

Motivational modes and learning in Parkinson's disease

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Learning and motivation are intrinsically related, and both have been linked to dopamine. Parkinson's disease results from a progressive loss of dopaminergic inputs to the striatum and leads to impairments in motivation and learning from feedback. However, the link between motivation and learning in Parkinson's disease is not well understood. To address this gap, we leverage a well-established psychological theory of motivation, regulatory mode theory, which distinguishes between two functionally independent motivational concerns in regulating behavior: a concern with having an effect by initiating and maintaining movement (Locomotion) and a concern with establishing what is correct by critically evaluating goal pursuit means and outcomes (Assessment). We examined Locomotion and Assessment in patients with Parkinson's disease and age-matched controls. Parkinson's disease patients demonstrated a selective decrease in Assessment motivation but no change in Locomotion motivation, suggesting that Parkinson's disease leads to a reduced tendency to evaluate and monitor outcomes. Moreover, weaker Assessment motivation was correlated with poorer performance on a feedback-based learning task previously shown to depend on the striatum. Together, these findings link a questionnaire-based personality inventory with performance on a well-characterized experimental task, advancing our understanding of how Parkinson's disease affects motivation with implications for well-being and treatment outcomes.

Keywords: motivation; Parkinson's disease; striatum; feedback learning; dopamine

INTRODUCTION

Adaptive behavior relies on learning in order to improve choices based on experiences, but motivation to do so is of equal importance. From a neurobiological perspective, learning and motivation have both been linked to dopamine. Numerous studies have linked firing of dopaminergic neurons or activity in brain regions that receive dopaminergic input to learning from reinforcement (Schultz *et al.*, 1997; O'Doherty *et al.*, 2003), and dopamine has been shown to play a critical role in motivated behavior, such as choosing to expend greater effort or wait longer in order to obtain larger rewards (Niv *et al.*, 2006; Salamone and Correa, 2012; Wang *et al.*, 2013).

Parkinson's disease (PD) is characterized by a progressive loss of dopaminergic inputs to the striatum that leads to impaired motor control, often considered a core symptom of the disease. The past decade has seen mounting evidence that learning and reward processing are also compromised in PD, consistent with the proposed role of dopaminergic signals in learning (Schultz, 1998; Frank *et al.*, 2004; Shohamy *et al.*, 2004; Foerde and Shohamy, 2011b). Additionally, it has long been speculated that PD is associated with a general motivation deficit (Todes and Lees, 1985; Glosser *et al.*, 1995; Menza, 2000; Dagher and Robbins, 2009). The prevalence of depression and apathy in the disease, along with reduced novelty seeking and reported decreases in susceptibility to addiction (Glosser *et al.*, 1995; Menza, 2000), is thought to result from a general depletion in dopaminergic circuits prior to diagnosis with PD (Aarsland *et al.*, 2012). The dorso-lateral striatum, which is the most severely affected region early in PD, is thought to be most directly related to the motor dysfunction, whereas motivational functions are more commonly associated with the ventral striatum (Liljeholm and O'Doherty, 2012). However, subtle deficits associated with less affected ventral striatal circuits may still give rise to affective, cognitive and behavioral changes. It is assumed

that this wide variety of deficits in PD share a single initial cause, and there is an emerging understanding that dopaminergic dysfunction and related striatal dysfunction have multifarious effects involving learning (Dagher and Robbins, 2009; Shohamy and Adcock, 2010), motivation (Salamone and Correa, 2002; Niv *et al.*, 2006) and performance (Smittenaar *et al.*, 2012). These wide-ranging effects highlight the need for a better understanding of how dopaminergic deficits in PD manifest in motivational and cognitive changes and, in particular, of the interrelation of these effects, both at the neural and psychological level.

Dopamine operates in both tonic and phasic modes, resulting in signals that convey distinct kinds of information. Phasic dopamine signals carry temporally specific learning signals (Schultz, 2000; Glimcher, 2011) and are commonly associated with reward. Notably, dopamine is associated with expectation and instrumental aspects of pursuing rewards (or wanting) rather than consummatory or hedonic aspects (liking) (see Salamone and Correa, 2012 for review). Tonic dopamine signals, according to recent proposals, may instead carry information about overall rates of responding or 'response vigor' that may be related to overall levels of reward available (Niv, 2007; Beierholm *et al.*, 2013; Wang *et al.*, 2013). That is, in a context where rewards are plentiful, it is advantageous to work vigorously to obtain as much reward as possible. Dopaminergic dysfunction should affect functions relying on both phasic and tonic signaling, and there is substantial evidence that this is the case in PD. Impaired learning from rewards has been widely documented (Knowlton *et al.*, 1996; Frank *et al.*, 2004; Hopkins *et al.*, 2004; Foerde and Shohamy, 2011a), and individuals with PD exhibit decreased movement vigor, even when they are able to accurately execute movements (Mazzoni *et al.*, 2007). Thus, PD appears to affect multiple aspects of motivation, perhaps through dysfunction in both phasic and tonic signaling (Dayan and Balleine, 2002; Niv *et al.*, 2006).

