Alterations in Reward Network Functional Connectivity is Associated with Increased Food Addiction in Obese Individuals

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Background

- Associations have been demonstrated between obesity and abnormal ingestive behaviors, primarily "food addiction," in 40% of individuals seeking bariatric surgery (Pedram et.al, 2013).
- Food Addiction (FA) describes addictive intake of hyperpalatable foods beyond the homeostatic needs of the individual primarily for pleasure (Lerma-Cabrera et.al, 2016; Carter et.al, 2016).
- The Yale Food Addiction Scale (YFAS) is a validated measure that is used as a common diagnostic criteria for substance use to operationalize food addiction (Gearhardt et al., 2009).
- Females with obesity display twice the rate of food addiction and more frequent cravings compared to males (Striegel-Moore et.al, 2009).
- Individuals with obesity and food addiction show greater activation in the reward network, in regions like the basal ganglia, due to the decreased expression of dopamine receptors (Tomasi & Volkow, 2012). The persistent activation of the dopaminergic pathway results in unregulated food intake and impaired inhibitory control (Adinoff et.al, 2004).
- Females with FA display greater activations in regions associated with visual cue identification and emotional regulation compared to male counterparts (Chao et.al, 2017). This could translate to alterations in their responses to negative-emotion-inducing stimuli and increased frequency of emotional overeating (Steward et al., 2017; Wang et.al, 2009).

Aims and Hypothesis

Aims

- To identify differences in resting state connectivity for obese individuals with food addiction compared to those without, as well as sex differences within obese individuals with food addiction.

Hypothesis

- Individuals with food addiction will show greater connectivity in regions of the reward network compared to those with no food addiction
- Females with food addiction will show greater connectivity between the brainstem, salience, and emotional regulation networks compared to their male counterparts

Methods

- 150 participants (females: N=103, males: N=47; food addiction: N=40, no food addiction: N=110) with BMI ≥ 25 kg/m^2 underwent functional resting state MRIs
- Participants were administered the Yale Food Addiction Scale (YFAS), to determine diagnostic criteria for food addiction (YFAS Symptom Count ≥ 3 with clinically significant impairment or distress) and completed ingestive behavior questionnaires.
- Descriptive statistical analyses were performed using SPSS Statistics software and the general linear model (GLM) procedure was utilized to assess group difference between the groups across all clinical variables.
- The following five contrasts were used in our analyses :
  - High FA > Low FA
  - High FA Female > High FA Male
  - High FA Female > Low FA Female
  - High FA Male > Low FA Male
  - Low FA Female > Low FA Male
- Connectivity differences were analyzed using a generic linear model in the CONN Toolbox and images were segmented using the Schaefer 400, Harvard-Oxford Subcortical, and Ascending Arousal Network atlases. Permuted statistical values from ROI-to-ROI analyses were further corrected using the false discovery rate (FDR) with $p_{(FDR)} < 0.05$.
- General Linear Model (GLM) procedure in SPSS was used to compute age-controlled partial correlations between significant brain connectivity and clinical variables ($q_{(FDR)} < 0.05$).

