Characterizing impulsivity and resting-state functional connectivity in normal-weight binge eaters

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Abstract

Objective: Binge eating is characterized by episodes of uncontrolled eating, within discrete periods of time. Although it is usually described in obese individuals or as a symptom of Binge Eating Disorder (BED), this behavior can also occur in the normal-weight (NW) population. An interesting premise suggests that impulsivity might contribute to the onset of binge eating and the progression toward weight gain. Drawing upon this evidence, here we explored impulsivity in NW individuals reporting binge-eating episodes through a functional connectivity approach. We hypothesized that, even in the absence of an eating disorder, NW binge eaters would be characterized by connectivity pattern changes in corticostriatal regions implicated in impulsivity, similarly to the results described in BED individuals.

Methods: A resting-state functional magnetic resonance imaging study tested 39 NW men and women, with and without binge eating (binge eaters, BE and non-BE). Brain functional connectivity was explored by means of graph theoretic centrality measures and traditional seed-based analysis; trait impulsivity was assessed with self-report questionnaires.

Results: The BE group was characterized by a higher degree of trait impulsivity. Brain functional connectivity measures revealed lower degree centrality within the right middle frontal gyrus, left insula/putamen and left temporoparietal regions and a lower functional connectivity between the right middle frontal gyrus and right insula in the BE group.

Discussion: The results support previous evidence on BED of altered functional connectivity and higher impulsivity at the roots of overeating behavior, but further extend this concept excluding any potential confounding effect exerted by the weight status.

KEYWORDS
binge eating behavior, functional connectivity, functional magnetic resonance imaging, impulsivity, normal weight, resting-state

INTRODUCTION

Binge eating is characterized by episodes of rapid food intake within a short period of time, accompanied by a feeling of loss of control. Although it is usually described as a symptom of binge eating disorder.
(BED) or bulimia nervosa (BN), binge eating can also occur in healthy individuals. In such circumstances, the loss of control eating is not accompanied by one or more of the criteria defining a full-syndrome of BED (i.e., objective large size of the binge, frequency of bingeing, marked distress) or BN (i.e., compensatory behaviors such as self-induced vomiting or laxative/diuretic abuse; American Psychiatric Association, APA, 2013; Cotrufo, Barretta, Monteleone, & Maj, 1998). Nevertheless, when binge eating becomes more frequent and compulsive over time, it can eventually lead to weight gain, obesity and BED (Davis, 2013; Stice, Marti, & Rohde, 2013); hence, increasing attention has been devoted to understanding the cognitive and neural mechanisms that may represent potential contributing factors for the development of overeating. One compelling premise places impulsivity at the roots of loss of control eating (Loxton, 2018) and both behavioral and neurobiological investigations seem to support this hypothesis. On the behavioral side, higher trait impulsivity and poor motor inhibitory control have been highlighted in both obese individuals with BED and BN individuals (Claes, Vandereycken, & Vertommen, 2005; Meule, 2013; Wu et al., 2013). On the neural side, task-based functional magnetic resonance imaging (fMRI) studies reveal that both BED and BN are associated with alterations within the corticostratial circuits, with functional changes of the prefrontal cortex (PFC), anterior cingulate cortex, striatum, and insula (Donnelly et al., 2018; Kessler, Hutson, Herman, & Potenza, 2016). All these regions have distinct but central roles in self- and eating regulation (Davis et al., 2013; Everitt et al., 2008; Small, 2010): the PFC allows the modulation of responses to environmental stimuli by exercising top-down inhibitory control (Miller & Cohen, 2001), the striatum underlies habits formation and reward sensitivity (Corbit & Janak, 2010), while the insula is involved in interoception and feeding regulation (Everitt et al., 2008; Small, 2010). Altogether, the evidence indicates that BED and BN may be characterized by functional changes—mainly a decreased activity—within the same networks supporting behavioral regulation and impulsivity, namely the frontostriatal circuitry (Donnelly et al., 2018).