Additionally, dopamine neurons arise from two main clusters in the midbrain, the substantia nigra pars compacta and the ventral tegmental area, which project to distinct anatomical targets. PD progresses from primary involvement of substantia nigra neurons that project to dorsolateral striatum in the early stages of disease, toward also affecting neurons projecting to the ventral striatum (Bernheimer *et al.*, 1973;

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Kish *et al.*, 1988; Hornykiewicz, 1989; Cools, 2006). Together, these aspects of dopaminergic function suggest that dopamine can be involved in different forms of motivation characterized by neuroanatomical specificity and distinct signaling modes, thereby accounting for the varied deficits stemming from dopamine dysfunction. Paired with a stereotypical disease progression in PD from dorsolateral to ventromedial degeneration of midbrain and striatum function, some specificity in the effects of PD on motivation should be expected and these effects are likely to change with disease progression.

As outlined above, important progress has been made in understanding distinctions between different forms of motivation and learning based on computational and neurobiological models. In contrast, psychological and personality level theories targeting motivation have not generally been sensitive to such distinctions. Instead, broad measures of apathy and depression have been used to demonstrate differences in PD patients, but these measures may not always have the resolution to provide tighter links across neural, computational and psychological levels of analysis. Linking self-report measures of motivation with experimental tasks that have been characterized in terms of their computational or neural underpinnings could provide the initial steps needed to bridge across levels of analysis.

Recent work has explored the interface of motivation and cognition in healthy individuals by linking psychological theories of motivation with classification learning and decision making (Markman *et al.*, 2005; Maddox *et al.*, 2006; Worthy *et al.*, 2007; Maddox and Markman, 2010; Otto *et al.*, 2010). A similar approach might illuminate the interplay of motivation and cognition in PD. One promising source of insight into understanding motivation and learning in PD comes from regulatory mode theory (Kruglanski *et al.*, 2000; Higgins *et al.*, 2003). Regulatory mode theory describes two functionally independent motivational concerns in regulating behavior. One mode, termed 'Locomotion', involves a concern with having an effect by initiating and maintaining movement, regardless of whether all alternatives have been fully considered ('get going'). A distinct and independent, and potentially complementary, motivational concern termed 'Assessment' involves establishing what's right and correct through critical evaluation and comparison of all possibilities. Assessment entails an emphasis on discovering and precisely understanding the relative worth of alternative goal pursuit means and outcomes, and, as a consequence, involves a desire to carefully observe feedback from the environment to stay in line with norms and goals ('get it right') (Kruglanski *et al.*, 2000). Given this distinction, Locomotion motivation should be most strongly related to 'movement vigor' or the 'energizing' functions described for dopamine above, whereas Assessment motivation should be most strongly related to the learning functions of dopamine. Regulatory mode has been characterized extensively in healthy populations (Kruglanski *et al.*, 2000; Higgins *et al.*, 2003), where it has shed light on motivational processing and performance. Yet it remains unknown whether, and how, regulatory modes are altered in PD.

We sought to address this gap by studying how PD affects Locomotion and Assessment *and* by determining how motivational modes in PD are related to the well-characterized learning deficits in this population. We focused on two main questions: First, does the dopaminergic dysfunction, as seen in PD, affect the motivational modes of Locomotion and Assessment uniformly? Second, are changes in motivational modes in PD related to striatal-dependent feedback learning?

We used the Regulatory Mode Questionnaire (Kruglanski *et al.*, 2000) to measure chronic motivation and computed scores on the Locomotion and Assessment scales. Importantly, the Regulatory Mode Questionnaire consists of questions whose content does not overlap with diagnostic interviews for diagnosis of PD, and it has

been used to predict performance and decision making across a range of settings in healthy individuals (see Kruglanski *et al.*, 2000; Higgins *et al.*, 2003; Kruglanski *et al.*, 2013).

In order to measure striatal-dependent feedback learning deficits, we used a probabilistic learning task in which feedback was delivered either immediately or after a delay. Previously, we found that the timing of feedback modulates whether learning depends on the striatum (for immediate feedback) or on the hippocampus (for delayed feedback) (Foerde and Shohamy, 2011a; Foerde *et al.*, 2013b; see also Maddox *et al.* (2003), Maddox and Ing, 2005). Thus, this task provides a 'within-subject' measure of the selective impairment of learning that depends on the striatum, which is the region most compromised in PD.

Guided by current understanding of motivation in PD, we considered several different relations between PD and regulatory mode. Given that PD is associated with loss of motor control and changes in the computations underlying the exertion of movement vigor (even in PD patients on dopamine replacement therapy; Mazzoni *et al.*, 2007), one possibility was that Locomotion—the motivation to move from state to state, manage to make things happen or get going—would be weaker in PD patients. However, given that PD is also associated with intrinsic monitoring problems (e.g. enhanced walking when externally cued by painted footsteps or an auditory beat), another possibility was that Assessment—the motivation to establish what's correct, critically evaluate alternatives or get it right—would be weaker among PD patients. Finally, both Locomotion and Assessment, although functionally independent, could be weaker among PD patients.

