were obtained with a multislice ^{1}H MRSI sequence with lipid inversion (TR/TE/TI = 1800/25/165 ms), in three parallel planes, each 15mm thick, 6 mm apart, angulated parallel to orbital-meatal line and covering the major cerebral lobes. Mean atrophy corrected concentrations of NAA, choline-, creatine-containing metabolites, and myo-inositol were calculated for GM and WM in major lobes. For statistical analyses, the volumetric measures and metabolite concentrations were considered as the response variables for a linear model that incorporated the covariates age, BMI and gender, also allowing for gender by BMI interaction. The interaction term was included to account for differential relationships between BMI and volumes or metabolite concentrations for males relative to females. The significance levels were adjusted to account for the number of regions assessed in particular analyses, i.e., $\alpha = 0.05/8 = 0.006$ for each metabolite and $\alpha = 0.05/13 = 0.004$ for volumes.

Results: The interaction between gender and BMI was not significantly associated with any regional volume or metabolite concentration. Higher BMI, both in males and females, was significantly associated with lower NAA concentrations in frontal GM, frontal, parietal, and temporal WM, as well as lower choline concentrations in frontal WM (all $p<0.002$). BMI was not significantly associated with regional creatine or myo-inositol concentrations, nor lobar GM, WM, or CSF volumes. Female gender was associated with 3-5% higher frontal GM NAA and higher frontal WM NAA and creatine ($p<0.003$).

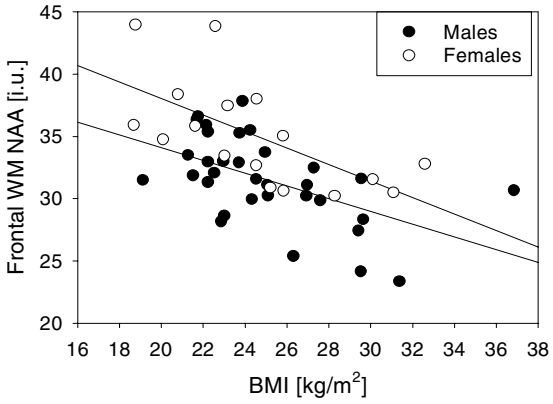

Figure 1. Frontal white matter concentrations of N-acetyl-apartate as a function of BMI, separately for men and women.

Discussion: These preliminary, retrospective results suggest that BMI is associated with brain NAA and choline metabolite concentrations in middle aged adults. If confirmed in a prospective study, these results may shed some light on neurobiological processes underlying early development of late-life dementia.

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