# The association of elevated body mass index with reduced fractional anisotropy using Tract-Based Spatial Statistics and Tract-Specific Analysis

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**Objective:** We aim to explore the regional pattern of white matter alteration in metabolic subjects with at least one cardiovascular risk factor. In addition, we investigate whether white matter alteration was related to body mass index (BMI).

**Methods:** Seven men aged 43.3 ± 4.4 years with BMI ≥ 24 kg /$m^2$ and having risk factors for cardiovascular disease were recruited to serve as metabolic subjects. Age-matched 7 men aged 42.3 ± 5.3 years with a BMI < 23 kg/m2 without any risk factor were recruited to serve as control subjects. MRI scans were performed using a 3.0 Tesla unit (Achieva; Philips Medical Systems, Best, the Netherlands) and an eight-channel array receiving head coil. A single shot echo planar 32-direction diffusion weighted sequence with a b-value of 1000 s/$mm^2$ was used. The general scan parameters were: TR/TE = 5443 msec / 70 msec; acquisition matrix = 128 × 128; field of view = 224 × 224; slice thickness = 3 mm (50 slices). We performed statistical analysis of the fractional anisotropy (FA) values with a tract-based spatial statistics (TBSS) technique using FMRIB's software library 4.1 (FSL). Differences of FA values between the metabolic group and control group were evaluated with a permutation-based randomized test. We conducted tract-specific analysis of the FA values using dTV II and VOLUME-ONE 1.72 developed by Masutani et al. (University of Tokyo Department of Radiology). Tractography of right inferior fronto-occipital fasciculus (IFOF) of all subjects were assessed using two-region-of-interest (two-ROI) method. To generate diffusion tensor tractography of the right IFOF, the seed ROIs were set in the anterior part of the right external capsule, the target ROIs were posterior part of those. JHU White Matter Tractography Atlas supplied with FSL guided the placement of the ROIs. Mean FA values in registered voxels within the core of the IFOF tracts were then measured. Statistical analyses were performed using SPSS 16.0 for Windows (SPSS Inc., Chicago, IL, USA). Student's t-test was used for group differences in clinical characteristics and white matter FA values (ROI-based analysis). Pearson correlation coefficient was used to evaluate the relationship between BMI and measured mean FA values of right IFOF. P values < 0.05 were considered statistically significant.

**Results:** Clinical characteristics of the participants and FA values are summarized in Table 1. Metabolic subjects demonstrated significantly lower FA values in the part of the right external capsule, the entire corpus callosum and part of deep white matter of the right frontal lobe compared with control subjects (Figure 1). Tractographies of the right IFOF were obtained as gently curved tracts that were passing backward from the right frontal lobe, along the lateral border of the right caudate nucleus, and passing into the occipital lobe in all subjects. The mean FA values of right IFOF was 0.41 ± 0.03 for the metabolic subjects and 0.44 ± 0.05 for the control subjects (Table 1) and the difference was statistically significant (P < 0.05). A significantly statistical negative correlation was observed between BMI and FA values of right IFOF (r = -0.56, p < 0.04).

**Table 1. Clinical characteristics of the participants and fractional anisotrophy [a]**

| | Control subjects 7 males, (BMI<23) | Metabolic subjuects 7 males, (BMI≥24) | P Value (t-test) | |
|---|---|---|---|---|
| Age (years) | 42.29 (5.28) | 43.29 (4.39) | 0.71 | |
| Body mass index [b] | 22.45 (0.42) | 25.80 (1.36) | < 0.05 | [c] |
| Abdominal circumferen | 81.14 (5.46) | 90.71 (6.27) | < 0.05 | [c] |
| Systolic BP | 115.86 (8.11) | 134.43 (9.81) | < 0.05 | [c] |
| Diastolic BP | 76.71 (91.43) | 91.43 (4.89) | < 0.05 | [c] |
| HDL cholesterol | 56.43 (9.95) | 60.14 (18.85) | 0.65 | |
| Triglyceride (mM) | 95.14 (30.87) | 183.29 (45.34) | < 0.05 | [c] |
| Blood glucose | 95.86 (7.06) | 101.00 (9.15) | 0.26 | |
| FA of right IFOF [d] | 0.44 (0.05) | 0.41 (0.03) | < 0.05 | [c] |

[a] Values are expressed as mean (SD).
[b] Body mass index was calculated as weight in kilograms divided by the square of height in meters.
[c] P < 0.05
[d] Fractional anisotrophy of right inferior fronto-occipital fasciculus

**Discussion / Conclusions:** We revealed significant decrease of FA values in the part of the right external capsule and in the entire corpus callosum and a negative correlation was observed between BMI and FA values of right IFOF. The IFOF is unique in that it connects all 4 major lobes of the brain, 24 potentially serving an important role in linking all the components in what is commonly called the "social brain"(Jou RJ. 2011 AJNR). We conclude that elevated BMI may correlates with white matter alteration in metabolic subjects.

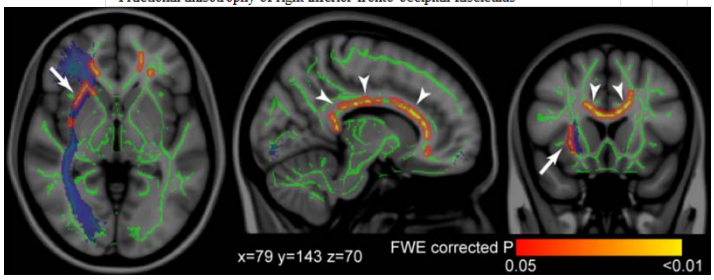


Figure 1. Results of tract-based spatial statistics analysis for fractional anisotrophy (FA). Areas with significantly decreased FA values in metabolic subjects compared with control subjects are shown by colors ranging from red to yellow (P < 0.05, the family-wise error correction for multiple comparisons). We revealed significant decrease of FA values in the part of the right external capsule (arrow) and in the entire corpus callosum (arrow head). Results are superimposed upon the MNI152-1mm template supplied with FSL. The mean FA skeleton is shown in green. The right inferior fronto-occipital fasciculus is shown for reference in blue. MNI space coordinates are provided in mm.