Additionally, in order to begin understanding whether dopaminergic dysfunction exerts independent influences on learning and motivation, we sought to determine whether differences in regulatory mode motivation are linked to those specific learning deficits that are associated with dopaminergic dysfunction in the striatum. We reasoned that if learning deficits associated with striatal dopamine dysfunction were associated with motivational mode scores, this would point to a link between striatal dopamine dysfunction and motivational changes.

MATERIALS AND METHODS

Participants

Fifty-seven participants with a diagnosis of idiopathic PD were recruited from the Center for Parkinson's Disease and Other Movement Disorders at the Columbia University Medical Center's Department of Neurology with the assistance of Dr Lucien Cote and through online databases for volunteers interested in participating in research on PD (Fox Trial Finder, PDtrials). Only patients in mild or moderate disease stages (Hoehn and Yahr stage 1–3) were recruited. Seventy healthy controls, matched to the PD patients on age and education, were recruited from Columbia University and the community surrounding Columbia University (Table 1). All participants provided informed consent in accordance with the guidelines of the Institutional Review Board of Columbia University and were paid \$12/h for their participation.

Participants were excluded if they had suffered brain injury, were diagnosed with neurological or psychiatric disorders other than PD or were on antidepressant, antipsychotic or anxiolytic medication. All participants completed a battery of neuropsychological tests and were excluded if they exhibited general cognitive impairment [scoring 27 (2.5 s.d. below the mean) or below on the Mini-Mental State Exam, MMSE] or showed signs of depression [scoring 7 (2.5 s.d. above the mean) or above on the cognitive subscale of the Beck Depression Inventory, BDI]. This left 42 PD patients and 53 older adult controls. The PD and healthy control groups did not differ in age, education or neuropsychological assessments ($P > 0.25$). PD patients were tested

Table 1 Demographic and neuropsychological characteristics of participants

	Regulatory mode participants				Feedback learning participants ^a			
	AC (<i>n</i> = 53)		PD (<i>n</i> = 42)		Control (<i>n</i> = 24)		PD (<i>n</i> = 24)	
Age	65.2	7.9	64.1	7.2	63.3	7.3	65.2	8.2
Male/Female	14/39		17/25		6/18		11/13	
Education	16.3	1.4	16.6	2.6	16.2	1.6	16.1	2.1
MMSE	29.6	0.7	29.4	0.8	29.5	0.6	29.3	0.8
COWAT	46.9	13.9	46.5	12.6	45.3	12.4	43.9	11.0
NAART	15.5	9.2	15.2	7.5	15.2	8.3	17.0	6.9
Digit Span	12.3	2.1	12.0	1.7	12.3	2.2	12.0	1.6
BDI ^b	3.3	2.9	6.4	5.1	3.0	2.0	6.5	5.3
BDI cognitive	1.0	1.2	1.4	1.5	0.8	1.2	1.4	1.5
PD duration			6.4	5.1			6.7	6.1
UPDRS Motor			18.5	11.1			28.5	14.2
H-Y			1-3				1-3	

Table displays mean and s.d. for AC and PD patients.

COWAT = Controlled Oral Word Association Test; NAART = North American Adult Reading Test.

^aNote that the feedback learning participants are a subset of the Regulatory Mode Questionnaire participants.

^bThe PD group had significantly higher overall BDI scores ($P = 0.002$) but did not differ significantly on the cognitive subscale ($P = 0.17$). This was also the case for the Feedback learning participants (BDI: $P = 0.039$; BDI cognitive subscale: $P = 0.25$).

either on medication (ON state: $n = 27$) or off medication [OFF state: $n = 15$; either withdrawn from medication ($n = 10$) or not yet receiving dopaminergic treatment ($n = 5$)]. Withdrawal from medication entailed omission of medications taken for PD in the morning such that withdrawal had occurred overnight (~16 h), as is common practice in the field (Cools et al., 2001b; Frank et al., 2004; Shohamy et al., 2006).

Procedure

Participants filled out the Regulatory Mode Questionnaire to assess motivation and completed a neuropsychological battery to assess overall cognitive function and mood (MMSE, North American Adult Reading Test, Controlled Oral Word Association Test, Digit Span and the BDI). A subset [$n = 48$: PD, $n = 24$ (11 ON and 13 OFF medication); Control, $n = 24$] of participants also completed a computerized feedback learning task. Some participants did not complete the feedback learning task as they were recruited to participate in other tasks not reported here.

Locomotion and Assessment scales

The Regulatory Mode Questionnaire comprises the Locomotion and Assessment scales (see Kruglanski et al., 2000) and requires participants to determine how much they agree with each of 30 statements. An example statement associated with the Assessment scale is 'I often critique work done by myself and others'. An example item from the Locomotion scale is 'By the time I accomplish a task, I already have the next one in mind'. Agreement with these statements is indicated on a 6-point scale ranging from 1 (strongly disagree) to 6 (strongly agree). Scores for Assessment and Locomotion were computed across appropriate items for each scale.