1.1 | Resting-state fMRI investigations of binge eating

In the last decade functional connectivity approaches have been developed, aiming at providing a description of how multiple brain regions interact and how this may relate to cognitive, behavioral or personality aspects (Rosazza & Minati, 2011). Among these, resting-state fMRI (rsfMRI) allows for the investigation of spontaneous fluctuations of blood-oxygen level-dependent (BOLD) signal arising from neuronal activity, when participants are at rest and not engaged in any particular task (Biswal, 2012). This approach aims to identify task-independent and more fundamental functional patterns underlying different states and/or disorders (Fox & Greicius, 2010). RsfMRI has been adopted to describe functional connectivity in relation to eating and weight disorders (García-García et al., 2015; Stopyra et al., 2019), and preliminary evidence converges in identifying altered functional connectivity patterns in regions mainly implicated in impulsivity-related aspects (such as, prefrontal, subcortical and parietal regions) in overeating conditions (García-García et al., 2015; Moreno-Lopez, Contreras-Rodriguez, Soriano-Mas, Stamatakis, & Verdejo-Garcia, 2016; Park, Seo, & Park, 2016). For example, functional connectivity changes within the frontoparietal circuit have been linked to dis-inhibited eating behavior (as assessed by Three Factor Eating Questionnaire, TFEQ; Stunkard & Messick, 1985) and body mass index (BMI) in normal- and overweight individuals (Park et al., 2016). Additionally, using a graph theory approach (Bullmore & Sporns, 2009), García-García et al. (2015) report that obese individuals—compared to healthy-weight controls—are characterized by a lower degree centrality (see Section 3.2 of this article for details on degree centrality) within the right middle frontal gyrus (MFG), a region part of the dorso-lateral PFC known to be involved in inhibitory control and monitoring of behavior (Bari & Robbins, 2013).

However, most of previous studies trying to characterize impulsivity as a possible key factor at the roots of eating disorders consider overweight populations with a history of weight gain and overeating. The combination of these two factors prevents from disentangling whether the reported functional changes are either reconfigurations of the brain connectivity as a result of weight gain, or possible pre-existing predisposing factors for weight gain. Hence, the neural underpinnings of binge-eating behavior may be unraveled by the study of binge-eating behavior in a normal-weight (NW) population.

1.2 | Objective

The present study sought to characterize behavioral and neural correlates of impulsivity in NW individuals with binge eating. To this purpose, we recruited two groups of individuals, one with and one without binge-eating episodes (BE and non-BE, respectively) and collected: (a) trait impulsivity measures and (b) rsfMRI data. Given the well-established association between impulsivity and overeating (Meule, 2013), we expected to observe higher trait impulsivity in BE compared to non-BE. Moreover, consistent with the evidence of altered connectivity between cortical “control” regions and subcortical “drive” structures in highly impulsive individuals (Davis et al., 2013), which may reflect a failure in cognitive control over the drive for immediate rewards, we hypothesized to observe a similar result for BE compared to non-BE in those regions involved in inhibitory and reward-related processes (i.e., prefrontal and subcortical regions). Drawing upon the evidence on the neural basis of BED and BN (Donnelly et al., 2018) and obesity (García-García et al., 2015; Baek et al., 2017), we expected BE to be characterized by a decreased connectivity within the frontostriatal circuit, compared to non-BE. Lastly, we expected these differences to be correlated with trait impulsivity measures.

To our knowledge, this is the first study investigating the link between functional connectivity pattern and impulsivity in a non-clinical population of NW binge eaters. The comparison of groups of individuals with and without binge eating may be informative in describing the role of impulsivity as a potential neurobehavioral...
substrate of such behavior, without overweight and obesity-related confounding effects.

2 | METHODS

2.1 | General procedure

Participants were recruited through local advertisements at the University of Padua. During the initial screening, participants were requested to fill out an ad-hoc questionnaire to verify the absence of exclusion criteria for the study (Section 2.2) and a self-report assessment of eating behavior and impulsivity (Section 2.3); and to report their height and weight in order to compute BMI. If they did not meet any of the exclusion criteria, the MR measurement was scheduled for a subsequent appointment (approximately 1 week after the screening). Given that hunger might be an additional factor to consider in the assessment of resting-state brain activity, we ensured comparable hunger states of participants by instructing them not to come hungry to the imaging session and to consume a small meal right before their appointment (Loeber et al., 2013; Price et al., 2016). Hence, participants were asked to refrain from drinking caffeinated beverages and from smoking for 3 h preceding their MRI session, which took part between 2 p.m. and 6 p.m. The study was conducted according to the guidelines provided by the Declaration of Helsinki and the ethical requirements of the University of Padua (protocol n. 2025).

2.2 | Participants

We recruited normal-weight (NW) male and females, from 20 to 35 years old and divided them in two groups according to the occurrence of binge eating episodes. Binge eating status was certified by means of the behavioral questions of the eating attitude test (EAT 26—Garner, Olmsted, Bohr, & Garfinkel, 1982), assessing the presence of binge eating episodes and the absence of compensatory behaviors (i.e., excessive physical activity, purging etc.). Participants reporting at least one binge eating episode per month in the last 3 months constituted the BE group, while participants declaring to have never had binge eating episodes in the past constituted the non-BE group. To further confirm the surmised binge eating status we used the binge eating scale (BES—Gormally, Black, Daston, & Rardin, 1982): participants who reported no episodes of overeating were expected to score lower than 8 in the BES to be included in the non-BE group (Filbey, Myers, & Dewitt, 2012).

