

ABSTRACT

BACKGROUND: Craving sweets is common in patients with Parkinson's disease (PD), but this symptom has not been systematically studied. **METHODS:** Patients with idiopathic PD and unaffected spouses of PD patients completed a Food Frequency Questionnaire (FFQ) for sweet foods they eat now, and identified if they felt craving for any of them. If yes, they completed a Food Craving Questionnaire (FCQ). All subjects answered a Symptom Checklist focusing on depression, anxiety, and obsessive-compulsive disorder, and completed smell testing (Q-SIT) and taste threshold testing for sweet, salty, sour, and bitter substances. PD subjects also completed an FFQ and FCQ relating to symptoms before developing PD. Demographic data was recorded. **RESULTS:** 62 patients (mean age 64.4 yrs, 35 male) and 23 controls (mean age 64.4 yrs, 7 male) were enrolled. Mean PD duration was 7.1 yrs (SD 4.9 yrs), mean UPDRS Part 3 score (N=50) was 26.7 (SD 12.2), and mean Hoehn & Yahr stage was 1.9 (SD 0.6). Of the 85 subjects, 32 (61.6%) patients and 9 (39.1%) controls identified themselves as cravers (p<0.32). Of those stating they craved sweets, 11 PD patients (34.4%) scored over the 75th percentile on the FCQ (mean 5.9, SD 0.5) but only 1 control (11.1%) scored over the 75th percentile (p=0.17). Craving did correlate with duration of PD (p=0.04), but no correlation was found between craving and age, gender, levodopa equivalents, depression, anxiety, OCD, Q-SIT scores, or craving before PD diagnosis. Thresholds for all tastes were similar between PD patients and controls, all subjects had relatively preserved sense of taste for sweets, and Q-SIT scores were lower for all PD patients than controls (p<0.0005). **CONCLUSIONS:** This pilot study demonstrates that a higher proportion of PD patients identified themselves as craving sweets than controls, and a higher proportion scored over the 75th percentile on a score of craving. Craving sweets significantly correlated with duration of PD, but not with other factors. Sense of smell and taste did not affect craving. Larger studies are needed to further define craving sweets in PD, and to correlate craving with other behaviors such as obsessive-compulsive disorder. Craving for sweets in PD may be an expression of dopamine-mediated reward systems.

METHODS

Inclusion Criteria:
 ♦ Any patient seen at the Parkinson's Disease Center and Movement Disorders Clinic and diagnosed with probable idiopathic PD according to the Gelb criteria (Gelb et al, 1993) were asked to participate.
 ♦ Control subjects were comprised of spouses of PD patients.

Exclusion Criteria:
 ♦ Unable to complete taste or smell test on his/her own.
 ♦ Unable to complete questionnaires on his/her own or with the help of a spouse or caregiver.

After informed consent was obtained, patients and controls were asked to complete the following questionnaires and tests with the assistance of a research coordinator:
 ♦ **Quick Smell Identification Test (Q-SIT; Sensonics, Inc.):** A short scratch-and-sniff test of three odors based on the University of Pennsylvania Smell Identification Test (Doty et al, 1984).
 ♦ **Taste threshold testing:** Various concentrations of solutions (see Table 1) representing the four taste sensations [sweet (sucrose), salty (sodium chloride), bitter (quinine hydrochloride), sour (citric acid)] and plain water were soaked onto circles of filter paper and dried. Subjects placed each filter disc (in a blinded fashion in a predetermined random order) on their tongue for at 5-10 seconds and were asked to identify the taste (Mueller et al, 2003).
 ♦ **Modified Symptom Checklist-90-R (SCL-90-R):** The original SCL-90-R is a self-report measure addressing nine primary psychiatric dimensions in 90 questions. Subjects answered questions corresponding to the anxiety, depression, and obsessive-compulsive scales only (total questions = 33). The questions were administered and scored according to Ostroff et al, 1976.
 ♦ **Sweet Food Frequency Questionnaire (FFQ):** Modified from the Arizona FFQ (Martinez et al, 1999). Subjects quantified the average frequency of intake of sweet foods before and after development of PD symptoms.
 ♦ **Food Craving Questionnaire (FCQ):** Modified from the Alcohol Craving Questionnaire, Short Form, Revised (ACQ-SF-R) (Singleton et al, 2003). If subjects stated they craved sweets, they answered 12 questions about their craving based on the food item they reported wanting or eating the most. Scored according to published guidelines (Singleton et al, 1994). Those with a score >75th percentile within their group (PD patients or controls) were considered "cravers".

