Archival Report

Biological Psychiatry

Ventral and Dorsal Striatum Networks in Obesity: Link to Food Craving and Weight Gain

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ABSTRACT

BACKGROUND: The food addiction model proposes that obesity overlaps with addiction in terms of neurobiological alterations in the striatum and related clinical manifestations (i.e., craving and persistence of unhealthy habits). Therefore, we aimed to examine the functional connectivity of the striatum in excess-weight versus normal-weight subjects and to determine the extent of the association between striatum connectivity and individual differences in food craving and changes in body mass index (BMI).

METHODS: Forty-two excess-weight participants (BMI $>$ 25) and 39 normal-weight participants enrolled in the study. Functional connectivity in the ventral and dorsal striatum was indicated by seed-based analyses on resting-state data. Food craving was indicated with subjective ratings of visual cues of high-calorie food. Changes in BMI between baseline and 12 weeks follow-up were assessed in 28 excess-weight participants. Measures of connectivity in the ventral striatum and dorsal striatum were compared between groups and correlated with craving and BMI change.

RESULTS: Participants with excess weight displayed increased functional connectivity between the ventral striatum and the medial prefrontal and parietal cortices and between the dorsal striatum and the somatosensory cortex. Dorsal striatum connectivity correlated with food craving and predicted BMI gains.

CONCLUSIONS: Obesity is linked to alterations in the functional connectivity of dorsal striatal networks relevant to food craving and weight gain. These neural alterations are associated with habit learning and thus compatible with the food addiction model of obesity.

Keywords: Body mass index change, Excess weight, Food craving, Functional connectivity, Obesity, Striatum

http://dx.doi.org/10.1016/j.biopsych.2015.11.020

In rich societies, the ubiquitous availability of appetizing high-calorie foods has increased the relevance of brain reward systems in governing food intake (1). In this context, recent theories have proposed a food addiction model of obesity, by which sensitization of the brain centers that represent reward and habits (i.e., the striatum) can lead to food craving, inability to cut down food intake, and weight gain (2–4).

The food addiction model is grounded in neuroimaging evidence showing that obese individuals display increased food cue-evoked activation in cortical-striatal regions that code food-related reward value (i.e., ventral striatum) and hedonic properties (i.e., insula/somatosensory cortices) and food choices (i.e., medial prefrontal/orbitofrontal cortex) (5–11). Moreover, food cue-evoked activation in these regions is associated with subjective measures of craving (9–13) and body mass index (BMI) gains (14–16). These regional alterations are plausibly associated with abnormalities in a broader network between the striatum and prefrontal regions representing food value. For example, neuroimaging studies have shown that functional connectivity between the ventral striatum and the medial prefrontal cortex correlates with external food sensitivity in healthy samples (17). Moreover, positron emission tomography studies have shown that obese individuals, akin to addicts, display reduced dopamine D_2 receptors in the striatum (18) linked to lower orbitofrontal cortex metabolism (19).

The food addiction model also assumes that severity of obesity is associated with neuroadaptations in the dorsal striatum network (4). This assumption is based on preclinical studies showing that self-administration of addictive drugs leads to neuroadaptations in the dorsal striatum (2,3,20). This is further illustrated by human neuroimaging studies on drug craving: in severe substance users, drug-related cues activate dorsal striatum regions implicated in habits processing (21,22). Therefore, dorsal striatal neuroadaptations have been implicated in the transition between incentive-based and habit-based control of behavior. Hence, greater involvement of the dorsal striatum is predicted as food intake becomes addictive or compulsive (3,4). In obese patients, high-calorie food intake is subjectively perceived as less pleasurable but strongly driven by habits (23,24), and they show increased dorsal striatum activation in response to food cues (6,7,25) and reduced activation during food receipt (6,7).

Altogether, ventral and dorsal striatum networks are relevant to the pathophysiology of obesity and to the association

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ISSN: 0006-3223

between obesity and addiction-related characteristics, such as craving and persistent high-calorie food intake. We aimed to contrast the functional connectivity of ventral and dorsal striatum networks in excess-weight versus normal-weight participants and to determine the association between functional connectivity in the striatum and individual differences in food craving and weight gain. We applied a seed-based resting-state functional connectivity approach to assess ventral and dorsal striatum networks (26). Resting-state fluctuations reflect cognitive and emotional biases that contribute to shape individuals' preferences; thus, striatal connectivity measures may have predictive validity in relation to craving and food intake (27,28). We hypothesized that excess-weight participants compared with normal-weight control subjects would show increased functional connectivity in the ventral and dorsal striatum. Increased dorsal striatal connectivity would be associated with greater food craving and weight gain.

