Structural connectivity of the reward network in obesity and its association with eating behavior

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Introduction

Obesity or excess bodyweight results from an imbalance in energy expenditure and food intake which is controlled by different neural circuits such as the hypothalamus and the reward network[1]. Central structures of the dopamine-dependent reward network are the nucleus accumbens, the orbitofrontal cortex (OFC), the putamen and the caudate nucleus[2]. Recently, it has been shown that obesity is associated with reduced structural connectivity of this network[3] but it remains unclear whether reduced structural connectivity relates to differences in eating behavior.

Goals: In this study, we aim to replicate and extend previous results on structural connectivity differences in obesity and investigate potential associations with eating behavior.

Research questions: Is obesity (defined as body mass index (BMI) > 30 kg/m^2) associated with white matter structural connectivity of the reward network in healthy adults and are obesity-related structural differences linked to self-reported eating behavior?

Methods

Study sample:

- 146 healthy obese and lean participants from the LIFE ADULT- study[4] (no stroke, major brain pathology or intake of centrally active medication; matched for age, sex and occurence of DTI-artifact)

	lean (N=73)	obese (N=73)
Age in years	48.04±8.23	47.7±9.14
Sex (male/female)	27/46	33/40
Ghost artifact (yes/no)	26/47	31/42
Body mass index (BMI in kg/m^2)	22.86±1.56 (19.1 – 24.99)	33.2±3.4 (30.03 – 50.15)

Magnetic resonance imaging (MRI)(3T Siemens Verio)

- T1-weighted MPRAGE with inversion time: 900 ms, repetition time (TR): 2300 ms, field of view: 256 x 240 x 176, voxel size: 1mm^3
- Diffusion-weighted EPI with TR: 13.8 s, echo time: 100 ms, field of view, 220 x 220 x 123 mm, voxel size of 1.7 mm^3, max b-value = 1000 s/mm^2, 60 directions

Three Factor Eating Questionnaire[5]

- Disinhibition (tendency of disinhibited eating)
- Cognitive control (control exerted over food intake)
- Hunger (subjective hunger feelings)

Preprocessing of MRI data:

- Cortical reconstruction and volumetric segmentation of T1-weighted MR images using Freesurfer v.5.3.0
- Correction of DTI data for susceptibility artifacts and eddy currents, diffusion tensor fitting and deterministic pathway tractography
- Weighted, undirected structural networks from 82 Desikan-Killiany regions with number of streamlines (NOS) and mean fractional anisotropy (FA) as weights
- Structural reward network from bilateral lateral and medial orbitofrontal cortex (OFC), caudate, putamen and accumbens
- Assessed graph metrics: averaged connectivity strength and clustering coefficient (CC) (for NOS and FA), normalized by global network metrics

Statistical analysis:

- Group comparison of graph metrics and behavioral data using independent two-sample t-tests
- Specificity analysis using permutation testing

Results

1

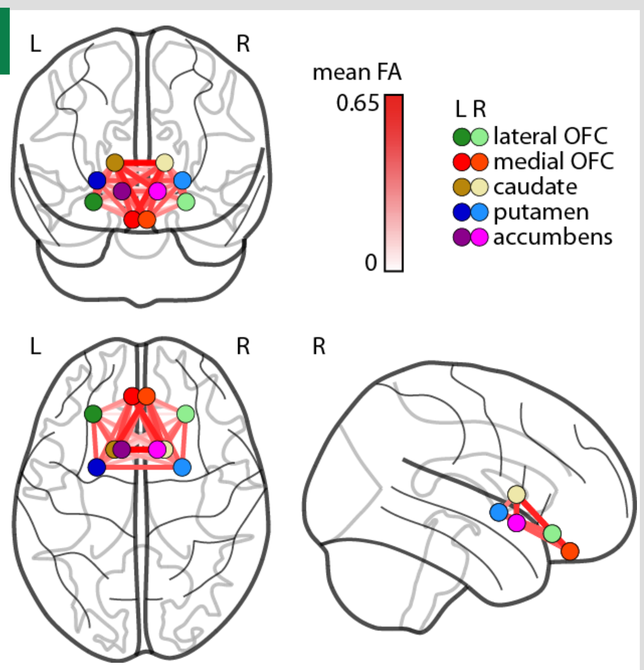

Figure 1: Mean FA connectivity in the reward network, averaged over all streamlines for both groups (N=146). The bilateral caudate connection had the highest mean FA.