Participants of both groups had a BMI (kg/m²) ranging from 18.5 to 24.9 (World Health Organization [WHO], 1995) and were righthanded according to the Edinburgh Handedness Inventory (EHI—Oldfield, 1971). For both groups specific exclusion criteria had to be fulfilled (i.e., no history of psychiatric, neurological disorders or head injuries, absence of relevant medical issues, psychoactive medication or psychotherapy). Further, all participants had to be checked with safety criteria for MRI examination (e.g., metal implants, pacemaker, claustrophobia, etc.). The final sample involved 21 participants for the BE group (17 females) and 21 participants for the non-BE group (16 females).

This study is part of a broader line of research that aims to characterize the role of impulsivity at the roots of binge eating behavior. The samples included in this study partially overlap with those described in a previous task-based fMRI investigation (Oliva, Morys, Horstmann, Castiello, & Begliomini, 2019).

2.3 | Measures: Self-reported questionnaires

All participants completed self-reported assessment related to eating behavior and impulsivity, including:

1. EAT 26 (Garner et al., 1982): a questionnaire assessing the characteristic symptoms and concerns of eating disorders (e.g., dieting, food preoccupation, oral control). In the present research, we focused on the behavioral questions of the questionnaires (Section 2.1).
2. BES (Gormally et al., 1982): a 16-items questionnaire used to assess binge-eating behavior with questions based upon both behavioral characteristics (e.g., amount of food consumed) and the emotional, cognitive response (e.g., guilt/shame, preoccupation with food and eating).
3. Yale Food Addiction Scale (YFAS—Gearhardt, Corbin, & Brownell, 2009): a self-reported measure used to identify those who are most likely to be exhibiting markers of substance dependence with the consumption of high-calorie foods.
4. Barratt Impulsiveness Scale (BIS-11—Patton, Stanford, & Barratt, 1995): a 30-items self-reported questionnaire yielding impulsivity measures on three scales: attentional (inability to focus or concentrate), motor (tendency to act without thinking) and nonplanning impulsivity (lack of future planning and forethought). The BIS-11 has acceptable internal consistency (Cronbach’s alphas ranging from .79 to .83; Patton et al., 1995). In the current sample, the internal consistency was good for the BIS-11 total scale (Cronbach’s $\alpha = .82$) and all the subscales: attentional impulsiveness (Cronbach’s $\alpha = .65$), nonplanning impulsiveness (Cronbach’s $\alpha = .71$) and motor impulsiveness (Cronbach’s $\alpha = .66$).
5. Behavioral inhibition/behavioral activation systems scale (BIS/BAS—Carver & White, 1994): a 24-items questionnaire that assesses individual differences in the sensitivity of two attitudinal styles. The BAS regulates appetitive motives, whose goal is to move toward something desired, while the BIS refers to the motivation of avoiding aversive outcomes. This scale yields four factors: a single BIS subscale and three BAS subscales: Reward responsivity, drive, and fun seeking. In the current sample, the BIS/BAS total scale had good internal consistency (Cronbach’s $\alpha = .81$). Internal consistency was good for the BIS subscale (Cronbach’s $\alpha = .8$), for Reward Responsivity (Cronbach’s $\alpha = .67$) but low for Fun Seeking (Cronbach’s $\alpha = .59$) and the Drive subscale (Cronbach’s $\alpha = .39$). Hence, the last two subscales were excluded from the analyses.
2.4 | Magnetic resonance imaging

2.4.1 | Acquisition

Whole-brain fMRI data were obtained using a 1.5 T Siemens Avanto MRI scanner (Siemens Medical Systems, Erlangen, Germany) equipped with a standard Siemens eight-channel coil. Two-hundred and forty resting-state functional volumes were collected using a gradient-echo, echo-planar (EPI) T2* weighted sequence (37 contiguous axial slices, ascending interleaved sequence, 56 × 64 voxels, 3.5 mm × 3.5 mm × 4.0 mm resolution, Field of View, FOV = 196 mm × 224 mm, flip angle = 90°, TE = 49 ms). Volumes were acquired continuously with a repetition time (TR) of 3 s. The fMRI measurement lasted 12 min, during which participants were lying down and wore LCD video goggles (VisuaStim XGA, Resonance Technology Inc., resolution 800 × 600, refresh rate 60 Hz), and were instructed to rest and look at a fixation cross (overlaid onto a black background) at the center of the screen. A high resolution structural scan was collected using T1-weighted 3D_MPRAGE sequence in sagittal orientation (duration = 9 min; 224 sagittal slices; FOV = 320 × 320; 0.7 mm isotropic voxels, TR = 20 ms, TE = 4.89 ms; flip angle = 20°; band = 130 Hz/Px).

