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Reward sensitivity in Parkinson's patients with binge eating

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ABSTRACT

Background: Parkinson's disease (PD) patients who are treated with dopamine replacement therapy are at risk of developing impulse control disorders (ICDs) (such as gambling, binge eating, and others). According to recent evidence, compulsive reward seeking in ICDs may arise from an excessive attribution of incentive salience (or 'wanting') to rewards.
Objectives: In this study, we tested this hypothesis in patients with PD who developed binge eating (BE).
Methods: Patients with BE, patients without BE, and healthy controls performed different experimental tasks assessing food liking and wanting. Participants first rated the degree of liking and wanting for different foods using explicit self-report measures. They then performed an affective priming task that measured participants' affective reactions towards foods (liking), and a grip-force task that assessed their motivation for food rewards (wanting). All participants also completed several questionnaires assessing impulsivity, reward sensitivity, anxiety and depression, and underwent a neuropsychological evaluation.
Results: Patients with BE displayed an altered liking for sweet foods compared to controls but not to patients without BE. Furthermore, this difference emerged only when implicit measures were used. Importantly, an increased wanting was not associated with binge eating even if wanting, but not liking scores significantly correlated with LED levodopa, confirming the hypothesis of a distinction between the two components of rewards. Lastly, binge eating was associated with depression and lower working memory scores.
Conclusions: Take together these results suggest that binge eating in PD is associated with cognitive abnormalities, and to lesser extent affective abnormalities, but not with an increased incentive salience.

1. Introduction

Parkinson's disease (PD) patients who are treated with dopaminergic medications are at risk of developing impulse control disorders (ICDs), which include pathological and repetitive behaviors such as gambling, compulsive shopping, sexual behaviors, binge eating, compulsive use of dopaminergic medications and punding [1]. These disorders occur with percentages varying from 3.5% to 42.8% and they are believed to reflect the interaction of dopaminergic treatments (dopamine agonists and/or dopamine replacement therapy) with the individual's susceptibility and the underlying neurobiology of PD [2,3].

Several fMRI and PET studies support the hypothesis that ICDs, like addictive disorders, may be characterized by an excessive attribution of "incentive salience" (or 'wanting') to rewards. These studies have shown an increased activity in different reward brain regions after reward presentation in PD patients with ICDs compared to control patients [4–7], and that 'wanting' but not 'liking' ratings in these patients significantly correlate with the activity in the ventral striatum [5,7]. Even in behavioral tasks, ICDs patients have also shown to exhibit an increased willingness to work for a reward compared to patients without ICDs [5]. These findings are in line with the incentive sensitization theory, according to which the degree of 'wanting' for a reward increases disproportionately compared to the degree of which the reward is liked as patients develop an addictive disorder. Liking and wanting

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are indeed considered as separate reward components, mediating, respectively, the pleasure effect of a reward and the motivational drive toward it [8].

Among ICDs, binge eating (BE) is described as recurrent episodes of increased eating coupled with a perceived lack of control [9]. It occurs in 4.3% of PD patients taking dopaminergic medications, it is more common in women [10,11], and it is often associated with increased body weight [12]. In binge eater patients without PD, this disorder has been related to the mechanisms implicated in addictive disorders, including elevated motivation to seek out palatable foods, greater neural activation in reward-related circuitry to high-calorie foods, and impairment in cognitive control [13]. However, to date the hypothesis of an enhanced incentive salience attribution to reward in ICDs has never been tested in patients with BE.

To fill this gap, PD patients with BE, PD patients without BE and healthy controls performed several tasks assessing food liking and wanting. First, in order to measure the patients' conscious and subjective experience of food rewards, we had them rate the degree of "liking" and "wanting" for different foods using explicit self-reports. Second, participants performed an affective priming task that measures attitude and affective reactions towards foods, and a grip-force task, in which motivation towards rewards was indirectly operationalized as the exerted effort. Participants also underwent a series of neuropsychological tests and completed several questionnaires evaluating impulsivity, reward sensitivity and the presence of anxiety and depression.

2. Methods

2.1. Subjects

Thirty-one dopaminergic treated patients with PD and twenty healthy controls (C) took part in the study. PD patients were recruited from the movement disorders clinic of "Cattinara" hospital in Trieste (Italy). Patients were assessed by a neurologist and asked to fill the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease-Rating Scale (QUIP-RS) [14]. Since no validation on the Italian population is available, we used a translated version of the questionnaire. Sixteen PD participants were identified as binge eaters (PD + BE), with ten exhibiting at least one additional ICDs (see supplementary material, Table S1). The other fifteen PD patients (PD) had no history of BE or other ICDs. Patients' disease severity was assessed using the Unified Parkinson's Disease Rating Scale-Part III (UPDRS-III) and the Hoehn and Yahr scale (H&Y) [15]. In addition, for each patient a daily L-dopa equivalent dose (LED total) was calculated based on [16]. The study was approved by SISSA Ethics Committee and all participants provided written informed consent. For details on demographical and clinical data, see Table 1.

