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Motivational engagement in Parkinson's disease: Preparation for motivated action

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ABSTRACT

The current study investigated whether motivational dysfunction in Parkinson's patients is related to a deficit in preparing for motivated behavior. Based on previous studies, it was hypothesized that PD patients would show reduced preparation for action specifically when faced with threat (of loss) and that reduced action preparation would relate to self-report of apathy symptoms. The study measured an electrocortical correlate of preparation for action (CNV amplitude) in PD patients and healthy controls, as well as defensive and appetitive activation during emotional perception (LPP amplitude). The sample included 18 non-demented PD patients (tested on dopaminergic medications) and 15 healthy controls who responded as quickly as possible to cues signaling threat of loss or reward, in which the speed of the response determined the outcome. Results indicated that, whereas PD patients showed similar enhanced action preparation with the addition of incentives to controls, PD patients showed generally reduced action preparation, evidenced by reduced CNV amplitude overall. Results suggest that PD patients may have behavioral issues due to globally impaired action preparation but that this deficit is not emotion-specific, and movement preparation may be aided by incentive in PD patients.

1. Introduction

Parkinson's disease (PD) is a degenerative disease of the central nervous system, typically recognized by cardinal motor symptoms of tremor, rigidity, bradykinesia, and postural instability. In addition to motor symptoms, PD patients experience a number of cognitive and emotional changes, including high rates of depression, anxiety, and apathy (Schneider et al., 2008; Pedersen et al., 2009), even when compared to other disabled medical populations (Pluck and Brown, 2002). Although research has made significant strides in understanding the pathophysiology underlying motor symptoms in PD (e.g. Delong, 1990), emotional and motivational changes are less well understood and remain some of the most debilitating symptoms of the disease (Weintraub et al., 2004; Visser et al., 2008). To better understand the nature of motivational and emotional dysfunction in Parkinson's disease, the current study investigated physiological correlates of these constructs in the laboratory, from preparation for motivated behavior to emotional perception.

According to the defense cascade model of emotion (Lang et al., 1997), emotion can be considered an action disposition, characterized by a physiological cascade where, as threat becomes more imminent, physiological reactivity shifts from enhanced orienting to preparation for action, in order to avoid a threat or capture a reward (Lang et al., 1997). Theoretically, affective pathology could be related to deficits at any level of the response cascade, from preparation for action or goal-directed behavior to oriented perceptual intake. Löw et al. (2008) developed an experimental paradigm to simulate the defense cascade in the laboratory, which measures physiological correlates of preparation for imminent action and emotional perception (Löw et al., 2008). In the current study, this paradigm was adapted for use in exploring motivational and emotional processes in Parkinson patients.

A number of theorists have proposed that disordered motivation in PD or "apathy" (Marin, 1991) may be due to a deficit in preparing for and initiating goal-directed behavior (Levy and Dubois, 2006). Apathy is defined as a primary deficit in motivation associated with reduced goal-directed behaviors (Marin, 1991) and is highly prevalent in frontal-subcortical diseases such as Parkinson's. In addition, data suggest that apathy may be related to Parkinson's disease pathology itself, as Zahodne et al. (2012) found that apathy follows a similar trajectory as motor symptom progression in Parkinson's. Stuss and Alexander (2000) suggested that apathy results from a variety of deficits in the central nervous system, including affective (flattening of emotional responsiveness), behavioral (reduced initiation of spontaneous behavior), and executive dysfunction (difficulty planning/executing), processes that are interrelated and frequent concomitants of Parkinson's disease. The hypothesis examined in the current study is that motivational

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dysfunction in PD is a deficit primarily in preparation for motivated behavior.

Previous studies have reported that PD patients show reduced potentiation of the startle reflex compared to healthy control participants when viewing aversive pictures (Bowers et al., 2006; Miller et al., 2009; Zahodne, 2011), and at least one of these studies also found that attenuated startle reflex is positively related to apathy symptoms (Bowers et al., unpublished data). On the other hand, whereas Parkinson patients demonstrate normal sympathetic arousal when viewing affective pictures, reduced exploration via voluntary eye movements is found (Dietz et al., 2011), prompting the hypothesis that PD patients may be impaired at the level of initiating motivated behavior, rather than showing deficits in affective arousal when confronted with emotionally engaging cues. This hypothesis is consistent with findings of reduced startle potentiation in PD, as the startle eye-blink is a somato-motor reflex that reflects readiness for defensive behavior (Lang et al., 1997; Carlsen et al., 2004).

When electrocortical responses in PD patients are measured during affective picture viewing, PD patients demonstrate reduced cortical response specifically to aversive (not pleasant or neutral pictures; Dietz et al., 2013) as evidenced by reduction of the late positive potential or "LPP", a positive-going event-related potential that is maximal 400–700 ms over centro-parietal sensors (e.g., Cuthbert et al., 1995; Schupp et al., 2000). Similar to the startle reflex data, reduced LPP to unpleasant pictures is also associated with higher self-reported apathy in Parkinson patients. Findings of reduced cortical response and reduced startle potentiation during unpleasant picture viewing in Parkinson patients suggest that the defensive motivational system—the brain's innate physiological response to threatening stimuli (Bradley et al., 2001)—may be specifically impaired in Parkinson's disease. Based on these findings, we hypothesized that motivational dysfunction in PD would be evidenced by diminished preparation for defensive behavior, and that the deficit is related to self-report of apathy symptoms.