2.4.2 | Preprocessing

Data were preprocessed and analyzed using SPM12 (www.fil.ion.ucl.ac.uk/spm) working in Matlab environment (MathWorks, Natick, MA). The ArtRepair (AR) toolbox was used to detect slices corrupted by event-related motion artifacts and/or signal spikes. Preprocessing steps included (a) realignment, (b) co-registration, (c) normalization. After these steps, the WM and CSF signals were masked out and global AR was applied to detect outlier volumes. The final output was a 4D residual functional timeseries in native space for each participant. These data were registered to the MNI152 template with 3-mm resolution using affine transformation. Spatial smoothing, with a 6 mm FWHM Gaussian kernel was applied after centrality measures and/or signal spikes. Preprocessing steps included (a) realignment, (b) co-registration, (c) normalization. After these steps, the WM and CSF signals were masked out and global AR was applied to detect outlier volumes. The final output was a 4D residual functional timeseries in native space for each participant. These data were registered to the MNI152 template with 3-mm resolution using affine transformation. Spatial smoothing, with a 6 mm FWHM Gaussian kernel was applied after centrality measures and seed-based connectivity analyses (Alakörrkö et al., 2017). After preprocessing, the images of one woman participant of the non-BE group and two women participants of the BE group had to be excluded from the analysis due to artifacts in the data acquisition. The resulting sample was 20 non-BE and 19 BE.

2.4.3 | fMRI analysis: Functional connectivity measures

We used Graph theory approaches to assess between-group differences in local and global functional connectivity (Bullmore & Sporns, 2009). Graph theory methods provide metrics of centrality: they enable the localization of important brain regions (i.e., central hubs) considering the connection patterns associated with them (Buckner, Sepulcre, & Talukdar, 2009; Zuo et al., 2012). In this study, we used two centrality measures: Degree and eigenvector centrality (DC and ECM, respectively; Bullmore & Sporns, 2009).

In more detail, DC attributes a value to a voxel on the basis of its connections to other voxels in the brain: the more the connections, the stronger the value (Buckner et al., 2009). In more concrete terms, DC provides information on the integrity of the resting state networks (Fox & Greicius, 2010). On the other side, ECM enables the identification of nodes connected to hubs (i.e., central nodes) of specific networks and assumes that a node is relevant if its neighbors are central within the network (Lohmann et al., 2010; Zuo et al., 2012). Since a node might have high DC while having a low ECM or vice-versa, the combined use of both metrics might give a comprehensive account of the functional connectivity within the network (Lohmann et al., 2010).

For DC, we computed individual correlation maps within gray matter using AFNI (3dDegreeCentrality; Cox, 1996) as implemented in the Nipype framework (Gorgolewski et al., 2011). According to García-García et al. (2015), we thresholded the resulting maps at a value of r = 0.5, where only values above this threshold were considered for the second level analysis. For ECM, individual maps were computed within gray matter using AFNI (3dECM; Cox, 1996) within the Nipype framework. Here, the sparsity was set to 1%, which means that only the strongest 1% of correlations was considered for the second level analysis. For both analyses, the signal of white matter and cerebrospinal fluid was removed.

2.4.4 | fMRI analysis: Seed based connectivity

The analysis of connectivity patterns was complemented by seed-based connectivity analysis (SCA; Fox & Greicius, 2010). In SCA, connectivity is computed as the correlation of time series within a seed with all other voxels in the brain. We chose as seeds the areas showing group differences in functional centrality measures. We extracted mean time series for each of the resulting seed and correlated it with remaining voxels in the brain within an identical whole-brain brain mask for each participant (Pearson’s correlation). This analysis was done using a custom-made script within the Nipype framework. Resulting connectivity maps were then Fisher-z transformed and entered into the second level analysis.

2.4.5 | Second-level analyses

Second-level analyses were conducted with SPM12. Differences in resting-state functional connectivity were assessed through a two-step procedure. First, ECM and DC maps for BE and non-BE were compared, in order to assess differences in functional centrality. Second, brain regions showing significant differences in ECM and DC maps were entered into the seed-based analysis, comparing the individual correlational maps between the two groups. In all second-level analyses, BES individual scores were entered as covariate to control for the possible effect of this variable. Since BES score was the criterion used to assign participants to one of the two groups, the inclusion
of this value in the model allowed us to both maintain the differences between the groups regarding this variable and to control for within-group differences in the interpretation of the results. In addition, in order to control for the potential impact of weight status on resting-state brain activity, we include BMI as a covariate in all second-level analyses. Statistical images were first assessed for cluster-wise significance with a primary cluster-defining threshold of \( p = .001 \), then the thresholded cluster was considered significant at a FWE rate of \( p < .05 \).

### 2.4.6 | Brain-behavior correlations

To directly investigate the relationship between brain and behavioral measures, we tested the correlation between resting-state centrality data and self-reported measures. Using "MarsBaR" toolbox (Brett, Anton, Valabregue, & Poline, 2002), we extracted the parameters of two clusters highlighting significant differences between the groups in DC analysis. Next, a correlation of the resulting values with the total and subscales' scores of the BIS-11 was performed with SPSS.