2

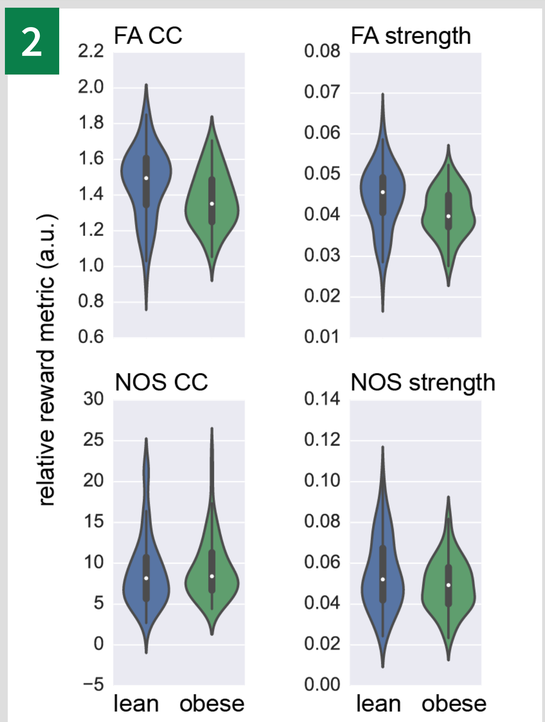

Figure 2: Reduced relative FA strength and FA CC in obese compared to lean participants. No significant difference for NOS strength and NOS CC.

3

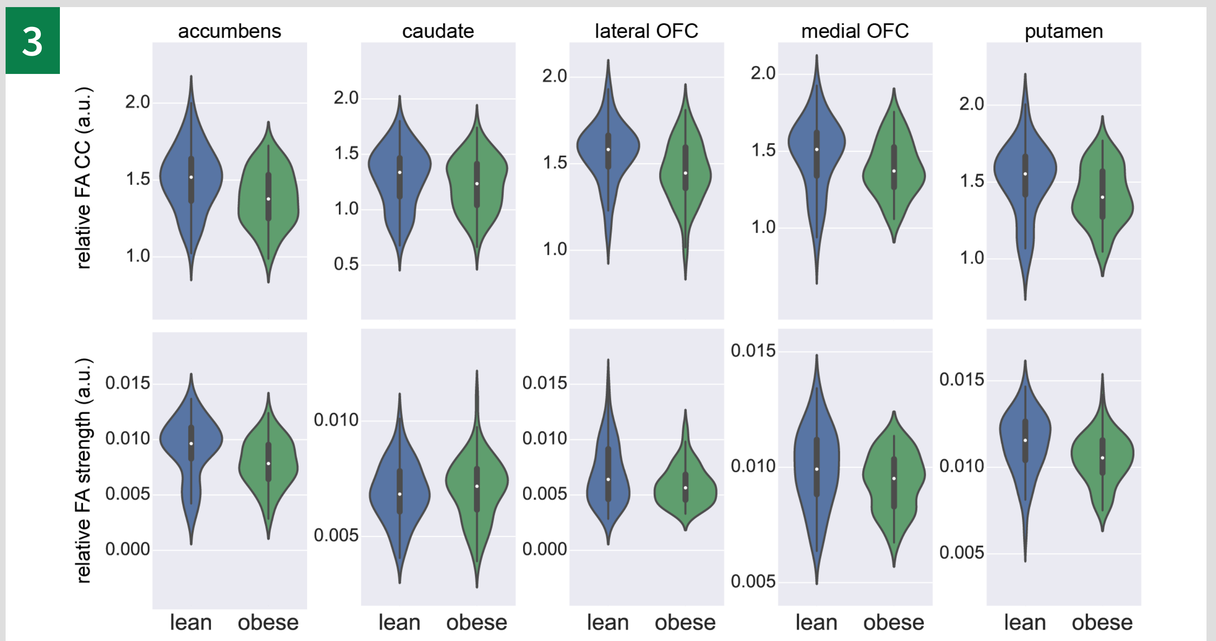

Figure 3: Reduced relative FA strength and CC in accumbens, lateral OFC and putamen of obese compared to lean participants (two sample t-test, all p< 0.01)