Feedback learning task

Forty-eight of the participants completed a probabilistic learning task, which previously has been shown to be sensitive to striatal function in humans and is known to be sensitive to learning impairments in PD (Knowlton et al., 1996; Poldrack et al., 2001; Shohamy et al., 2004; Foerde et al., 2006; Foerde and Shohamy, 2011a). Note that the majority of these data, with the exception of four PD patients, have been

reported previously in Foerde and Shohamy (2011) and Foerde et al. (2013b). In this type of task, participants learn to associate cues with outcomes through trial and error. Because there is no one to one mapping between cues and outcomes, optimal learning involves the use of response-contingent feedback across multiple trials to incrementally learn the most probable outcome.

We used a version of the task with two within-subject conditions that differed in the timing with which feedback was delivered during probabilistic learning: feedback was either immediate or delayed by a few seconds (Immediate vs Delayed Feedback conditions). In previous work, we have shown that Immediate Feedback learning depends on the striatum and is impaired in PD, whereas Delayed Feedback learning depends on the hippocampus and is spared in PD (Foerde and Shohamy, 2011a; Foerde et al., 2013b).

On each trial, participants saw a cue (one of the four different butterflies) and had to predict which of the two outcomes (different colored flowers) that cue was associated with (Figure 1A). Each butterfly was associated with one flower on 83% of the trials and with the other flower on 17% of the trials (Figure 1B). Response-contingent feedback was presented after a fixed delay of either 1 s (Immediate condition; striatal dependent) or 7 s (Delay condition; striatal independent), such that two butterflies were associated with each feedback timing condition. Participants' choices remained on the screen during the delay in order to minimize working memory demands. The assignment of cues to outcomes and conditions was counterbalanced across participants. Immediate and Delayed feedback trial types were interleaved throughout training. Feedback consisted of a verbal response ('CORRECT' or 'INCORRECT') presented on the screen for 2 s (Foerde and Shohamy, 2011a). A 7 s response deadline was imposed, and a reminder to respond appeared after 4 s.

Participants completed a short practice to ensure that they understood the task and were able to respond in the allotted time. Next, they completed 96 learning trials of the task (Learning phase), followed by a Test phase with 24 trials, in which participants saw the butterflies from the Learning phase and were told to continue performing based on what they had learned. The Test phase structure resembled the Learning phase, with the exception that no feedback was given and the timing of all trial parts was equivalent across trial types.

Performance on the feedback learning task was assessed in terms of making optimal choices—the degree to which participants selected the most likely outcome for each cue. Thus, regardless of the feedback outcome (correct vs incorrect) on each trial, a participant was scored as making a correct response if the flower associated with a butterfly on 83% of trials was selected. The overall optimal proportion correct was calculated separately for the Immediate and Delayed feedback conditions for both the learning and test phases.

RESULTS

Regulatory mode

First, we tested whether Locomotion differed between PD patients and healthy controls (matched to the PD patients on age and education). Although Locomotion and Assessment are considered independent constructs, they were significantly, moderately correlated in our sample ($r = 0.28$, $P = 0.003$). Thus, we compared Locomotion between groups in a univariate analysis of variance (ANOVA) with Assessment as a covariate. PD patients and age-matched controls (AC) did not differ on the Locomotion scale [AC: $M_{\text{adjusted}} = 4.47$, standard error (SE) = 0.10; PD: $M_{\text{adjusted}} = 4.50$, s.d. = 0.12; $F(1,92) = 0.06$, $P = 0.81$; Figure 2A]. Second, we tested whether Assessment differed between PD patients and healthy controls. We compared PD patients and controls using a univariate ANOVA with Locomotion as a covariate. We found that PD patients scored significantly lower on the Assessment scale

