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Hedonic and Behavioral Deficits Associated with Apathy in Parkinson's Disease: Potential Treatment Implications

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Abstract

Many individuals with Parkinson's disease (PD) experience apathy independent of depression. In this study we examined hedonic and behavioral deficits related to apathy in 50 PD patients and 42 healthy older adults who completed standardized measures. Regression analyses revealed that apathy was associated with anticipatory, but not consummatory, anhedonia and reduced goal-directed behavior, independent of PD diagnosis, age, education and depressive symptoms. These findings suggest that apathy is characterized by deficits in anticipatory pleasure and behavioral drive rather than consummatory pleasure or reward responsiveness. Therefore, PD patients with apathy would likely benefit from psychotherapeutic treatment that encourages structured, goal-directed plans for pleasurable events and stimulation which provide adaptive hedonic effects. In addition, given the proposed shared mechanism of dopamine depletion within the ventral striatum in apathy and anticipatory anhedonia, future trials of dopamine-eliciting activities (e.g. exercise and other non-pharmacologic methods) appear warranted to improve these symptoms in PD.

Keywords

Parkinson's disease; anhedonia; apathy

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Author Roles

Lizabeth L. Jordan, M.S. participated across all steps of the of project and manuscript preparation, including conceptualization and conduction of this research project as well as the review of statistical analyses and writing of the manuscript.

Laura B. Zahodne, Ph.D. assisted with data collection and statistical analyses as well as the writing of the manuscript's results and discussion sections.

Michael S. Okun, M.D. was involved with recruitment and medical evaluation of the PD patients at the University of Florida's Center for Movement Disorders and Neurorestoration. In addition, Dr. Okun provided valuable review and critique of the written manuscript. Dawn Bowers, Ph.D. supervised the conceptualization and conduction of the research project and statistical analyses. In addition, Dr. Bowers participated in the writing and review of the manuscript.

Introduction

Parkinson's disease (PD) is associated with apathy, a motivational defect, and decreased anticipation of reward/punishment contingencies.^{1, 2, 3} Although up to 70% of PD patients experience apathy, its underlying components are not well characterized. In this study, we examined whether anhedonia, the inability to experience pleasure, might contribute to apathy in PD. Anhedonia has been characterized as comprising of two types of pleasure deficits: anticipatory and consummatory.^{4, 5} Anticipatory anhedonia refers to the inability to generate desire for a future reward ("wanting"), whereas consummatory anhedonia is the inability to experience pleasure upon receipt of a reward ("liking"). Recent studies suggest that PD patients may have intact "consummatory" pleasure, based on self-ratings of reactions to emotional stimuli.^{6, 7, 8, 9, 10} Indeed, a recent study measuring daily affect reported that individuals with PD do *not* demonstrate anhedonia in response to positive life events.¹⁰ In contrast, high rates of PD apathy may reflect deficient expectancy for pleasure.²

The aims of this study were two-fold. *First*, we examined whether anhedonia *in general* was linked to apathy, or whether this apathy-anhedonia relationship was specific for "anticipatory" rather than "consummatory" anhedonia. *Second*, based on work by Gard et al.⁴ showing that anticipatory pleasure activates approach motivation (i.e., processes that underlie seeking out desired goals), we examined relationships between apathy and approach/avoidance motivation using validated measures. In light of previous research linking anticipatory anhedonia to decreased approach motivation), we hypothesized that apathy in PD would be associated with decreased pursuit of goals, but not reward responsiveness.^{4, 11}

Methods

Participants & Procedures

Participants included 50 patients with idiopathic PD from the University of Florida's Center for Movement Disorders and 42 healthy controls from the Gainesville, Florida community. Patients had undergone extensive neurologic screening in order to establish a definitive diagnosis of PD based on the UK Brain Bank criteria.¹² Exclusion criteria were: (1) suspected dementia (MMSE <25); (2) current uncontrolled psychiatric disorder (e.g., substance abuse, major depressive disorder); or (3) history of neurological illness (other than PD). Patients were tested "on" dopaminergic medications. Informed consent was obtained according to local and federal guidelines.

Measures

The following self-report questionnaires were administered to all participants:

Apathy Scale (AS)—The Apathy Scale (AS) is a 14 item self-report questionnaire recommended by the Movement Disorder Society (MDS) to assess apathy in PD.^{6, 13} AS scores range from 0 to 42, and higher scores indicate greater apathy. The recommended clinical cut-off for apathy is 14.

