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Research report

Brain structure and cognitive correlates of body mass index in healthy older adults

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HIGHLIGHTS

- We examine white matter tracts and cognitive performance with BMI in old age.
- High BMI was related to low FA in the uncinate fasciculus.
- No relationships between BMI and cognition were observed.
- BMI-related white matter alterations precede cognitive dysfunction.

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ABSTRACT

Obesity, commonly measured with body mass index (BMI), is associated with numerous deleterious health conditions including alterations in brain integrity related to advanced age. Prior research has suggested that white matter integrity observed using diffusion tensor imaging (DTI) is altered in relation to high BMI, but the integrity of specific white matter tracts remains poorly understood. Additionally, no studies have examined white matter tract integrity in conjunction with neuropsychological evaluation associated with BMI among older adults. The present study examined white matter tract integrity using DTI and cognitive performance associated with BMI in 62 healthy older adults (20 males, 42 females) aged 51–81. Results revealed that elevated BMI was associated with lower fractional anisotropy (FA) in the uncinate fasciculus, though there was no evidence of an age by BMI interaction relating to FA in this tract. No relationships were observed between BMI and other white matter tracts or cognition after controlling for demographic variables. Findings suggest that elevated BMI is associated with lower structural integrity in a brain region connecting frontal and temporal lobes and this alteration precedes cognitive dysfunction. Future studies should examine biological mechanisms that mediate the relationships between BMI and white matter tract integrity, as well as the evolution of these abnormalities utilizing longitudinal designs.

1. Introduction

Obesity has become an increasingly prevalent health concern in recent decades, especially in the United States and other Western cultures [1,2]. Recent estimates indicate that nearly one third of adults in the United States are classified as obese [2]. High body weight, commonly quantified by body mass index (BMI), is associated with increased risk for chronic health conditions such as diabetes, cardiovascular disease, and late life dementia [3,4]. If uncorrected, these obesity-related consequences can contribute to decreased quality of life, increased cost of health care, and increased mortality [5].

Elevated BMI has also been associated with alterations in brain structure and function. A recent meta-analysis suggested that high BMI is related to poor cognitive performance, especially in domains of executive function, processing speed, and memory [6]. Other

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studies have demonstrated poor cognitive performance in relation to high BMI after controlling for demographics and cardiovascular comorbidities [7–9]. In addition, neuroimaging methodologies incorporating structural magnetic resonance imaging (MRI) have reported smaller volumes of gray and white matter in obese individuals compared to normal-weight individuals, especially in frontal and temporal structures [10–13]. Though these volumetric approaches are valuable for assessing the amount of regional tissue composition in the brain, they are unable to provide information regarding the microstructural integrity of brain tissue.

Diffusion tensor imaging (DTI) provides detail regarding the integrity of neural microstructure in the brain. The advantage of DTI over other neuroimaging sequences is the opportunity to quantify microstructural characteristics of white matter not captured by standard magnetic resonance imaging [14]. Several studies have demonstrated that the integrity of white matter is adversely affected in individuals with high BMI [15–17]. White matter regions such as the corpus callosum, cingulate portion of the cingulum bundle, and fornix are shown to exhibit lower fractional anisotropy (FA) associated with high BMI, indicating that the directionality of water diffusion within these areas is reduced in individuals with elevated BMI [15,17,18]. Few studies, however, have examined BMI as it relates to FA in white matter tracts connecting to frontal and temporal lobes given volumetric evidence for this relationship. Assessment of these tracts may provide insight into early disruptions in white matter microstructure that lead to cortical atrophy and cognitive dysfunction associated with high BMI.

While many studies suggest that high BMI relates to lower white matter integrity and cognitive performance [19,8,9,16], few studies have examined these measures in a healthy older adult sample. Evidence suggests that elevated body mass may have a compounding effect on the cascade of biological process related to aging, which may be a key factor related to aging brain variability [20]. Activation of age-related physiological processes, including oxidative stress, vascular inflammation, and endothelial cell dysfunction, may be partially modified by obesity, potentially resulting in increased risk of ischemic stroke and white matter damage [3,21,22]. Increased quantities of adipocytes seen in obese individuals may exacerbate the cellular inflammatory response, which have a detrimental impact on the cellular integrity of brain tissue, particularly oligodendrocytes that comprise white matter [23,24]. Some studies have demonstrated an interactive effect of advanced age and high BMI affecting white matter integrity [16], yet many of these studies have focused exclusively on corpus callosum integrity rather than inclusion of cortical association tracts [16,25]. Investigating the integrity of these tracts in relation to high BMI is important for identifying disruption to white matter microstructure that may contribute to later cognitive dysfunction.