METHODS AND MATERIALS

Participants

Forty-two subjects with excess weight (BMI >25) and 39 subjects with normal weight enrolled in the study. Participants were recruited via general hospitals and community advertisement (i.e., local press, radio, and social media) and enrolled if they were aged 18 to 45 and had BMI >18. Exclusion criteria were 1) history of brain injury or diseases impacting the central nervous system; 2) history of substance use, major depression, or psychosis; 3) self-reported use of psychotropic medication; and 4) morbid obesity (BMI ≥ 40). The two groups had similar sociodemographic characteristics (Table 1). The Universidad de Granada Human Research Ethics Committee approved the study, and all participants provided informed consent.

Participants were involved in two assessment sessions. At baseline, they 1) were measured and weighed to calculate BMI via an automated scale; 2) underwent a functional magnetic resonance imaging (fMRI) scan; 3) rated their food craving immediately after fMRI scan; and 4) had a 30-minute diet counseling session with a professional dietitian who provided specific strategies to lose weight (i.e., excess-weight group only). At 12-week follow-up, excess-weight participants (n = 28, 67% of the original sample) were reassessed to calculate change in BMI relative to baseline. Twelve weeks is the standard benchmark to assess the outcome of weight loss interventions (29).

Measures

Imaging Data Acquisition and Preprocessing. All participants were scanned at the same time of the day (4:00 to 6:00 PM) and after lunch, which is typically between 2:00 and 4:00 PM. Prescanner ratings of hunger (0–100 visual analog scale [VAS]) did not differ between groups (Table 1). Participants underwent a 6-minute resting-state scan. They were instructed to lie still with eyes closed. We used a 3.0 Tesla clinical magnetic resonance imaging scanner, equipped with an eight-channel phased-array head coil (Intera Achieva Philips Medical Systems, Eindhoven, The Netherlands). A T2*-weighted echo-planar imaging was obtained (repetition time = 2000 ms, echo time = 35 ms, field of view = 230 × 230 mm, 96 × 96 pixel matrix; flip angle = 90º, 21 4-mm axial slices, 1-mm gap, 180 whole-brain volumes). The sequence included four initial dummy volumes to allow the magnetization to reach equilibrium.

Food Craving. Participants viewed six photographs of highly appetizing food stimuli, all rich in sugar and fat content (e.g., cheesecake, chocolate), and were instructed to rate their level of craving using VAS (range 0–10). The dependent measure was the mean score of the six VAS ratings. To increase the task's validity, all participants were pre-exposed to these foods in a catered tasting session conducted 1 week before the scan (Supplemental Figure S1).

Table 1. Demographics and Clinical Characteristics of the Study Groups

	Normal Weight (n = 39)	Excess Weight (n = 42)
Age (Years)	33.07 (6.73)	33.59 (6.16)
Education (Years)	18.18 (3.75)	17.50 (3.77)
Sex (Men/Women)	18 (46.2%)/21 (53.8%)	20 (47.6%)/22 (52.4%)
BMI Baseline (kg/m^2)[a,b]	22.09 (1.74)	30.51 (3.63)
BMI Change (kg/m^2)[c,d]	−.03 (.72)	−.60 (1.66)
Food Craving	5.47 (1.36)	5.93 (1.39)
Hunger Before fMRI	15.03 (19.07)	16.27 (18.72)
Hunger After fMRI	39.59 (28.62)	44.20 (25.45)
Impulsivity (Delay Discounting Area Under the Curve)[e]	.55 (.19)	.58 (.23)
Compulsivity (Reversal Learning Perseveration Error Rate)[f]	1.66 (.69)	1.67 (.74)

Except for sex, all values are mean (± SD).
BMI, body mass index; fMRI, functional magnetic resonance imaging.
[a] $p \leq .01$.
[b] BMI minimum/maximum values, normal weight 19/24.8, excess weight 25.20/38.30.
[c] Data for 24 normal-weight and 28 excess-weight participants at 12 weeks follow-up.
[d] Minimum/maximum values, normal weight −1.70/1.30, excess weight −4.60/4.70.
[e] Data from two normal-weight and two excess-weight participants are missing.
[f] Data from one excess weight are missing.