On the other hand, some data support a hypothesis of generally reduced preparation for action in PD that is not specific to defensive motivation. For example, several studies have found that PD patients show a smaller contingent negative variation (CNV) prior to a simple motor response than controls (Tsuda, 1982; Amabile et al., 1986; Oishi et al., 1995; Verleger et al., 1999; Pulvermüller et al., 1996). The CNV is a slow event-related potential that is largest in the anticipatory period just prior to a motor response (Simons et al., 1979). The CNV is also modulated by affective arousal or the addition of an incentive tied to the behavioral response (Simons et al., 1979; Chwilla and Brunia, 1991; Kotani et al., 2001, 2003; Masaki et al., 2006; Ohgami et al., 2004, 2006). Although PD patients, compared to controls, have shown reduced CNV amplitude in a variety of simple motor tasks (e.g. go/no-go task, Pulvermüller et al., 1996), the question investigated here is whether the CNV will be differentially modulated by incentive.

Thus, the current study measured electrocortical activity in PD patients and controls using a task adapted from Löw et al. (2008) in which ERPs to salient cues are measured during preparation for action. On each trial, specific cues are presented that signal the possibility of either loss or reward which the participant can either avoid (loss) or gain (reward) based on the speed of their response to an imperative stimulus, and the amplitude of the CNV leading up to the motor response is measured. It is hypothesized that Parkinson's patients will show blunted activation of the defense system, evidenced by smaller CNV in PD patients compared to controls during threat (of loss) condition. An alternative hypothesis is that PD patients will show reduced preparation for action across all conditions, regardless of incentive, which would indicate that the deficit in preparation for action is broad and not specific to motivated behavior.

A secondary aim of the current study was to replicate findings of reduced LPP amplitude during unpleasant picture viewing in PD patients (Dietz et al., 2013). To do so, unpleasant, pleasant, or neutral pictures were presented on pseudorandomized trials, separate from preparation for action trials, and the amplitude of the late positive potential was measured and correlated with self-report of apathy symptoms. A deficit in defensive motivational activation would be evidenced by reduced LPP amplitude during unpleasant picture viewing compared to controls (based on Dietz et al., 2013) that varies with self-reported apathy.

2. Material and methods

2.1. Participants

A total of 18 non-demented patients with idiopathic Parkinson's disease (PD) and 15 healthy age-matched controls participated in the study. The Parkinson patients were recruited through the clinics of the University of Florida's Center for Movement Disorders and Neurorestoration (CMDNR); the control participants were spouses of patients or recruited from the community.

To be included in the Parkinson group, participants: a) had a clinical diagnosis of idiopathic PD (Hughes et al., 1992) based on the presence of at least two of three cardinal motor signs of PD (i.e., bradykinesia, resting tremor, rigidity) and a positive response to dopaminergic therapy based on improved motor subscore of the Unified Parkinson's Disease Rating Scale-Third Edition (UPDRS-III; Fahn et al., 1987) and b) were on stable regimen of Parkinson medication (6 months) prior to participating in this study. Patients were tested "on" their dopaminergic medications in order to accurately reflect their day to day functional state, especially given that emotion and motivation dysfunction persist in Parkinson's patients despite dopaminergic therapy (possibly due to the fact that motor and limbic functions have different optimal dopaminergic dosages; Cools, 2006). Indices for gauging disease severity were obtained as part of normal clinical care and included in correlational analyses only if within six months of the testing session. Specific measures included the motor scale of the UPDRS-III and staging from the Hoehn–Yahr scale.

Specific exclusion criteria employed during recruitment for the Parkinson group included (a) evidence of secondary or atypical parkinsonism, b) brain surgery including deep brain stimulation, pallidotomy, thalamotomy, or fetal cell transplants, c) evidence of dopamine dysregulation disorder; or d) dopamine-related dyskinesias that would affect EMG or ERP recordings, e) neurologic disturbance (other than Parkinson disease for the PD group) or chronic medical illness (i.e., HIV, metastatic cancer, etc.). Other exclusion criteria, assessed at the time of the testing session, included: a) significant cognitive disturbance based on MMSE <25; b) current or past history of major psychiatric disturbance based on the self-report (e.g., schizophrenia, bipolar, anxiety disorders, major depressive disorder (anxiety and depressive disorders were screened out only for patients whose disorders preexisted the Parkinson diagnosis, as we intended to include patients with a range of affective symptoms due to PD in the current study for the purposes of correlational analyses). Axis I disorders were screened with a structured clinical interview. Participants who were taking anti-depressant medications were included, since many of the PD patients seen at the UF Center for Movement Disorders and Neurorestoration are prescribed anti-depressants even in the absence of a diagnosis of major depressive disorder for sub-clinical depressive symptoms and/or mood maintenance.

2.2. Screening evaluation (Parkinson patients and control group)

All participants were fully informed of the nature of the study and written informed consent was obtained according to University of Florida and federal guidelines. All participants received neurocognitive, psychiatric, and mood screening to rule out dementia and other significant psychopathology, mood disturbance, or other factors (i.e., medical history) that would interfere with their participation in this study. This screening evaluation occurred on the same day as the acquisition of