Snaith Hamilton Pleasure Scale (SHPS)—The Snaith Hamilton Pleasure Scale (SHPS) is a 14-item questionnaire widely used in clinical research to estimate global anhedonia.¹⁴ Importantly, the Movement Disorder Society (MDS) "suggests" the use of the SHPS as a useful measure of assessing anhedonia in PD populations.⁶ SHPS scores range from 14 to 56.²⁰ Higher scores indicate greater anhedonia.¹⁵

Temporal Experience of Pleasure Scale (TEPS)—The Temporal Experience of Pleasure Scale (TEPS) is an 18-item questionnaire with anticipatory and consummatory pleasure subscales.⁹ We modified two items from the original TEPS Consummatory subscale to ensure relatability for older adults living in Florida for our sample.^a Lower scores on the TEPS indicate greater anhedonia.

Behavioral Inhibition and Approach Scale (BIS/BAS)—The Behavioral Inhibition and Approach Scale (BIS/BAS) is a 24-item questionnaire with 4 motivated behavior subscales:¹⁶ BIS (anticipatory anxiety and sensitivity to punishment); BAS Reward Responsiveness (positive behavioral responses to reward occurrence); BAS Drive (pursuit of desired goals), BAS Fun Seeking (desire for *new* rewards). We modified one item for our population.^b Lower scores on all BIS/BAS scales indicate greater deficits.

Beck Depression Inventory, 2nd Edition (BDI-II)—Finally, the Beck Depression Inventory is 21-item questionnaire used to quantify depressive symptoms.¹⁷ BDI-II Scores range from 0 to 63. Higher scores indicate greater depression.

Statistical Analyses

Descriptive statistics were used to characterize the sample. Independent samples t-tests examined group differences, and seven separate multivariate regression models explored relationships between apathy, anhedonia, and motivated behavior. More specifically, the dependent variables in the regression analyses were scores from the SHPS (Aim 1), TEPS (Aim 2), and BIS/BAS scales (Aim 2). Independent variables were AS scores and group membership (i.e. PD or healthy control). Age, education, and BDI-II scores were used as covariates in these analyses. These covariates were chosen because they significantly differed between groups and/or correlated with AS.

Results

Data was collected from 42 healthy control participants and 50 PD patients. The healthy control participants (mean age = 71 years-old) were significantly older than the PD patients (mean age = 65 years-old, $t(89) = 2.86$; $p < .01$). When tested on their PD medications, the group mean performance of the PD patients on Part 3 of the Unified Parkinson's Disease Rating Scale was 27.94 (standard deviation = 10.40, $N = 35$). Hoehn & Yahr scores on medication were available for 39 of the PD patients; approximately 46% of these patients scored in Stage 2, 33% in Stage 2.5, and 20% in Stage 3. Compared to control participants, patients reported greater psychopathology on the BDI-II ($t(57.73) = -5.83$; $p < .001$), Apathy Scale ($t(73.94) = -2.78$; $p < .01$), SHPS ($t(90) = -4.07$; $p < .001$), and TEPS Consummatory ($t(90) = 2.77$; $p < .01$). Forty-four percent of PD patients were apathetic, compared to 20% of healthy controls when using standard cutoff criteria of 14 from the Apathy Scale ($\chi^2(1) = 5.91$; $p = .01$). PD patients with apathy had greater global anhedonia (SHPS: $t(46) = -2.85$, $p < .01$), greater anticipatory anhedonia (TEPS: $t(25.77) = 2.89$, $p < .01$), and reduced pursuit of desired goals (BAS Drive: $t(46) = 2.73$, $p < .01$) than patients without apathy.

Of the seven regression models examined, four significant regression models were identified (Table 1). In summary, increased apathy scale scores significantly predicted greater overall anhedonia (SHPS, $B = .30$, $p < .01$), greater anticipatory anhedonia (TEPS Anticipatory, $B = -.45$, $p < .05$), and reduced pursuit of desired goals (BAS drive, $B = -.15$, $p < .05$). The latter two

^aItems 9, 11, and on the TEPS questionnaire were modified to the following: 9) I love it when people *rub my back* [originally, play with my hair], 10) When I'm on my way to *my grandchildren's house* [an amusement park], I can hardly wait to *see them* [ride the roller coaster], and 10) I appreciate the beauty of a *colorful sunset* [colorful sunset].

^bItem 23 on the BAS Reward Responsiveness subscale was changed to "It would excite me to win *the lottery* [previously, a contest]."

relationships were independent of PD diagnosis, age, education, and depressive symptoms (as indexed by the Beck Depression Inventory-II). However, the regressions did *not* reveal a significant relationship between apathy and consummatory anhedonia, desire for rewards, positive behavioral responses to rewards, or subjective distress resulting from negative events.