Statistical Analysis:
 ♦ Differences between cravers and non-cravers were tested by Student's t-test with unequal variances, and chi-square tests using Fisher's exact method.
 ♦ In the patients identified as cravers, correlations between the FCQ score and various factors were performed.

RESULTS

Table 1. Concentrations of solutions used for filter discs

Sweet	10%	25%	60%
Salty	1.25%	5%	20%
Sour	0.25%	1%	4%
Bitter	0.025%	0.1%	0.5%

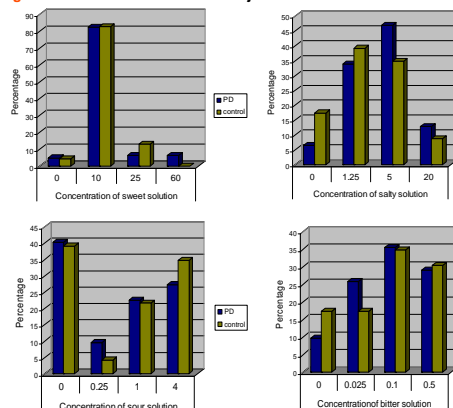
Table 3. FCQ scores

Self-identified		>75th percentile	
PD	Controls	PD	Controls
4.51 (SD = 1.3)	3.92 (SD = 1.3)	5.99 (SD = 0.5)	6.5 (N/A)
N=33 (53%)	N=9 (39%)	N=10 (16%)	N=1 (4%)

Table 2. Characteristics of all subjects

	PD patients (N = 62)	Controls (N = 23)	p value
Mean age	64.4 years	64.4 years	0.98
Gender	35M / 27F	7M / 16F	--
Mean PD Duration (± SD)	7.1 years (±4.9)	N/A	--
Mean UPDRS - Pt. 3 (± SD) (N = 50)	26.7 (±12.2)	N/A	--
Mean Hoehn & Yahr (± SD) (N = 50)	1.9 (±0.6)	N/A	--
Mean FFQ (± SD)	14.6 (±9.0)	13 (±6.2)	0.35
Mean FCQ (± SD)	4.51 (±1.32) (N=33)	3.92 (±1.31) (N=9)	0.33
Mean Q-SIT (± SD)	1.27 (±0.9)	2.17 (±0.7)	<0.05
Mean Depression subscale of SCL-90-R (± SD)	0.97 (±0.1)	0.67 (±0.1)	0.07
Mean Anxiety subscale of SCL-90-R (± SD)	0.9 (±0.1)	0.5 (±0.1)	0.02
Mean OCD subscale of SCL-90-R (± SD)	1.15 (±0.1)	0.8 (±0.1)	0.063

Figure 1. Taste thresholds for all subjects*



* No significant differences in taste thresholds between PD patients who crave sweets and controls

RESULTS (continued)

Table 4. Characteristics of PD patients who crave sweets

	PD cravers* (N=10)	PD non-cravers (N=52)	P value	Controls (N=23)	P value (vs. PD cravers)	Control craver* (N=1)
Age, yrs (SE)	65.4 (±11.2)	64.1 (±10.8)	0.76	64.4 (±10.3)	0.82	74.4 (N/A)
Gender	4M/6F	31M/21F	--	7M/16F	--	1F
UPDRS-3 (SE)	31.4 (±10.7) N=8	25.8 (±12.4) N=42	0.22	N/A	--	N/A
H&Y (SE)	2.2 (±0.37) N=8	1.9 (±6.1) N=42	0.077	N/A	--	N/A
PD duration (SE)	10.1 (±6.2)	6.5 (±4.5)	0.11 †	N/A	--	N/A
Levodopa equivalents, mg (SE)	344 (±259)	493 (±457) N=48	0.17	N/A	--	N/A
FFQ (SE)	18.3 (± 8.0)	13.9 (± 1.26)	0.14	13.0 (±6.2)	0.08†	15 (N/A)
Q-SIT (SE)	1.0 (± 1.1)	1.3 (±0.90)	0.38	2.17 (± 0.072)	0.007 †	3 (N/A)
SCL-90-R Anxiety (SE)	1.12 (± 1.04)	0.83 (± 1.0)	0.42	0.50 (± 0.72)	0.10	0.3 (N/A)
SCL-90-R Depression (SE)	1.45 (±1.12)	0.88 (± 0.11)	0.15	0.673 (± 0.058)	0.67†	0.5 (N/A)
SCL-90-R OCD (SE)	1.45 (± 0.90)	1.1 (± 0.11)	0.27	0.80 (± 0.72)	0.06†	0.2 (N/A)