Lower reward network structural connectivity in obese compared to lean:
All regions were significantly structurally connected (mean FA > 0, p<0.001, see Figure 1). Relative FA strength and FA CC were significantly reduced in obese compared to lean participants (p<0.0125). Relative mean NOS connectivity strength showed a similar effect but did not survive the Bonferroni-corrected threshold and there was no difference between lean and obese for NOS CC (see Figure 2). Node-wise analyses reveiled that FA strength and clustering coefficient were reduced for accumbens, lateral OFC and putamen but not for caudate and putamen in obese compared to lean participants (see Figure 3).

Specificity of the result for the reward network:
Only 0.5% of random networks had larger group difference T-values in FA strength and CC (nominal p-values: FA strength p=0.0049, FA CC p=0.0042).

Negative association of structural connectivity and TFEQ measures
Obese participants scored significantly higher on the disinhibition and hunger scales of the TFEQ than lean participants. In an exploratory linear regression analysis we used log-transformed disinhibition as an outcome measures and relative FA CC as well as age and sex as predictors and found a negative association of FA CC and log(disinhibition) (N=124, β= -0.19, p=0.032).

4

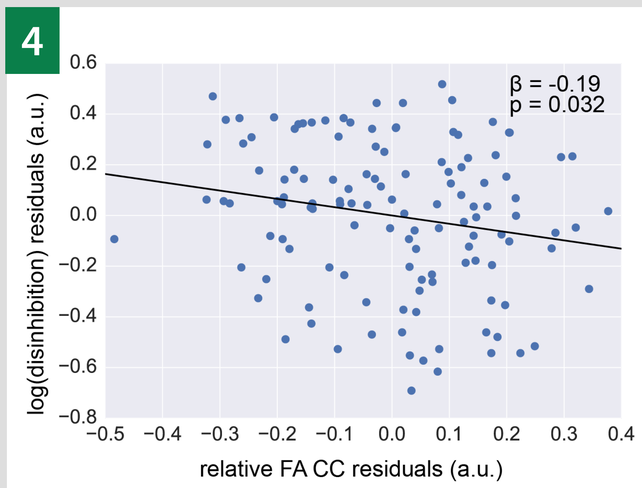

Figure 4: Negative association of FA CC and log(disinhibition) across both groups

Discussion

In line with the literature, we found overall reduced FA strength and CC of the reward network in obese compared to lean participants. NOS connectivity measures did not significantly differ between groups which might be due to the lower sensitivity of this measure, reflecting the mere number of connections. The result was specific for the reward network as shown by comparison to random networks of equal size and laterality. In a node-specific analysis, mean FA strength and CC of accumbens, lateral OFC and putamen were significantly reduced in obese compared to lean participants. OFC and accumbens are important in inferring and signalling reward value[6] and reduced clustering and connectivity strength of these nodes might reflect impaired reward processing in obesity. Based on findings from task-based fMRI studies it has been previously hypothesized that initial hypersensitivity to reward in overweight individuals or those predisposed to obesity promotes overeating which in turn leads to a malfunction of the striatum, further enhancing overeating[7]. In line with this interpretation, we found reduced mean FA strength to be associated with a higher tendency for disinhibited eating when correcting for age and sex.

Reductions of white matter diffusion anisotropy in obesity have been previously reported[8], but it still remains unclear whether these differences are cause or consequence of obesity. Similarly, our cross-sectional data does not allow us to infer causality.

In further studies we thus intend to employ genetic designs such as mendelian randomization and longitudinal data from the follow-up of the LIFE-Adult Study to further investigate the association of obesity and reward network structural connectivity.

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Conference, Year