### TABLE 1  Descriptive characteristics: Between-group comparisons for age, body mass index and self-reported measures

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>BE (n = 19) M ± SD</th>
<th>Non-BE (n = 20) M ± SD</th>
<th>Two-sample t-test t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>23.89 ± 3.4</td>
<td>25.31 ± 3.2</td>
<td>1.35</td>
<td>.186</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.53 ± 2.04</td>
<td>21.25 ± 2.07</td>
<td>1.94</td>
<td>.06</td>
</tr>
<tr>
<td>BES</td>
<td>17.79 ± 3.7</td>
<td>3.3 ± 2.3</td>
<td>14.6</td>
<td>&lt;.001**</td>
</tr>
<tr>
<td>YFAS</td>
<td>3.05 ± 1.5</td>
<td>0.25 ± 0.5</td>
<td>7.78</td>
<td>&lt;.001***</td>
</tr>
</tbody>
</table>

**BIS-11**

- Attentional subscale: 17.58 ± 3.7 vs. 15.15 ± 3.2 (t = 2.2, p = .035*)
- Motor subscale: 20.68 ± 4.2 vs. 18 ± 3.4 (t = 2.2, p = .034*)
- Nonplanning subscale: 25.63 ± 5.8 vs. 22.55 ± 4.2 (t = 1.9, p = .006***)
- Total score: 63.9 ± 11.3 vs. 55.7 ± 7.9 (t = 2.6, p = .013*)

**BIS/BAS**

- BAS reward responsiveness: 7.95 ± 2.2 vs. 8.35 ± 2.6 (t = 0.51, p = .612)
- BIS: 13.68 ± 2.5 vs. 16.85 ± 3.8 (t = 3.07, p = .004***)

Abbreviations: BAS, behavioral activation system; BE, binge eaters; BES, binge eating scale; BIS, behavioral inhibition system; BIS-11, Barratt impulsiveness scale; BMI, body mass index; M, mean; Non-BE, non-binge eaters; SD, standard deviation; YFAS, Yale food addiction scale. Significance is indicated by the asterisks (*\( p < .05 \); **\( p < .01 \); ***\( p < .001 \)).
23 software. Spearman’s correlations were considered significant at the level of .01 (two-tailed).

3 | RESULTS

3.1 | Descriptive characteristics and self-reported measures

Table 1 shows the descriptive characteristics and results of self-reported measures of the groups (BE = 19; non-BE = 20). BE and non-BE groups did not differ for BMI, age and sex (men: ~30%). The BE group scored higher in the measures of impulsivity toward food (BES, YFAS), general trait impulsivity (BIS-11 total and subscales’ scores). The non-BE group scored higher in the BIS subscale of the BIS/BAS questionnaire.

3.2 | Centrality measures: Degree centrality

The comparison "non-BE > BE" showed a lower DC for BE in the right MFG, left middle/inferior temporal cortex, left superior parietal lobe, and left insula. The opposite comparison ("BE > non-BE") did not yield any significant result (Figure 1; Table 2).

3.3 | Centrality measures: Eigenvector centrality

No differences were observed in ECM. Thus, SCA was run based on DC results only.

3.4 | Seed-based connectivity analysis

All the results described in the following paragraphs are ascribable to DC parameters only.

3.4.1 | Seed: Right middle frontal gyrus

BE participants exhibited lower functional connectivity compared to non-BE between the seed located in the right MFG and: (a) right anterior insula and (b) right middle/inferior frontal gyrus. The opposite

<table>
<thead>
<tr>
<th>Cluster</th>
<th>Peak</th>
<th>MNI</th>
<th>Side</th>
<th>Region</th>
</tr>
</thead>
</table>
|         | k    | p(FWE-corr) | t     | z     | x | y | z |              |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      |               |      | mea

Notes: t and z scores; stereotactic coordinates according to the MNI space; brain side and region. Statistic threshold: Results were considered significant at $p < .001$ that additionally met a FWE correction at cluster level ($p < .05$).

Abbreviations: BE, binge eaters; non-BE, non-binge eaters; FWE, family wise error; k, number of voxels; L, left; R, right.

FIGURE 2  Seed-based connectivity: Middle frontal gyrus. Figure shows results for the non-BE > BE comparison, with right middle frontal gyrus as seed. Statistical parametric maps were overlaid onto Montreal Neurological Institute (MNI) render, provided by the MRicroGL software. The color bar is representative of the t-scores given in the table below. Images are shown in neurological convention [Color figure can be viewed at wileyonlinelibrary.com]
TABLE 3  Seed-based connectivity: right middle frontal gyrus

<table>
<thead>
<tr>
<th>Cluster</th>
<th>Peak</th>
<th>MNI</th>
<th>Side</th>
<th>Region</th>
</tr>
</thead>
<tbody>
<tr>
<td>k</td>
<td>p(FWE-corr)</td>
<td>t</td>
<td>z</td>
<td>x</td>
</tr>
<tr>
<td>35</td>
<td>0.025</td>
<td>4.71</td>
<td>4.11</td>
<td>42</td>
</tr>
<tr>
<td>34</td>
<td>0.029</td>
<td>4.62</td>
<td>4.04</td>
<td>27</td>
</tr>
</tbody>
</table>

Notes: t and z scores; stereotaxic coordinates according to the MNI space; brain side and region. Statistic threshold: Results were considered significant at p < .001 that additionally met a FWE correction at cluster level (p < .05).

