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Laboratory of Working Memory and Cognition

Lab Link

Individual differences in brain structure and functional connectivity related to body mass index (BMI) and body fat percentage (BFP)

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Background and Aims

- Obesity affects more than 850 million adults worldwide and is one of the leading causes of death in first-world countries.
- There are also well-established associations between higher adiposity, elevated impulsivity and decreased cognitive performance.
- Previous studies have investigated the neural correlates of these obesity-related cognitive effects, and have included: studies of gray and white matter volumes; white matter microstructure; **or** metabolic/functional activity. However, to the best of our knowledge, none have investigated all of these factors in a single cohort.
- Therefore, the primary aim of this study was to identify differences in brain structure **and** function related to normal individual variability in body composition.
- This was achieved by:
  1) Acquiring two independent measures of body composition - i.e., body mass index (BMI) and body fat percentage (BFP); and
  2) Comparing these to magnetic resonance imaging measures of local gray matter volume, white matter volume, white matter microstructure, and functional connectivity using voxel-based morphometry (VBM), diffusion tensor imaging (DTI), and resting state functional MRI (rs-fMRI).

Body Composition (BMI and BFP)

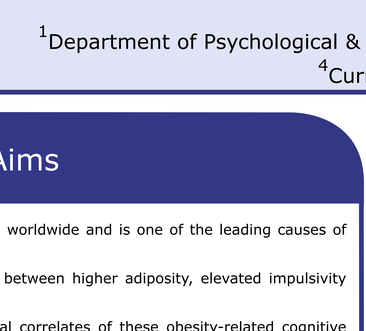
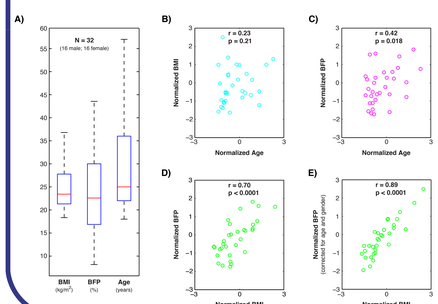


*Figure 1: **A)** Age, **B)** Body Mass Index (BMI), **C)** Body Fat Percentage (BFP), and **D)** Muscle Mass Percentage (MMP) for our study population (female; male; overall). *BMI less than 18.5 (dotted green line) is considered underweight; BMI between 18.5 and 25 (dotted black line) is normal; BMI between 25 and 30 (dotted red line) is overweight; and BMI greater than 30 is obese.*

- 32 healthy adults were recruited from the community at large and screened for prior neurological or psychiatric trauma or illnesses, alcohol or drug abuse, etc.
- Participants were recruited to span a broad range of age and weight, although sex was evenly balanced.
- BMI was calculated using height and weight, whereas BFP was measured using a Tanita BC-350 bioelectric impedance scale.
- As shown in both **Figure 1** and **Figure 2**: Age ranged from 18 to 57 years (with a slight bias toward younger subjects); BMI ranged from 18 to 37; and BFP ranged from 7.5 to 44.



- BFP, but not BMI, was significantly correlated with age (**Figure 2B-C**).
- BMI was significantly correlated with BFP (**Figure 2D**), but even after regressing out age and gender, there were still small differences between BMI and BFP (**Figure 2E**).
- After body composition measurements were acquired for each participant, 3T MRI scans were performed.

*Figure 2: **A)** Body Mass Index (BMI), Body Fat Percentage (BFP) and Age among the 32 healthy study participants, as well as correlations between: **B)** normalized BMI and Age; **C)** normalized BFP and Age; and **D)** normalized BFP and BMI. **E)** Partial correlations were also performed between normalized BFP and normalized BMI to factor out the effects of age and gender.*

Gray and White Matter Volumetric Analyses (VBM)