In the present study we examined FA in the superior longitudinal fasciculus (SLF), uncinate fasciculus (UF), cingulate portion of the cingulum bundle, and posterior sections of the corpus callosum associated with BMI. We also investigated the impact of high BMI on cognitive performance on tests of executive function, processing speed, and memory, which represent cognitive domains associated with the specific tracts of interest [26–28]. We hypothesized that while age would relate to DTI and cognitive measures, elevated BMI would be independently associated with lower white matter tract integrity and cognitive performance.

2. Method

2.1. Participants

A total of 62 individuals between the ages of 51 and 81 were included in the study. Participants were recruited from the local community in addition to the Research Participant Registry of the Washington University Institute of Clinical and Translational Sciences. Demographics and health history were obtained as part of cognitive assessment procedures within one month of MRI acquisition. All participants were required to be fluent English speakers to participate in the study protocol. Individuals with a self-reported history of medical conditions with potential to impact cognitive function (e.g., thyroid disease) were excluded. Also, individuals with a history of neurological disease (e.g., dementia, multiple sclerosis, Parkinson's disease), diabetes, significant head injury (defined as loss of consciousness greater than five minutes), alcohol or drug abuse, or MRI contraindication (e.g., claustrophobia) were not considered for inclusion. Individuals were excluded if they reported a current diagnosis of a DSM Axis I psychiatric condition (e.g., schizophrenia) with the exception of treated depression. The Mini-Mental State Examination (MMSE) was used to screen for current symptoms of dementia, excluding individuals with scores below 24. Trained experimenters measured each individual's height and weight. All study participants provided informed consent and were provided compensation for their participation in the study. Approval was obtained from the local university Institutional Review Boards and all participants provided informed consent according to Institutional Review Board guidelines for participation in all study procedures.

2.2. Neuroimaging acquisition

MRI scan acquisitions were obtained using a head-only Magnetom Allegra 3T MRI scanner located at Washington University in St. Louis. During the duration of data acquisition, all hardware, software, acquisition protocols, and pulse sequences remained unchanged to ensure quality assurance of neuroimaging data. High-performance gradients with a maximum strength of 40 mT/m in a 100-μs rise time and maximum slew rate of 400 T/m/s (simultaneously on all three axes) were used to limit scan times. Every scan session was initiated by a scout scan surveying three orthogonal planes to ensure correct head position. Structural MRI data were obtained utilizing T1-weighted magnetization-prepared rapid acquisition gradient echo (MP-RAGE) sequence, T2-weighted turbo spin echo (TSE), and T2-weighted fluid-attenuated inversion recovery (FLAIR). An initial pilot sample from the same parent study was used to establish slice coverage and field of view parameters. Total scan time was limited to less than 1 h.

2.3. DTI acquisition and analysis

To obtain diffusion weighted images, a custom single-shot multislice echo-planar tensor-encoded pulse sequence was used, with 31 non-collinear diffusion gradient directions comprising the 24 main direction used for data processing (diffusion weighting of $b = 996$ s/mm^2) and five baseline I_0 acquisition sequences ($b = 0$ s/mm^2). To ensure whole brain coverage, acquisition parameters (TE = 86.2 ms, TR = 7.82 s) were optimized across 64 contiguous 2.0 mm slices for each contrast. Additional imaging parameters included a 128×128 acquisition matrix with 256×256 mm field of view (isotropic $2.0 \times 2.0 \times 2.0$ mm voxels). Scan data were averaged with two scan repeats (total of 72 acquisitions). Raw (k-space) data were saved, stored, then reconstructed floating-point diffusion weighted images using a custom method of image reconstruction. Each of the participants' diffusion weighted images and diffusion-encoding vectors were registered via affine registration to the first I_0 volume with the mutual information metric of FSL FLIRT to correct for motion in the scanner and eddy current artifacts [29]. Brain tissue was extracted with the FSL Brain Extraction Tool. Diffusion tensors and their associated FA were estimated using linear least squares. To identify specific white matter tracts, the Johns Hopkins University (JHU) DTI atlas was mapped to each participant through