Abbreviations: BE, binge eaters; non-BE, non-binge eaters; FWE, family wise error; k, number of voxels; L, left; R, right.

comparison (non-BE > BE) did not reveal any significant results (Figure 2; Table 3).

3.4.2  Seeds: Left putamen; left inferior temporal gyrus; left superior parietal lobule

For all the remaining seed regions, SCA did not reveal any significant result for both contrasts (BE > non-BE; non-BE > BE).

3.5  Brain-behavior correlations

Drawing upon the relevance of the corticostriatal network at the roots of behavioral inhibition and impulsivity (Fuster, 2002), we tested the correlations between the extracted DC parameters of the clusters—resulting from the DC analysis—in the right MFG and left insula/putamen and the BIS-11 total and subscales scores. No significant correlations with the subscales and total scores of the BIS-11 were found, neither for the right MFG nor for the left insula-putamen (Table S2).

4  DISCUSSION

In the present research, we characterized impulsivity as a trait and as functional connectivity pattern during resting-state in NW individuals with binge eating but without any weight or eating disorders. As hypothesized, the groups showed different levels of general trait impulsivity, assessed by the BIS-11 (Patton et al., 1995). In line with previous evidence (Lyke & Spinella, 2004; Meule, 2013), BE had higher scores in the motor, nonplanning and attentional subscales, indicating higher impulsive tendencies not only towards food but also expressed in general terms. Furthermore, BE exhibited lower scores in the BIS subscale: this subscale measures the regulation of aversive motives (Carver & White, 1994), and lower scores in the BE might indicate a diminished tendency for avoidance and a greater propensity to respond in this group. Contrary to our expectations, the groups did not differ in the reward responsiveness subscale of the BIS/BAS questionnaire. Since this subscale refers to reward in a general sense (not specifically to food), it could be that our groups did differ for sensitivity to reward concerning food but not for sensitivity toward generic rewards.

With regard to functional centrality, we highlighted between-group differences in DC but not in ECM. The lack of significant between-group differences in the ECM, even if consistent with previous results in obese individuals (García-García et al., 2015), is hard to interpret and needs additional exploration. Nevertheless, this result may suggest that the changes in BE are more related to differences in terms of number of connections of the nodes (i.e., DC indexes) rather than differences in their eigenvector value. The DC analysis indeed revealed that BE, compared to non-BE, had a lower DC in the right MFG, left anterior insula/putamen, inferior temporal gyrus and superior parietal lobule. These regions are known to be involved in inhibitory control (right MFG and insula-putamen; Fuster, 2002), interoception (anterior insula; Craig, 2002) and multimodal sensory integration (temporal and parietal regions; Macaluso & Driver, 2005). A recent fMRI study also reported lower functional connectivity in some overlapping regions (i.e., insula, temporal cortex and the dorsal-lateral PFC—including the right MFG) in overweight adolescents compared to lean counterparts (Moreno-Lopez et al., 2016).

In line with our hypothesis, we found a lower DC in the right MFG. Recently, rsfMRI evidence has revealed changes in functional connectivity in networks important for executive control (i.e., PFC), in overweight and obese individuals compared to NW (Kullmann et al., 2013), and lower DC in the MFG has been described in obese compared to NW adults (García-García et al., 2015). In the latter study, lower DC in the MFG appeared to characterize brain activity during both a resting-state condition and a visual task performance. The authors concluded that the MFG might represent a key region in the pathophysiology of obesity (García-García et al., 2015). Of relevance to this study, we have previously demonstrated differences in the right MFG between NW BE and non-BE in a task-based fMRI investigation focusing on the neural correlates of food-specific response inhibition in binge eating (Oliva et al., 2019). Specifically, the results revealed a differential engagement of frontostriatal regions between the groups during a food-specific Go/No-Go task: the BE showed lower activation of the right MFG, putamen and temporoparietal regions, compared to non-BE, while performing the task (Oliva et al., 2019). The consistent involvement of the right MFG—both at rest and
during the task—suggests that this region might be pivotal for inhibitory mechanisms at the roots of overeating conditions. Moreover, since the differences in brain activity ascribable to the right MFG seem to arise in the absence of an overweight condition, the modulation of activity within this region might be a potential trait of overeating also in NW, and not only in obese conditions.

