Gender Differences in the Dependence of Body Weight and Brain Connectivity Revealed by Diffusion Tensor Imaging

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Introduction: Recent studies showed that obesity is associated with changes in brain structure (1,2). It was also suggested that cerebral changes may be similar to those observed in drug addiction. However, the underlying mechanisms are unclear. To address these questions, we investigated the dependence between body weight and brain structure using diffusion-tensor imaging (DTI). Correlations between the body mass index (BMI) and fractional anisotropy (FA) were computed in female and male subjects separately. Axial and the radial diffusivity were additionally studied, which had been investigated by Song et al. (3,4) in animal models including the shiverer mouse.

Methods: High-resolution diffusion-weighted (DW) images (60 directions, b = 1000 s/mm², GRAPPA accel. fact. 2, NEX = 3) were acquired on a whole-body 3T TIM Trio scanner (Siemens, Erlangen, Germany) with a 12-channel head array coil.. The measurement of 72 axial slices with an isotropic resolution of 1.7 mm covered the entire brain. A set of 49 subjects was analyzed (23 female; age=26.4±5.0 y, BMI 18.5-50.7, mean 29.1, std=7.0).

Brain masks were extracted from T_1-weighted structural scans and co-registered into the Talairach space. The DW images were corrected for subject motion and registered to the T_1 anatomy with isotropic voxel size of 1mm using rigid-body transformation computed with FLIRT (5). For each voxel, a diffusion tensor was fitted to the data, and the FA was computed. Non-linear registration was used for inter-subject alignment (6). Using the deformed FA images, a mean image was created and thinned to create a mean skeleton, which represents the centers of all tracts common to the group (7). Finally, each subject's aligned FA were projected to the mean skeleton and fed into voxel-wise cross-subject statistics based on a general linear model containing BMI, gender, and age as covariates. In order to investigate gender differences, the statistical analysis was also performed for the female and male subjects separately. In addition to the FA, axial and radial diffusivity was investigated. Axial diffusivity is defined by the eigenvalue of the primary eigenvector and is also referred to as parallel diffusion. Radial diffusivity is the mean of the eigenvalues of the second and third eigenvectors, and it is also attributed to perpendicular diffusion.

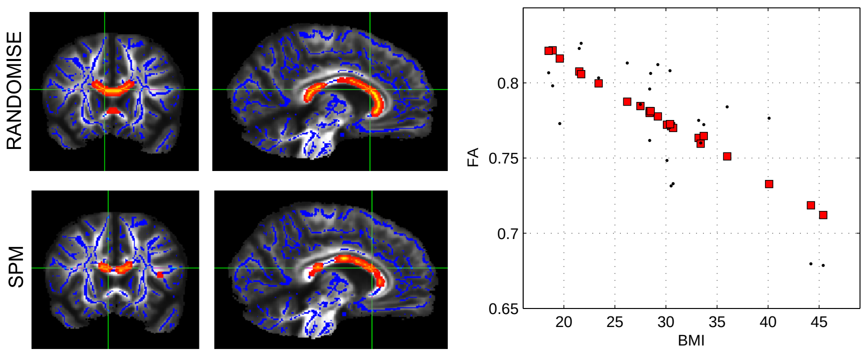

Figure 1. Coronal and sagittal brain slices showing a negative correlation between FA and BMI in female subjects (color-coded in red/yellow). The result was obtained using the randomise tool of FSL (p<0.05, corrected ; top row), and the statistics in SPM8 with p<0.001, uncorrected (bottom row). The plot on the right side shows the FA/BMI-values of all female subjects in a selected voxel (green cross-hair in the brain slices). Black dots and red squares show original and age-corrected FA values, respectively.

Results & Discussion: For female subjects, we observed significant negative correlations between FA and BMI in the whole corpus callosum. This result was obtained both with SPM8 and the randomise tool of FSL (Fig 1). In contrast, for the male subjects, no significant (neither negative nor positive) FA-BMI correlations could be observed (even without correction for multiple comparisons). For both female and male subjects, significant negative correlations between axial diffusivity and BMI were observed in all regions of the corpus callosum (Fig 2). The dependence between the radial diffusivity and body weight was again gender-specific: Only for the female subjects, significant positive correlations were obtained between radial diffusivity and BMI in the anterior part of the corpus callosum.

To summarize, women showed a much stronger dependence of body weight and brain structure than men. In female subjects, the BMI was significantly correlated with all diffusion parameters—FA, axial diffusivity, and radial diffusivity (i.e., a large BMI was associated with a small FA, a small axial diffusivity, and a large radial diffusivity). It is currently not known, which gender-specific mechanisms might lead to the observed differences in brain microstructure. Further work is thus advocated to investigate potential underlying mechanisms including fiber density or myelination.

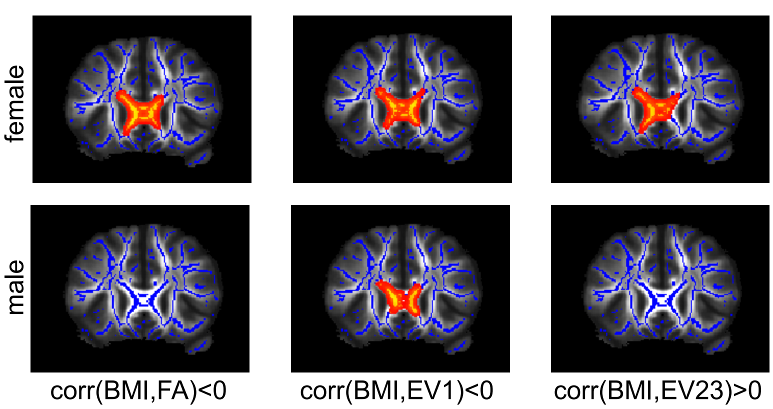

Figure 2. Gender-specific correlations between body weight and FA (left column), axial diffusivity (middle column), and radial diffusivity (right column) in female (top row) and male (bottom row) subjects. Significant correlations (color-coded in red/yellow) were obtained using the randomise tool of FSL (p<0.05, corrected for multiple comparisons).

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