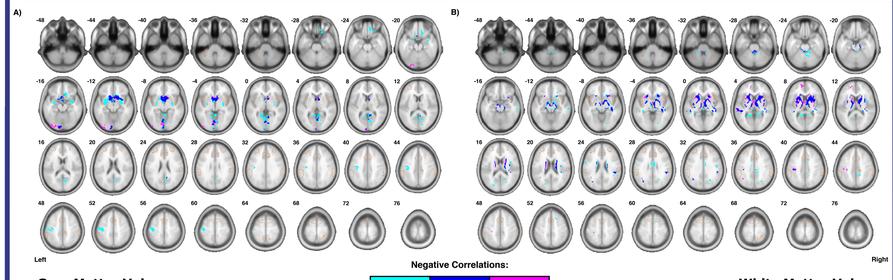


*Figure 3: Individual differences in regional cortical volumes are correlated with body composition (i.e., BMI and/or BFP), corrected for age, gender and total intracranial volume. **A)** Gray matter volumes were negatively correlated with BMI in three clusters and negatively correlated with BFP in two clusters. No gray matter structures demonstrated significant positive correlations with either BMI or BFP. **B)** White matter volumes were negatively correlated with BMI in six clusters and negatively correlated with BFP in seven clusters. No white matter structures demonstrated significant positive correlations with either BMI or BFP. *Note: all brain images are displayed in neurological orientation, and are in normalized MNI space. Regions of the Salience Network (SN) are shown with a light brown outline.*

- Processing of whole-brain T_1-weighed images (1mm isotropic) was performed using SPM8 and the VBM8 toolbox, and included: unified segmentation; non-linear (DARTEL) normalization to MNI space; image modulation; and 5 mm 3D smoothing.
- By running separate cluster-level GLM analyses for gray and white matter images, we found that:
  1) Several gray matter regions (i.e., the amygdala, basal ganglia, lingual gyri, precuneus, as well as the precentral and postcentral gyri) demonstrated significant volume reductions with higher BMI and/or BFP (**Figure 3A**).
  2) Several white matter regions (i.e., the cingulum, corpus callosum, inferior fronto-occipital fasciculus, inferior and superior longitudinal fasciculi, and regions proximal to the basal ganglia) also demonstrated volume reductions with higher BMI and/or BFP (**Figure 3B**).
  3) Neither gray nor white matter analyses (corrected for age, gender and intracranial volume) revealed local volumetric increases.

White Matter Microstructural Analyses (DTI)

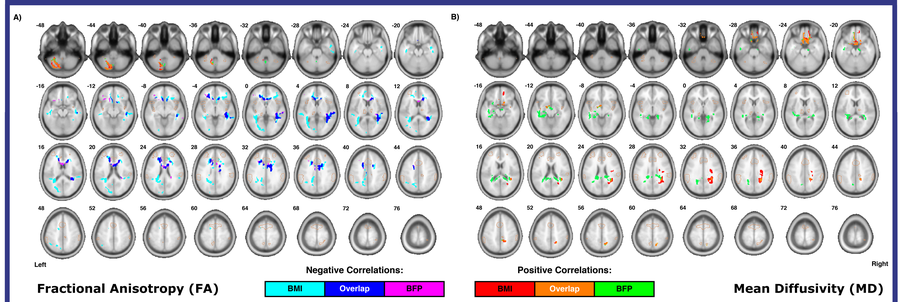


*Figure 4: Individual differences in regional white matter microstructure are correlated with body composition (i.e., BMI and/or BFP), corrected for age and gender. **A)** Fractional anisotropy (FA) values were negatively correlated with BMI in three clusters, negatively correlated with BFP in two clusters, and positively correlated with both BMI and BFP in one cluster. **B)** Mean diffusivity (MD) values were positively correlated with BMI in three clusters and negatively correlated with BFP in two clusters. No white matter structures demonstrated significant negative correlations with either BMI or BFP. *Note: all brain images are displayed in neurological orientation, and are in normalized MNI space. Regions of the Salience Network (SN) are shown with a light brown outline.*

- Processing of diffusion-weighed images (30 directions; b = 700 s/mm^2) was performed using CATNAP, MRIStudio, SPM8, and included: coregistration; gradient orientation; skull stripping; linear (AIR) and non-linear (LDDMM) normalization to MNI space; calculation of fractional anisotropy (FA) and mean diffusivity (MD) images; white matter masking; and 6 mm 3D smoothing.
- By running separate cluster-level GLM analyses for FA and MD images, we found that:
  1) The corona radiata, inferior fronto-occipital fasciculus, inferior longitudinal fasciculus, as well as orbitofrontal and temporal white matter demonstrated significantly reduced FA with higher BMI and/or BFP. Only the left cerebellum showed increased FA (**Figure 3A**).
  2) The cingulum, corpus callosum, cuneus and precuneus, as well as middle orbitofrontal and parahippocampal white matter demonstrated significant increases in MD with higher BMI and/or BFP. No regions exhibited significantly decreased MD (**Figure 3B**).