Table 1
Demographic, clinic and questionnaire data (mean and standard deviation). Subscales of the questionnaires are provided in Italics.

	PD + BE (n = 16)	PD (n = 15)	C (n = 20)
Gender (female)	8	7	10
Age(y)	67.1(8.2)	64.9 (12.9)	68 (6.4)
Education (y)	9.6 (4.2)	10.7 (2.9)	9.7 (3.4)
BMI	29.4 (5.9)*,**	25 (3.8)	25.2 (3.4)
PD duration (y)	8.5 (5.6)	6.8 (3.1)	–
UPDRS III	20.5 (9.6)	15.8 (8.1)	–
H&Y	1.7 (0.4)	1.7 (0.4)	–
LED total (mg)	788 (260.7)	695.7 (309.3)	–
LED-DA (mg)	181.5 (51.7)	220.6 (83.9)	–
LED-Levodopa (mg)	476.5 (231.2)	348.3 (280)	–
Total QUIP-RS score	31.6(15.4)*	10.2 (10.2)	–
eating	8.9 (2.2)*	2 (1.8)	–
gambling	1.31 (2)	0.4 (0.9)	–
buying	4.7 (2.5)*	1.6 (1.4)	–
sex	2.7 (2.7)	1.8 (1.8)	–
hobbyism	5.8 (4.9)*	1.6 (2)	–
punding	3.5 (3.5)	1.3 (1.7)	–
DDS	3.8 (5.1)	1.4 (2.5)	–
HADS *anxiety* [a]	8.6 (4)	6.4 (3.8)	6.3 (3.5)
HADS *depression* [a]	7.6 (4.3)*,**	4.8 (2.3)	4.8 (3.2)
BIS impulsivity	60.1 (9.5)	57.4 (10.2)	63.1 (8.3)
attentional	15.6 (3.3)	14.5 (2.7)	16.3 (3.3)
motor	20.3 (3.5)	18.8 (4.5)	20.5 (3.5)
non-planning	25.1 (4.7)	28.8 (7.4)	26.3 (4.7)
BAS	38.5 (3.8)	39.2 (7.1)	40.2 (5.6)
reward responsiveness	17.5 (2.8)	16.6 (3.1)	17.6 (2.3)
drive	11.8 (1.8)	12.5 (3.9)	11.9 (2.3)
fun-seeking	9.1 (2.6)	10 (4.5)	10.6 (1.9)

* = significantly different from PD, $p < 0.05$;** = significantly different from C, $p < 0.05$;y = years;mg = milligrams;*a* = one patient didn't complete the HADS.

2.2. Experimental evaluation

We collected participant's subjective ratings of hunger and fasting in order to control for macroscopic differences between subjects. We collected participants' weight and height, and calculated body mass index (BMI) by dividing weight in kilograms by the square of height in meters (kg/m^2). Participants were then asked to perform the experimental tasks, undergo a neuropsychological examination and complete several questionnaires.

2.2.1. Self-ratings of "liking" and "wanting" for foods

In this task, 20 food pictures were presented and participants were asked to respond to the questions: (1) "How tasty is this food for you?" (*Liking*) and (2) "How much do you want this food now"? (*Wanting*). The experimenter indicated patients' responses on a 100 visual analogue scale anchored at each end with "not at all" and "extremely" [17]. In addition, participants were also asked the question: "How often do you eat this food?" Foods normally not eaten (Frequency: 0–10) were removed from the analysis. On average 9.35% of food items were removed for each patient.

2.2.2. Liking: affective priming task

Participants were instructed that they would see a picture (prime), followed by a smiley symbol (target), and that their task was to indicate whether the smiley was a positive or negative one, by pressing the marked keys (see Ref. [18]). Participants were instructed to not pay attention to prime stimuli and to respond as quickly and accurately as possible. The prime stimuli were 20 food pictures and 10 food-unrelated filler pictures (e.g., a comb, a hanger, a wardrobe, etc.) used as filler. The target stimuli were a positive and a negative emoticon (☺ and ☹).

The allocation of responses (positive/negative) to the response buttons was counterbalanced among participants. RTs on trials with errors or RTs below and above 2SD were excluded from the analyses. Each trial consisted of 250 ms prime period, a blank screen of 50 ms, resulting in a stimulus onset asynchrony (SOA) of a 300 ms, a target (which remained on screen until a response was given), and an intertrial interval period of 1500 ms. Each of the prime was presented twice (once followed by the negative target and once followed by the positive one), resulting in 60 trials. In order to determine participants' attitude, a positivity index was constructed for each item type by subtracting from the RTs for negative emotions the RTs for positive emoticons. Thus, lower values of this index indicate a more negative attitude. Stimulus presentation and data collection were accomplished using the E-prime software installed on a desktop computer.

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