We further investigated the right MFG-seed with SCA, which revealed a lower functional connectivity between the right MFG and the right anterior insula, a region that provides an interface between stimulus-driven processing and brain regions involved in monitoring the internal milieu (Craig, 2002). Functional alterations within this region have been frequently reported in eating-related disorders (Avery et al., 2017; Brooks, Cedernaes, & Schioth, 2013; Moreno-Lopez et al., 2016) and could be linked to an approach toward food dominated by reward-seeking behaviors rather than by interoceptive information from the body (Mata, Verdejo-Roman, Soriano-Mas, & Verdejo-Garcia, 2015). Hence, our result of a diminished functional connectivity between MFG regions and the insula in the BE group points toward a possible disequilibrium between cognitive control and reward sensitivity processes. This picture of results has already been described in obese adolescents (Moreno-Lopez et al., 2016) and adults (Lips et al., 2014), and the fact that a similar pattern characterizes NW participants reporting binge eating episodes supports the premise that the involvement of networks associated with impulsivity in binge eating may not be only related to weight status.

Additionally, the left insula and putamen highlighted a lower DC in BE compared to non-BE. These regions have been identified as critical nodes in cravings, with their functional alterations being associated with enhanced vulnerability for compulsive habits and addiction (Everitt et al., 2008; Gilman et al., 2018). Given the role of the insula in food regulation (Tataranni et al., 1999), and putamen in habits formations (Dolan & Dayan, 2013), alterations within these networks might be at the roots of eating dysregulation and maladaptive habitual behaviors (e.g., compulsive eating; Kullmann et al., 2012). Since no significant evidence was obtained when the cluster in the left insula/putamen was used as a seed in the SCA, we might speculate that differences characterizing the groups could be more related to a lower number of connections for these regions rather than to differences in their functional connections with specific areas. A lower total number of connections might denote a diminished exchange of information with the entire network, not directly linked to a specific region.

Despite the involvement of both the right MFG and the insula/putamen in impulsivity-related processes, no significant correlations between the scores of the BIS-11 questionnaire and brain activity was observed. This finding might indicate that the between-group differences in terms of functional connectivity are not linked to the differences in impulsivity traits, assessed by the BIS-11. Drawing upon the multidimensional nature of impulsivity (Fuster, 2002), a more complete assessment of the diverse facets of impulsivity would help establish if these differences are related to specific impulsivity aspects or may indicate a more fundamental functional connectivity alteration.

5 | LIMITATIONS AND CONCLUSIONS

Our results indicate that the BE—compared to non-BE—are characterized by a higher trait impulsivity and a diminished functional connectivity in regions relevant for coding of motivationally significant and higher-level stimuli and for cognitive control. Although the possible causal relationships between these results and binge eating remains to be established with longitudinal investigations, we can conclude that these differences were not influenced by the presence of an excessive weight condition. Our findings suggest the intriguing possibility that high trait impulsivity together with diminished functional connectivity at rest involving prefrontal, subcortical and temporoparietal regions can act as a possible neurobehavioral substrate for the development of overeating behavior. In this perspective, future longitudinal studies are needed to explore whether these differences may constitute stable features of binge eating and potential risk factors for the development of clinically relevant weight and eating disorders.

The present study is characterized also by some limitations that need to be acknowledged. First, given the evidence of behavioral similarities and neurobiological overlaps between overeating and substance abuse conditions, a further step should consider a fine-grained initial assessment involving other-than-eating addicted behaviors (e.g., alcohol or drug dependence). In particular, a key part would be accounting for the number of smokers within the entire sample. Since we did not assess this aspect, in our study the between-group differences in resting-state functional connectivity of the brain’s mesocorticolimbic network might be at least partially attributable to smoking status and/or withdrawal symptoms due to the 3-h abstinence required by the study procedure (Franklin et al., 2018). Hence, a comprehensive characterization of addictive behavior traits as well as other psychopathological aspects (i.e., anxiety, depression) would allow for disentangling possible confounding phenomena arising from comorbidities or multi-addiction conditions. Besides, future studies should also include directly measured weight and height data to avoid the potential risk of estimation errors (Frank, Favaro, Marsh, Ehrlich, & Lawson, 2018). Lastly, the chosen resting-state condition (eyes open versus eyes closed during rsfMRI acquisition) is another important variable to consider in the interpretation of results, in terms of connectivity of a wide range of networks (e.g., visual, auditory and sensorimotor; Agcaoglu, Wilson, Wang, Stephen, & Calhoun, 2019). Hence, future studies—including the comparison between different resting-state conditions—should be warranted to confirm and extend the generalizability of our findings.