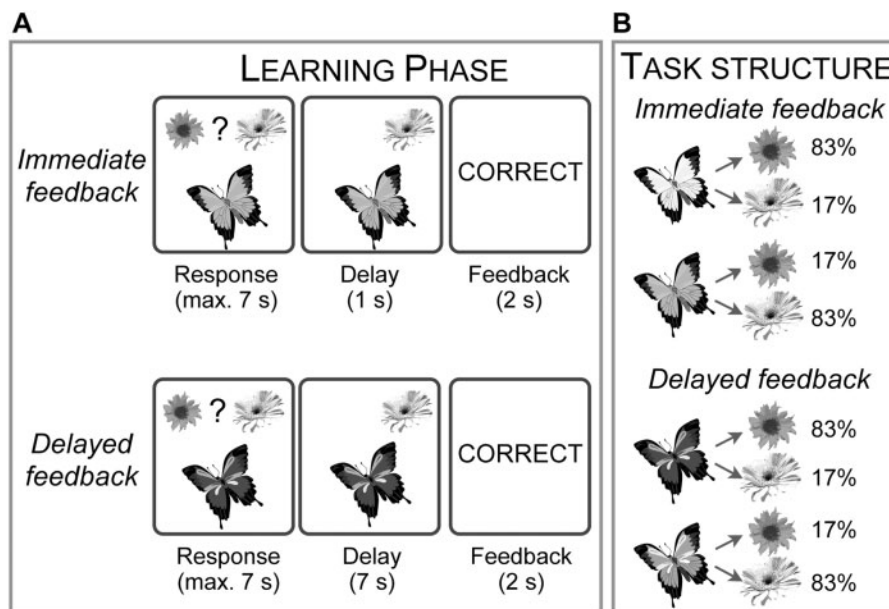


Fig. 1 Probabilistic learning with immediate and delayed feedback. Participants completed a probabilistic learning task in which feedback was delivered either immediately or delayed several seconds. In this task, learning from immediate feedback depends on the striatum, whereas learning from delayed feedback depends on the hippocampus. (A) In the Learning phase, participants used trial-by-trial feedback to learn which of the two outcomes were associated with four different butterflies. On each trial, as soon as a response was made, participants' choices were displayed along with the cue stimulus until feedback was provided. For one pair of cues feedback was presented immediately (1 s) after the response was made, and for another pair of cues feedback was presented with a delay (7 s). Feedback timing (Immediate vs Delayed) was manipulated within subjects, and trial types were interleaved in randomized order during learning. (B) The task required participants to learn which of the two flowers four different butterflies preferred. Each butterfly was associated with one flower on 83% of trials and with the other flower on 17% of trials. Two butterflies were associated with each feedback timing condition and this association was counterbalanced across participants.

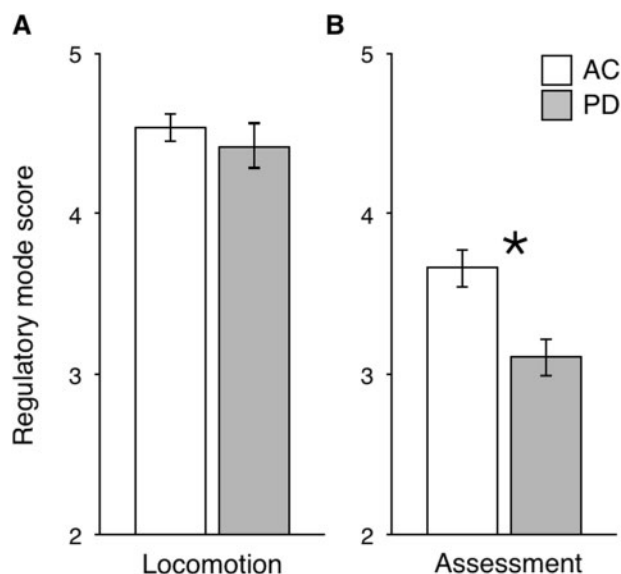


Fig. 2 Regulatory mode in Parkinson's disease patients and healthy controls. Parkinson's disease patients (PD) scored significantly lower than age-matched controls (AC) on the Assessment scale. Groups did not differ significantly on the Locomotion scale.

(AC: $M_{adjusted} = 3.64$, $SE = 0.11$; PD: $M_{adjusted} = 3.12$, $SE = 0.12$; $F(1,92) = 10.58$, $P = 0.002$; Figure 2B). Thus, PD patients differed from controls on Assessment specifically, and not generally in how they answered the questionnaire.

In order to determine whether age affected responses, we also compared Locomotion and Assessment scores of the healthy controls with a sample of young adults. The regulatory mode scales have been used

extensively in young adults and middle-aged adult populations, but not in older populations (50–85 years) such as our sample. We found no differences between young and old adults on either Assessment ($t(102) = -1.42$, $P = 0.16$) or Locomotion ($t(102) = 0.37$, $p = 0.71$), suggesting that differences between PD patients and AC in assessment were not due to age-related differences. Additionally, scores on the built-in 'Lie' scale did not differ between groups overall (one-way ANOVA: $F(2,143) = 0.22$, $P = 0.80$; $M_{YOUNG} = 2.4 \pm 0.78$, $M_{AC} = 2.4 \pm 0.80$, $M_{PD} = 2.3 \pm 0.80$).

Although the study was not designed to compare PD patients ON and OFF medication—the majority of the PD patients were tested while ON their regular dopamine replacement medication ($n = 27$), but some were tested while OFF dopaminergic medication ($n = 15$)—we report this comparison for completeness. ON vs OFF patients did not differ in Assessment scores ($t(40) = -0.67$, $P = 0.51$). Comparing only the patients' ON dopaminergic medication with AC, the difference in Assessment was still significant ($F(1,77) = 6.45$, $P = 0.013$), suggesting that remediation with dopamine replacement therapy did not strengthen Assessment motivation.

