



The late positive potential, emotion and apathy in Parkinson's disease

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ABSTRACT

Parkinson's disease is associated with emotional changes including depression, apathy, and anxiety. The current study investigated emotional processing in non-demented individuals with Parkinson disease (PD) using an electrophysiological measure, the centro-parietal late positive potential (LPP). Non-demented patients with Parkinson's disease ($n=17$) and healthy control participants ($n=16$) viewed pleasant, neutral, and unpleasant pictures while EEG was recorded from a 64-channel geodesic net. The Parkinson patients did not differ from controls in terms of early electrophysiological components that index perceptual processing (occipital P100, N150, P250). Parkinson patients, however, showed reduced LPP amplitude specifically when viewing unpleasant, compared to pleasant, pictures as well as when compared to controls, consistent with previous studies suggesting a specific difference in aversive processing between PD patients and healthy controls. Importantly, LPP amplitude during unpleasant picture viewing was most attenuated for patients reporting high apathy. The data suggest that apathy in PD may be related to a deficit in defensive activation, and may be indexed cortically using event-related potentials.

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1. Introduction

Parkinson's disease (PD) is a neurodegenerative disease related to the loss of dopamine neurons in the substantia nigra and a degeneration of multiple motor and non-motor basal ganglia circuits (Alexander, DeLong, & Strick, 1986). While the essential characterizing symptom of PD is abnormal motor activity, in the form of tremors, rigidity and bradykinesia, there are also significant impairments in cognitive and emotional functioning (Blonder, Gur, Gur, Saykin, & Hurtig, 1989). For instance, both depression and apathy are significantly higher in Parkinson's patients than in other medically debilitated populations (Kirsch-Darrow, Fernandez, Marsiske, Okun, & Bowers, 2006; Reijnders, Ehrt, Lousberg, Aarsland, & Leentjens, 2009), with previous research reporting rates of apathy (without depression) up to 17–30%, suggesting that apathy may be a unique feature of PD (Kirsch-Darrow et al., 2006; Oguru, Tachibana, Toda, Okuda, & Oka, 2010).

Among the possible mechanisms underlying emotional dysfunction in Parkinson's disease are amygdala abnormalities (Tessitore et al., 2002) and degeneration of non-motor basal ganglia thalamo-cortical loops, caused by dopamine depletion in

the ventral striatum, an area known to project to regions of the frontal cortex important in emotional behaviors (i.e., anterior cingulate cortex and lateral orbitofrontal cortex; Alexander et al., 1986; cf. Zgaljardic, Borod, Foldi, & Mattis, 2003). Whether emotional difficulties, particularly apathy, result from an affective disturbance or a behavioral deficit remains unclear (Brown & Pluck, 2000; Levy & Czernecki, 2006). For instance, PD patients report that emotion is experienced as intensely as healthy controls, but rate themselves as less emotionally expressive (Mikos et al., 2009), partially due to reduced emotional facial expressions (Bowers et al., 2006a).

Lang's motivational theory (Lang & Bradley, 2010) views emotion as reflecting activation in fundamental defensive and appetitive systems that have evolved to mediate attention and action in life-threatening and life-sustaining contexts. According to this view, emotional reactions to environmental cues reflect activation in basic defensive and appetitive neural circuits, indexing the extent of both defensive and appetitive motivation. Pictures depicting threatening and appetitive natural scenes encountered by humans in the world are cues that reliably activate these circuits (Lang & Bradley, 2010). Previous studies have found that individuals with PD showed reduced potentiation of the startle eye blink response, a defensive reflex, when viewing unpleasant pictures, compared to healthy controls (Bowers et al., 2006b; Miller, Okun, Marsiske, Fennell, & Bowers, 2009; Zahodne, 2012).