* as identified by FCQ > 75th percentile of scores within that group of patients
 † though not statistically significant, the numbers suggest a trend

♦ FCQ scores in the PD cravers did not correlate with age, levodopa equivalents, FFQ, Q-SIT, anxiety, depression, or OCD.
 ♦ FCQ scores did correlate with UPDRS scores (-0.69, p=0.06), H&Y score (-0.81, p=0.015), and PD duration (0.75, p=0.012).

CONCLUSIONS

♦ This pilot study demonstrates that a higher proportion of PD patients identified themselves as craving sweets than controls, and a higher proportion scored over the 75th percentile on the FCQ.
 > The difference in proportions was non-significant, likely due to inadequate sample size.
 ♦ Of those PD patients who stated they experienced craving (33), only 30% (10) were actually found to have elevated craving scores. This symptom may be over-reported in the PD population.
 ♦ PD patients identified as cravers were characterized by longer PD duration, lower levodopa equivalents, higher FFQ scores, and higher depression and OCD scores (all non-significant) compared to non-craving PD patients.
 ♦ Factors that *did* affect craving sweets include duration of PD and H&Y score.
 > These findings are of uncertain significance due to the small sample size
 ♦ Factors that *did not* affect craving sweets include:
 > Sense of smell - Q-SIT scores in PD cravers were significantly lower than controls, but not different from PD non-cravers.
 > Taste thresholds, which failed to differentiate PD patients from normal controls. Both PD patients and controls were more likely to identify sweet tastes correctly and had greatest difficulty identifying sour tastes. Enhanced taste reactivity likely does not play a role in craving in PD.
 > Medication dosages - levodopa equivalents were actually lower amongst PD cravers compared to PD non-cravers.
 > Mood disorders or OCD, although PD cravers had higher scores on depression and OCD subscales than both PD non-cravers and controls.
 ♦ Food frequency questionnaires did not significantly differentiate cravers from non-cravers, although the scores tended to be higher for PD cravers. This is most likely a result of recall bias.
 ♦ In view of these findings, craving for sweets in PD may be mostly an expression of dysfunction within dopamine-mediated reward systems.
 ♦ Larger studies are needed to further define craving sweets in PD, and to correlate craving with mood disorders (including obsessive-compulsive disorder).