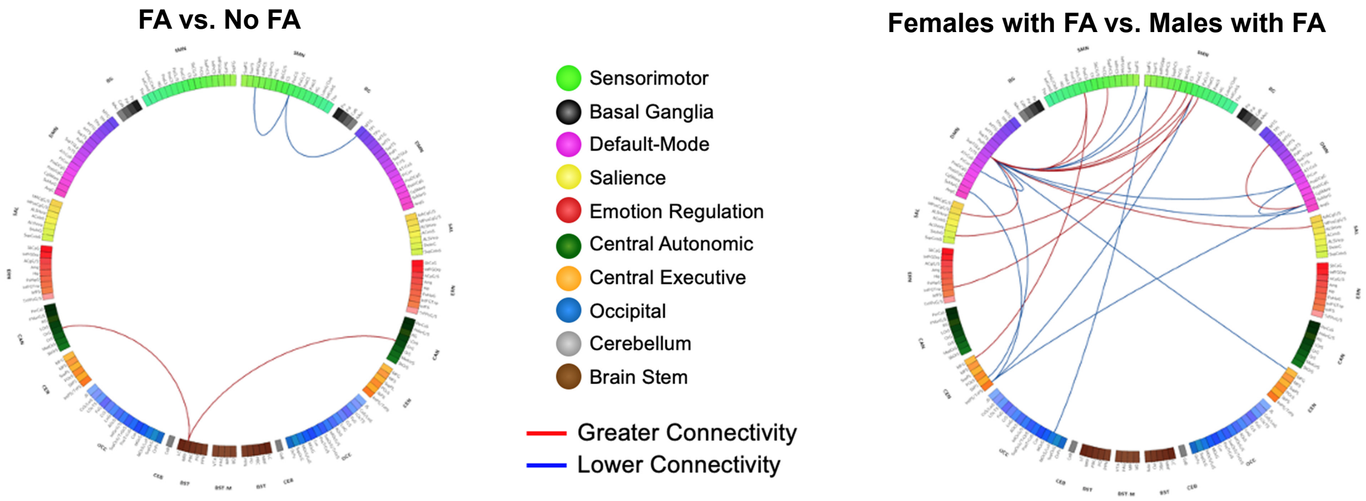
Results

- **Subject Characteristics:**
  - Individuals with FA had higher scores on the General Food Cravings Questionnaire (GFCQT) ($p<0.05$), higher anxiety ($p=0.02$) and depression ($p=2.00E-3$) compared to those with no FA.
  - Males with FA had higher scores on the Given Up ($p=4.00E-3$), Loss of Control ($p=9.00E-03$), and Clinical Significant Impairment components ($p=0.03$) of the YFAS compared to females with FA.
- **Connectivity Differences:**
  - Individuals with FA had greater brainstem connectivity, namely between the brainstem and middle frontal gyrus ($q=0.02$) and bilateral orbital gyri (Left and Right $q=0.02$) compared to those without FA.
  - Females with FA had greater emotional regulation network connectivity between the inferior frontal gyrus and paracentral lobule ($q=0.04$) and greater salience network connectivity between the short insular gyrus and paracentral lobule ($q=0.01$) compared to males with FA.
- **Associations between Brain Connectivity and Clinical Variables:**
  - Brainstem and emotional regulation network connectivity was positively associated with BMI ($r=0.61$, $q=0.04$) in females with FA compared to males with FA.
  - Brainstem (locus coeruleus) and central autonomic connectivity was positively associated with BMI ($r=0.329$, $q=0.01$) and negatively associated with food cravings in individuals with no FA compared to those with FA ($r=0.383$, $q=0.04$).

Table 1. Summary of Connectivity Differences

Network	Food addiction versus no food addiction	Females with food addiction versus males with food addiction	Females with food addiction versus females with no food addiction	Males with food addiction vs. males with no food addiction
Brainstem	Food addiction ↑		Females with food addiction ↑	Males with food addiction ↑↓
Emotional regulation	Food addiction ↓	Females with food addiction ↑	Females with food addiction ↓	
Salience		Females with food addiction ↑		Males with food addiction ↑
Sensorimotor	Food addiction ↓	Females with food addiction ↑	Females with food addiction ↓	Males with food addiction ↓
Central autonomic			Females with food addiction ↑	
Central executive		Females with food addiction ↓	Females with food addiction ↑	
Default mode		Females with food addiction ↓		Males with food addiction ↑

Figure 1. Connectogram of Resting State Connectivity Differences



Summary and Conclusions

- Individuals with food addiction exhibit greater connectivity in reward regions, consistent with the reward deficiency hypothesis which states that a decreased availability of D2 dopamine receptors creates a less responsive reward system (Volkow et.al 2011). To compensate this perpetual hypodopaminergic state, these individuals seek frequent, potent reward stimulation in the form of high sugar/fat foods in the case of food addiction, causing increased levels of food cravings and impaired satiety cues (Davis et.al 2013).
- Females with food addiction showed greater connectivity in emotional regulation and salience regions compared to male counterparts. This aligns with the self-medication model since females with food addiction engage in uncontrollable eating behaviors as an artificial coping mechanism to manage their emotional response to negative stimuli and therefore engage in the chronic consumption of ultra-processed food to lessen their emotional load and satiate their persistent cravings (Geliebter et.al, 2013; Volkow et.al, 2011)
- Greater connectivity in the locus coeruleus could indicate that the maladaptive food behaviors displayed by individuals with food addiction serve as a coping mechanism in response to pathological anxiety and stress (Morris et.al, 2020).
- These mechanistic pathways may have clinical implications for understanding the sex-dependent variability in response to diet interventions.

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