Overall, the investigation of nonclinical populations of binge eaters may be the ideal substrate to collect insights on the mechanisms underlying loss of control toward food, regardless of body weight. Besides, new insights on the role of impulsivity as a prodromal for overeating might be helpful for researchers and health care professionals to build appropriate interventions for overeating prevention and develop a more comprehensive model of this behavior.
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CONFLICT OF INTEREST
All Authors declare to have no financial, biomedical or any sort of con-
flict of interest.

AUTHOR CONTRIBUTIONS
R.O., C.B., and U.C. designed the research; R.O. recruited participants;
R.O. and C.B. collected the data; R.O., C.B., F.M., and A.H. collaborated
on the data analysis; R.O., C.B., F.M., A.H., and UC collaborated on the
writing of the manuscript.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the
responding author upon reasonable request.

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REFERENCES
(2019). Resting state connectivity differences in eyes open versus eyes
doi.org/10.1002/hbm.24559
Alakörkkö, T., Saarimäki, H., Glerean, E., Glerean, E., Saramäki, J., &
doi.org/10.1111/ejn.13717
American Psychiatric Association. (2013). Diagnostic and statistical manual
Avery, J. A., Powell, J. N., Breslin, F. J., Lepping, R. J., Martin, L. E.,
Patrician, T. M., & Simmons, W. K. (2017). Obesity is associated with
altered mid-insula functional connectivity to limbic regions underlying
appetitive responses to foods. Journal of Psychopharmacology, 31,
brain network properties in obesity: decreased global and putaminal
cortico-striatal network efficiency. Psychological Medicine, 47(4), 585.
https://doi.org/10.1017/S0033291716002646
https://doi.org/10.1016/j.pneurobio.2013.06.005
Biswal, B. B. (2012). Resting state fMRI: A personal history. Neuroimage,
Brett, M., Anton, J. L., Valabregue, R., & Poline, J. B. (2002). Region of
interest analysis using an SPM toolbox. Presented at the 8th
international conference on functional mapping of the human brain,
Japan. Neuroimage, 16, 2.
Brooks, S. J., Cedernaes, J., & Schioth, H. B. (2013). Increased prefrontal and
parahippocampal activation with reduced dorsolateral prefrontal and
insula cortex activation to foods in obesity: A meta-analysis of
pone.0060393
Buckner, R. L., Sepulcre, J., Talukdar, T., Krienen, F. M., Liu, H., Hedden, T.,
connectivity: Mapping, assessment of stability, and relation to
Alzheimer’s disease. The Journal of Neuroscience: The Official Journal of
the Society for Neuroscience, 29, 1860–1873. https://doi.org/10.1523/
JNEUROSCI.5062-08.2009
Bullmore, E., & Sporns, O. (2009). Complex brain networks: Graph theoret-
al analysis of structural and functional systems. Nature Reviews Neu-
roscience, 10, 186–198. https://doi.org/10.1038/nrn2575
Carver, C. S., & White, T. L. (1994). Behavioral inhibition, behavioral activa-
tion, and affective responses to impending reward and punishment:
The BIS/BAS scales. Journal of Personality and Social Psychology, 67,
traits in eating disorder patients. Personality and Individual Differences,
Corbit, L. H., & Janak, P. H. (2010). Posterior dorsomedial striatum is criti-
cal for both selective instrumental and Pavlovian reward learning.
1111/j.1460-9586.2010.07153.x
partial-syndrome and subclinical eating disorders: An epidemiological
study of female students in southern Italy. Acta Psychiatrica Scandi-
1998.tb10051.x
tional magnetic resonance Neuroimages. Computers and Biomedical
physiological condition of the body. Nature Reviews Neuroscience, 3(8),
655–666. https://doi.org/10.1038/nrn894
org/10.1155/2013/435027
Hariri, A. R. (2013). Impulsivity and the modular organization of
https://doi.org/10.1093/cercor/bhs126
Dolan, R. J., & Dayan, P. (2013). Goals and habits in the brain. Neuron, 80,
312–325. https://doi.org/10.1016/j.neuron.2013.09.007
Neuroimaging in bulimia nervosa and binge eating disorder: A system-
1186/s40337-018-0187-1
Everitt, B. J., Belin, D., Economidou, D., Pelloux, Y., Dalley, J. W., &
Robbins, T. W. (2008). Neural mechanisms underlying the vulnera-
bility to develop compulsive drug-seeking habits and addiction. Philosoph-
ical Transactions of the Royal Society B: Biological Sciences, 363(1507),
Filbey, F. M., Myers, U. S., & Dewitt, S. (2012). Reward circuit function in
high BMI individuals with compulsive overeating: Similarities with
neuroimage.2012.08.073
Fox, M. D., & Greicius, M. (2010). Clinical applications of resting state
https://doi.org/10.3389/fnsys.2010.00019
Toward valid and reliable brain imaging results in eating disorders.

**SUPPORTING INFORMATION**

Additional supporting information may be found online in the Supporting Information section at the end of this article.