REFERENCES

♦ Christensen L, Peltjohn L. Mood and carbohydrate cravings. *Appetite*. 2001 Apr;36(2):137-45.
 ♦ Derogatis LR, Rickels K, Rock AF. The SCL-90 and the MPI: a step in the validation of a new self-report scale. *Br J Psychiatry*. 1976 Mar;128:282-9.
 ♦ Doherty RL, Shahan P, Dann M. Development of the University of Pennsylvania Smell Identification Test: a standardized microencapsulated test of olfactory function. *Physiol Behav*. 1984;33:469-502.
 ♦ Gelb DJ, Oliver E, Gilman S. Diagnostic criteria for Parkinson disease. *Arch Neurol*. 1999 Jan;56(1):33-9.
 ♦ Henderson R, Kurlan R, Keruan JK, Como P. Preliminary examination of the comorbidity of anxiety and depression in Parkinson's disease. *J Neurophysiol Clin Neurosci*. 1992 Summer;4(3):257-64.
 ♦ Hurley MJ, Mash DC, Jenner P. Dopamine D(1) receptor expression in human basal ganglia and changes in Parkinson's disease. *Brain Res Mol Brain Res*. 2001 Mar;5(7):271-9.
 ♦ Kaneda H, Maeshima K, Goto N, et al. Decline in taste and odor discrimination abilities with age, and relationship between gustation and olfaction. *Chem Senses*. 2000 Jun;25(3):331-7.
 ♦ Kelley AE, Bakshi VP, Haber SN, et al. Opioid modulation of taste hedonics within the ventral striatum. *Physiol Behav*. 2002 Jul;76(3):365-77.
 ♦ Martinez ME, Marshall JR, Graver E, Whiteacre RC, Wood K, Ribbens GA, Alberts DS. Reliability and validity of a self-administered food frequency questionnaire in a chemoprevention trial of adenoma recurrence. *Cancer Epidemiol Biomarkers Prev*. 1999 Oct;8(10):941-5.
 ♦ Mojet J, Koster EP, Pinz JF. Do tastants have a smell? *Chem Senses*. 2005 Jan;30(1):9-21.
 ♦ Mueller C, Kallert S, Renner B, Slassay K, Temmel AF, Hummel T, Kobal G. Quantitative assessment of gustatory function in a clinical context using integrated "taste strips". *Rhinology*. 2003 Mar;41(1):2-6.
 ♦ Murray AM, Wehmueller FB, Marshall JF, et al. Damage to dopamine systems differs between Parkinson's disease and Alzheimer's disease with parkinsonism. *Ann Neurol*. 1995 Mar;37(3):300-12.
 ♦ Nirenberg MJ, Waters C. Compulsive eating and weight gain related to dopamine agonist use. *Mov Disord*. 2006;21(S24):4.
 ♦ Picini S, Berridge KC. Opioid site in nucleus accumbens shell mediates eating and hedonic "liking" for food: map based on microinjection Fos plumes. *Brain Res*. 2000 Apr;2886(1-2):71-86.
 ♦ Sienkiewicz-Jarosz H, Soroká A, Kurán W, et al. Taste responses in patients with Parkinson's disease. *J Neurol Neurosurg Psychiatry*. 2005 Jan;76(1):40-5.
 ♦ Singleton EG, Tiffany ST, and Henningfield J E (2003). The Alcohol Craving Questionnaire (ACQ-Now). In J. P. Allen & V. B. Wilson (Eds.), *Assessing Alcohol Problems: A Guide for Clinicians and Researchers* (2nd ed., pp. 271-281). NIH Publication No. 03-3745. Bethesda, MD: National Institute on Alcohol Abuse and Alcoholism.

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INTRODUCTION

♦ PD patients have been known to crave sweets, but this has not been systematically studied.
 ♦ To determine if PD patients had anhedonic responses to pleasant and unpleasant stimuli, Sienkiewicz-Jarosz et al (2005) studied their taste responses.
 > No difference between PD patients and controls in the perceived pleasantness of sweet samples
 > No statistically significant difference in craving for sweets between the two groups based on a single item visual analog scale.
 > PD patients had a lower taste threshold on electrogoniometry.
 > Olfactory deficits in PD may be compensated for by enhanced taste reactivity
 > However, formal smell and craving assessments were not performed.
 ♦ There is an age-related decrease in the size of the olfactory bulb and other cell structures involved in smell, whereas there is no diminution of taste receptor density with advancing age (Kaneda et al, 2000).
 > However, taste and smell senses are closely related, as most taste perceptions rely to some degree on olfactory sensations (Mojet et al, 2005).
 ♦ Craving carbohydrates is closely linked to mood; females are more likely to experience this phenomenon and it is more commonly associated with "negative" mood states (Christensen et al, 2001).
 > 40% of PD patients experience mood disorders (Henderson et al, 1992).
 ♦ A report of binge eating in PD patients after beginning a dopamine agonist described 7 patients who developed a compulsive type of eating, 3 of whom experienced food and sweet cravings (Nirenberg and Waters, 2006).
 > Binge eating and craving resolved after discontinuation of the drug.
 ♦ Animal models of craving suggest involvement of opiate pathways and the nucleus accumbens (Picini and Berridge, 2000; Kelley et al, 2002).
 > Degenerative and receptor changes within the nucleus accumbens occur in PD (Murray et al, 1995; Hurley et al, 2001)
 ♦ The aim of this study is to determine the prevalence of craving for sweets in our population of PD patients, and to determine if this phenomenon correlates with olfactory loss, taste loss, medications, or underlying affective disorder.