Relation between regulatory mode and feedback learning

Next, we sought to determine whether differences in regulatory mode motivation were linked to learning deficits previously associated with dopaminergic dysfunction in the striatum (Foerde and Shohamy, 2011a; Foerde et al., 2013b; Figure 3; the majority of the data included here were reported previously). In order test the link between Assessment and striatal-dependent learning, we focused on a subset of our participants ($n = 48$) who completed the immediate vs delayed feedback learning task described above. If Assessment is related to the striatal dysfunction underlying PD, then Assessment would be expected to be related specifically to learning from immediate feedback (shown previously to depend on the striatum) but not to learning from

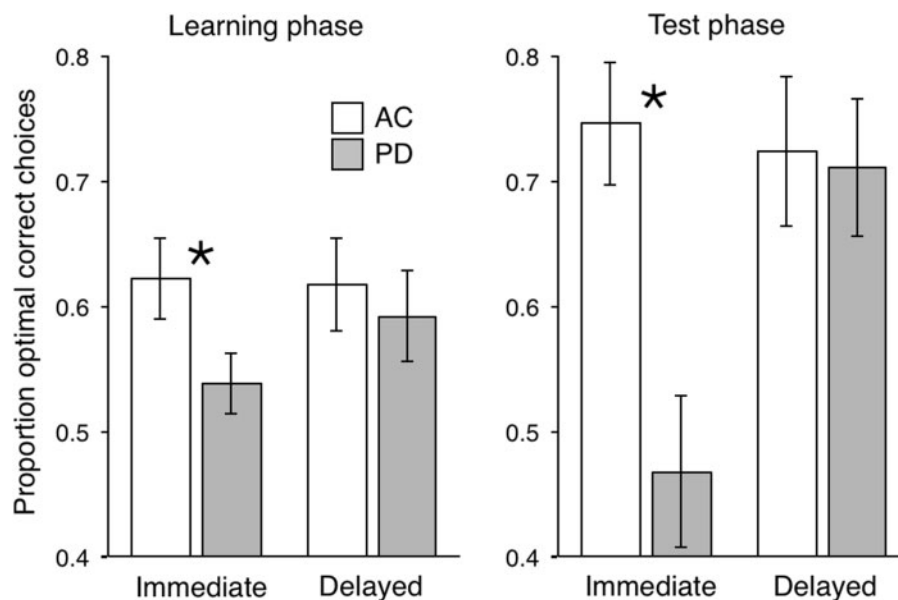


Fig. 3 Performance on immediate and delayed feedback learning task. PD patients were impaired in the Immediate feedback condition in learning and test phases. PD and AC did not differ in the Delayed feedback condition. The majority of data were previously reported in Foerde and Shohamy (2013) and Foerde et al. (2013b).

delayed feedback (shown previously to depend on the hippocampus). Therefore, we planned to test correlations between immediate and delayed feedback learning and Assessment scores.

Across groups, Assessment and Immediate feedback learning were positively correlated ($r=0.32$, $P=0.028$; Figure 4A). In contrast, there was no correlation between Assessment and Delayed feedback learning ($r=-0.07$, $P=0.66$; Figure 4B). The difference between these two correlations was borderline significant ($P=0.036$, one-tailed test for dependent correlations; Lee and Preacher, 2013). Thus, scores on the Assessment scale were specifically related to learning from immediate feedback, which has been shown to depend on the striatum (Foerde and Shohamy, 2011a; Foerde et al., 2013b).

Given the relationship between PD and both Assessment and Immediate feedback learning, we tested whether Assessment motivation mediated the Immediate feedback learning performance through a series of regression analyses (Figure 5). First, disease status (Group: AC/PD coded $-1/+1$) significantly affected Immediate feedback learning ($\beta=0.29$, $t(46)=2.08$, $P=0.043$). Second, disease status was marginally associated with Assessment scores in the reduced subset sample that completed the feedback learning task ($\beta=0.25$, $t(46)=1.72$, $P=0.09$). Finally, there was a near significant association between Assessment and Immediate feedback learning when controlling for disease status ($\beta=0.23$, $t(45)=1.85$, $P=0.07$) and the association between disease status and Immediate feedback learning was non-significant when controlling for Assessment ($\beta=0.23$, $t(45)=1.61$, $P=0.11$). To test the indirect effect, we used the Hayes and Preacher SPSS macro implementing the bootstrapping method (Preacher and Hayes, 2008); the 95% confidence interval (CI) was obtained using 5000 resamples. Results indicated a significant mediating role of Assessment on the relation between disease status and Immediate feedback learning ($\beta=0.0092$, 95% CI = 0.0002–0.0262).

DISCUSSION

Aspects of both learning and motivation are thought to depend on striatal dopamine function and multiple neurobiological mechanisms underpinning such effects on learning and motivation have been posited. Yet little is known about how this relates to broader psychological

theoretical frameworks and personality-based measures of motivation. Here, we determined whether questionnaire-based measures of chronic goal pursuit motivations, related to either movement (Locomotion) or monitoring (Assessment) functions, were affected by PD and were related to performance on an experimental task known to depend on the striatum.