Discussion

The present study confirmed previous research that PD is associated with increased apathy and anhedonia. Moreover, PD patients who report experiencing clinically significant apathy also report experiencing greater anticipatory anhedonia and diminished behavioral drive than PD patients without self-reported apathy. Thus, our results link PD apathy to specifically anticipatory, but not consummatory, anhedonic deficits. This finding is consistent with previous studies demonstrating that PD patients report intact emotional responses to emotional stimuli.¹⁰⁻¹⁶

Apathy, anticipatory anhedonia, and decreased pursuit of goals may share a common neurobiological substrate in PD, i.e. dopamine depletion in the nucleus accumbens. Previous studies have identified dissociable neural circuitry in anticipatory (dopaminergic dysfunction in the nucleus accumbens⁸) versus consummatory (prefrontal cortex) anhedonia.^{4,10} Similar to anticipatory anhedonia, apathy has been linked to dysfunction of fronto-striatal circuitry involving the anterior cingulate cortex and the ventral striatum in older individuals with¹⁸ and without¹⁹ PD. We hypothesize that patients with PD are more likely to experience apathy and anticipatory anhedonia due to dopamine depletion in the ventral striatum resulting from the disease process.^{18, 20, 21} This hypothesis has been supported in research with schizophrenia patients, who, like PD patients, report anticipatory anhedonia on the TEPS and presumably suffer from dopamine dysfunction.²³ In addition, treatment studies in Parkinson's patients report that dopaminergic medications reduce apathy and anhedonia.⁶

This present study implemented a series of linear regressions. Because analyses were hypothesis-driven, potential for Type I errors was reduced. Identification of significant results within a relatively small sample size further suggests that findings are unlikely to be spurious. Use of self-report measures may limit interpretation. For example, other apathy scales may have quantified apathy differently in our sample, and items modified from the TEPS and BAS questionnaires have not been previously validated. Finally, this study included only one measure of behavioral responses to negative events (i.e., BIS). It is possible that comprehensive anticipatory anxiety assessment would have revealed a negative association with apathy, which has been conceptualized to involve reduced anticipation of both positive and negative events.

Despite limitations, the results have important implications for the treatment of apathy in PD. Our findings suggest that once engaged in pleasurable events, patients with PD will be able to experience their adaptive hedonic effects. Therefore, we suggest psychotherapeutic treatment with structured, goal-directed plans for pleasurable events and stimulation. In addition, future trials of non-pharmacological methods (e.g. exercise and other stimulating activities) should aim to naturally increase dopamine or reduce dopamine breakdown, through non-pharmacological methods (e.g. exercise and other stimulating activities). Future research should investigate the utility of combining non-dopaminergic pharmacological treatments (e.g. acetylcholinesterase inhibitors) with psychotherapeutic interventions to improve anhedonia and apathy associated with PD. Importantly, we recommend non-dopaminergic pharmacological interventions because adding dopaminergic medications to regimens that optimally control motor symptoms may produce side effects (e.g., dyskinesias) in PD.

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Results of significant regression analyses

Table 1

Model. Dependent Variable	Model R^2	Effect of Independent Variable/Covariate on Dependent Variable, B (SE)			
		Apathy Scale	Group	Age	Education
Model 1. SHPS	.33**	.30 (.10)**	2.71 (1.10)**	ns	ns
Model 2. TEPS Anticipatory	.15*	-.45 (.19)*	ns	ns	ns
Model 3. TEPS Consummatory	.10*	ns	ns	ns	-.51 (.25)*
Model 4. BAS Drive	.03*	-.15 (.05)**	ns	ns	ns

Table 1 summarizes the four significant regression models identified in this study. As shown, Model 1 revealed that Apathy Scale scores and group membership significantly predicted SHPS scores. Model 2 indicated that only Apathy Scale scores significantly predicted to TEPS Anticipatory scores. Model 3 revealed that only the covariate Education significantly related to TEPS Consummatory scores. Finally, Model 4 indicated that only Apathy Scale scores significantly related to BAS Drive scores.

Note. SHPS: Snaith-Hamilton Pleasure Scale; BDI-II: Beck Depression Inventory, 2nd Edition; TEPS: Temporal Experience of Pleasure Scale; BAS: Behavioral Activation Scale; PD: Parkinson's disease. Asterisks indicate significant levels.

** $p < .01$

* $p < .05$.