Functional Connectivity Analysis (rs-fMRI)

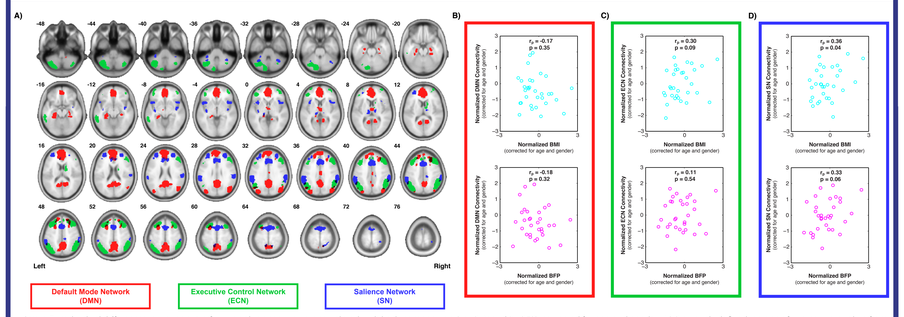


*Figure 5: Individual differences in resting state functional connectivity are correlated with body composition (i.e., BMI and/or BFP), corrected for age and gender. **A)** Previously defined regions of interest were taken from an anatomical atlas (Shirer et al., 2012) of the default mode network (DMN; red), the executive control network (ECN; green), and the salience network (SN; blue). Partial correlations (corrected for age and gender) were performed between body composition data (BMI or BFP) and: **B)** DMN connectivity, **C)** ECN connectivity, and **D)** SN connectivity.*

- Processing of resting state BOLD fMRI data (222 volumes; 7.4 minutes) was performed using the SPM8 Conn toolbox, and included: realignment; slice-time correction; coregistration; spatial normalization; 6mm 3D smoothing; motion compensation (CompCor); artifact detection and removal (ART); and band-pass filtering (0.01–0.08 Hz).
- Each subject's network connectivities were calculated by averaging bivariate correlations between all ROIs pairs (taken from a previously published atlas; **Figure 5A**), and these were plotted against BMI and BFP, correcting for age and gender (**Figure 5B-D**). Of the three networks investigated (i.e., the DMN, ECN, and SN), we observed:
  1) No significant relationships between DMN or ECN connectivity and either BMI or BFP (**Figure 5B-C**), and
  2) Significantly increased SN connectivity among higher BMI and BFP individuals (**Figure 5D**).

Discussion and Conclusions

- Although the association between BMI and BFP was not perfect (r=0.70), both measures were in good agreement regarding the neural correlates of obesity.
- Total brain size, as well as global gray and white matter volumes were positively correlated with BMI and BFP in our sample (**Figure 6**). However, many structures exhibited significant volumetric decreases with higher BMI and BFP.
- Several white matter regions also showed decreased FA and/or increased MD (both markers of decreased white matter integrity) among higher BMI and BFP individuals.
- Despite relatively under-developed gray and white matter structures and reduced white matter connectivity proximal to several nodes of the Salience Network (SN), functional connectivity within this network was significantly increased as a function of BMI and BFP.

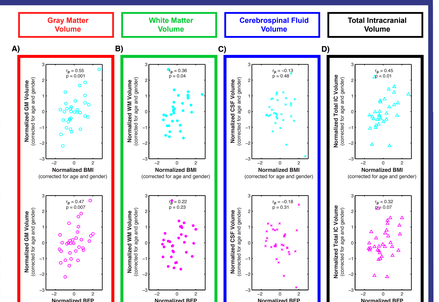


Figure 6: Individual differences in global brain volume related to body composition (i.e., BMI and BFP), corrected for age and gender, and broken down by tissue type.

In summary, we have shown that:

1) two independent measures of body composition (i.e., BMI and BFP) are correlated with aberrant changes in brain structure and functional connectivity, and

2) many of the affected regions/networks offer a biologically plausible explanation for previously reported deficits in reward processing and cognitive performance.

Thanks for stopping by. If you have any questions or would like an electronic reprint of this poster, please contact me at chase.figley@umanitoba.ca

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