Our results suggest that PD differentially affects Assessment motivation. Patients with PD had lower Assessment scores than healthy controls, but they did not differ in Locomotion. Additionally, the self-reported Assessment scores were correlated specifically with the ability to learn from immediate response-contingent feedback, a form of learning previously shown to depend on the striatum (Foerde and Shohamy, 2011a; Foerde et al., 2013b). The relation between these two separate measures suggests a link between the differences in Assessment in PD and the known feedback-based learning disruption in the disease. Such a link could tie Assessment motivation to the functioning of phasic dopamine signals that are critical for learning in the striatum.

It is increasingly clear that PD involves cognitive and motivational deficits as well as motor deficits, even in the early stages of the disease (White, 1997; Cools et al., 2001a; Frank et al., 2004; Shohamy et al., 2004; Jahanshahi et al., 2010), and the present results are consistent with such findings. Indeed, the lower scores on the Assessment scale, which captures a self-reported reduced motivation to get it right, are consistent with a substantial body of research demonstrating selective deficits in feedback-driven learning in PD (Frank et al., 2004; Shohamy et al., 2004; Cools, 2006; Foerde and Shohamy, 2011a).

Interestingly, recent theoretical (Daw et al., 2005) and empirical (Yin and Knowlton, 2006; Daw et al., 2011) work points to an important distinction between habitual vs goal-directed behavior. Feedback learning is often thought to be habitual in nature, but in past work we have found that feedback learning tasks may invite contributions from both habitual and goal-directed forms of learning (Foerde et al., 2006). The feedback learning task used in this study manipulated the timing of feedback, which we have shown determines whether learning depends on the striatum or the medial temporal lobes (Foerde and Shohamy, 2011a; Foerde et al., 2013b). In this previous work, we

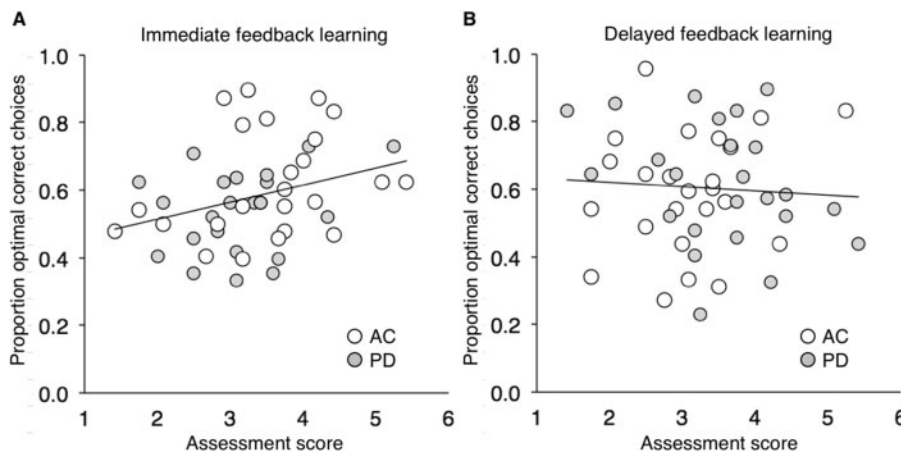


Fig. 4 Relationship between Assessment scores on the Regulatory Mode Questionnaire and learning from immediate and delayed feedback. (A) Across groups, Assessment and Immediate feedback learning were positively correlated ($r = 0.32$, $P = 0.028$). (B) In contrast, there was no correlation between Assessment and Delayed feedback learning ($r = -0.07$, $P = 0.66$).

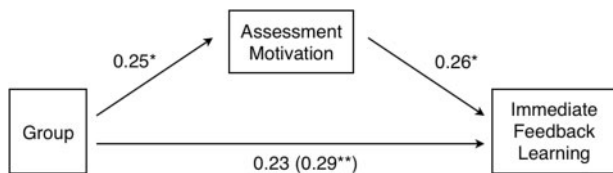


Fig. 5 A mediation analysis testing the hypothesis that Assessment mediates the relationship between disease status group and learning from immediate feedback. Standardized beta coefficients are listed along with P values. * $P < 0.1$, ** $P < 0.05$.

also found that learning that relied on the striatum was related to poorer memory of trial outcomes, which could suggest that such learning may be less goal-directed. However, recent work has shown that it may be difficult to distinguish between habitual vs goal-directed learning at the level of the striatum (Daw et al., 2011), and we cannot preclude the possibility that goal-directed learning played a role even when learning from immediate feedback. Given the characterization of the Assessment scale, it is tempting to speculate that it is more related to goal-directed responding. Although it is often assumed that PD patients suffer primarily from deficits in habitual learning, there is some evidence suggesting this may not be the case (de Wit et al., 2011; M. Sharp, K. Foerde, N.D. Daw, and D. Shohamy, manuscript in preparation) and that dopamine dysfunction may also affect goal-directed learning (de Wit et al., 2012). Moreover, it has been proposed that energizing functions of motivation may be most relevant for habitual responding (Niv et al., 2006). In future work, it would be important to further characterize the links between self-reported motivation and habitual vs goal-directed learning.

Notably, we did not find differences in Locomotion (nor any association with measures of disease severity, e.g. Unified Parkinson’s Disease Rating Scale, UPDRS). Yet motor impairments and energizing deficits in PD are well known (Mazzoni et al., 2007). There are several potential reasons a ‘disconnect’ between observable symptoms and self-reported motivation might occur. One possibility is that while PD patients may report that they still are motivated to take action, they are less effective in doing so. This would be consistent with the idea that a key problem in PD is the translation of internal motivation into selecting the appropriate action (Mogenson et al., 1980; Schmidt et al., 2008; Balleine and O’Doherty, 2010), and selection includes making the right or correct choice, which would involve assessment motivation. Another possibility is that the ‘implicitness’ of

Locomotion vs Assessment differs, such that individuals are less able to accurately report on some motivational functions than others (i.e. less able for the locomotion function)—a possibility that it could be fruitful to explore in future research in order to better understand how to evaluate motivational changes in PD.

The current results extend previous work documenting cognitive and motivational deficits in PD by linking a questionnaire-based goal pursuit personality measure with performance on a well-characterized experimental task that measures striatal learning. A considerable body of research, largely separate from the experimental investigations of cognitive learning deficits in PD, has investigated the idea that those with a predisposition to develop PD share a distinct set of traits—the ‘parkinsonian personality’ (Todes and Lees, 1985; Glosser et al., 1995; Menza, 2000; Dagher and Robbins, 2009). For example, patients with PD are described as rigid, introverted and low in novelty seeking (Glosser et al., 1995; Menza, 2000); traits that have been thought to fit with the idea that damage to the dopaminergic system is present prior to the onset of motor illness and gives rise to a variety of symptoms (Menza, 2000; Aarsland et al., 2012). Thus, an open question is whether the differences in Assessment motivation that we found are the result of changes associated with the onset of PD or reflect stable differences in people who go on to develop PD.

Limitations and future directions

One limitation of this study is that we lack direct measurements of striatal and dopaminergic functioning. Instead, by showing an association between questionnaire measures and an experimental task that was previously characterized in terms of its neural substrates (Foerde and Shohamy, 2011a; Foerde et al., 2013a,b), we provide a strong indirect link to dopaminergic and striatal changes as the neurobiological underpinning of motivational changes in PD. Future neuroimaging and pharmacological investigations will be needed to address this directly.

Another limitation is that we did not have sufficient sample size to evaluate the role of dopaminergic medication status by comparing patients tested ON vs OFF medication. The absence of significant differences in motivation between PD patients ON or OFF medication is consistent with our previous reports of no differences in learning from immediate feedback between PD patients ON and OFF medication (Foerde and Shohamy, 2011a; Foerde et al., 2013a,b), but due to the sample size, we interpret this null result with caution. Previous studies of cognition and learning have found effects of dopaminergic

medication status on both learning and performance on a variety of tasks, such that medication sometimes helps and sometimes hurts performance (Swainson et al., 2000; Cools et al., 2001a; Frank et al., 2004; Shohamy et al., 2006; Jahanshahi et al., 2010). Separately, studies have reported effects of medication status on measures of motivation, such as the Starkstein Apathy scale (Czernecki et al., 2002, 2008; Rektorova et al., 2008; Thobois et al., 2010, 2013; Starkstein, 2012). A question that arises is how pharmacological treatment aimed at alleviating motor symptoms affects motivation, which could be a critical issue in managing the care of patients with PD. Future studies should assess motivation in PD patients who are medication naïve to disentangle the effects of changes in dopaminergic medication once treatment is initiated from those of dopaminergic dysfunction in the striatum associated with the onset of PD.

Finally, a limitation that is shared by most studies attempting to systematically investigate motivation in PD is that we cannot determine whether PD changes motivational concerns or whether people who are diagnosed with PD fit particular profiles. In order to address these questions it will be necessary to track motivational changes longitudinally. It will be particularly useful to examine changes on well-characterized cognitive and motor tasks along with measures of motivation to understand how the neurobiological changes in the disease affect these functions uniformly and/or selectively. Further work in this arena is of particular interest because it holds the promise of identifying personality inventory-based markers of the disease prior to the onset of motor illness.

CONCLUSION

We found that PD was associated with changes in motivational concerns, selectively in concerns with critical evaluation and comparison of goal pursuit means and outcomes (Assessment) rather than concerns with initiating and maintaining movement (Locomotion). Moreover, we found that scores of Assessment motivation were correlated with performance on a separate learning task, one that requires the use of immediate response-contingent feedback to drive learning and which has previously been shown to depend on the striatum. Understanding how distinct motivational concerns are affected by PD and how various treatments impact motivation may have implications for patients' well-being and engagement with treatment options (e.g. propensity to exercise, participation in therapy). A richer understanding of motivation in PD may also help identify markers of disease prior to the onset of motor illness.

CONFLICT OF INTEREST

None declared.

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