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Reduced defensive activation may be mediated by a disturbance that is driven by amygdala dysfunction, as the amygdala plays a central role in fear potentiated startle circuitry (Davis, 1992; Lang, 1995). While such a deficit might suggest that Parkinson's patients are generally hypoaroused to emotional stimuli (Miller et al., 2009), in a more recent study we found that pupil dilation, an index of sympathetic arousal, was significantly enhanced in Parkinson's patients when viewing pleasant or unpleasant pictures, a pattern similar to that found in healthy controls (Dietz, Bradley, Okun, & Bowers, 2011). Electrophysiological indices of brain response during emotional processing could help address these discrepant results. One of the most reliable measures of emotion during picture processing is the amplitude of the late positive potential (LPP), a slow positive deflection over centro-parietal sensors that has been repeatedly found to be enhanced when viewing emotionally arousing pictures (e.g., Cacioppo, Crites, Gardner, & Berntson, 1994; Bradley, 2009; Cuthbert, Schupp, Bradley, Birbaumer, & Lang, 2000; Keil et al., 2002). The LPP begins around 300 ms following picture onset, can last up to 6 s and shows maximal positivity for sensors placed over the centro-parietal area of the brain (Bradley, 2009; Cuthbert et al., 2000). While LPP modulation is correlated with other measures of subjective and autonomic arousal (Cuthbert et al., 2000), it does not completely habituate with stimulus repetition, suggesting it may be a sensitive index of fundamental defensive and appetitive activation (Bradley, 2009).

Thus, in the current study, we measured the late positive potential while Parkinson patients and healthy controls viewed pleasant, neutral, and unpleasant pictures. Based on the pupillary findings of Dietz et al. (2011), one hypothesis is that PD patients will show normal affective modulation of the LPP. An alternative hypothesis, based on findings of blunted startle response in PD patients (Bowers et al., 2006b) is that PD patients will show a reduced LPP specifically when viewing unpleasant pictures. Because apathy may be a feature of Parkinson's disease that significantly affects emotional reactivity, an additional exploratory aim was to examine the relationship between apathy (measured by the apathy scale; Starkstein et al., 1992) and LPP modulation. Marin (1991) has defined apathy as a primary lack of motivation/goal-directed behavior which involves cognitive, affective, and behavioral domains. His proposed diagnostic criteria within the affective domain includes "unchanging affect" or "lack of emotional responsivity to positive or negative events," which suggests that patients high in apathy may show deficits when viewing either pleasant or unpleasant pictures.

Effects of hedonic content on earlier components of the ERP during picture viewing have proved somewhat less reliable, with some studies reporting differences and others not (Olofsson, Nordin, Sequeira, & Polich, 2008). We assessed the magnitude of a number of early ERP components (frontal N250, occipital P100, N150, P250 or EPN) that are involved in picture processing primarily to assess early sensory and perceptual processing in PD patients and controls. If PD patients specifically differ in terms of affective processing, differences in the early ERP components that index initial sensory and perceptual processing between PD patients and controls are not expected. For instance, Wieser et al. (2006) reported that PD patients did not differ from controls on the amplitude of an early occipital component (EPN) found during affective picture viewing.

2. Methods

2.1. Participants

Twenty-four non-demented Parkinson's patients and 18 healthy older adults participated in the current study. Parkinson's patients were recruited from the University of Florida Center for Movement Disorders and Neurorestoration and

Table 1

Demographic and clinical characteristics of Parkinson's and healthy older adult groups. Mean (standard deviation) is presented for quantitative variables and ratios are presented for categorical variables.

	Mean (SD) or ratio		P-Value
	Parkinson (N=17)	Control (N=16)	
Gender (M/F)	16/1	14/2	.10
Antidepressant (Y/N)	6/11	0/16	.01
Age	59.9 (8.4)	70.6 (9.0)	$p < .01$
Education	14.98 (2.7)	16.3 (3.3)	.19
BDI	10.1 (4.6)	3.1 (3.3)	$p < .01$
Apathy scale	13.0 (6.2)	7.4 (2.9)	$p < .01$
STAI	38.8 (8.4)	26.9 (8.9)	$p < .01$
Disease duration	6.6 (4.3)	–	
UPDRS motor "On"	39.1 (8.1)	–	
"Off"	27.9 (10.2)	–	
Levodopa equivalent dosage	752.3	–	

had been previously examined by a movement disorders specialist. All PD participants met UK brain bank criteria for idiopathic Parkinson's disease (Hughes, Daniel, Kilford, & Lees, 1992). Patients were tested while taking prescribed Parkinson's medications. The control group was recruited from the community and from spouses of PD patients. Participants were characterized as non-demented (Mini Mental State Exam > 25), free of any self-reported major psychiatric disturbance (e.g., major depression or anxiety, psychotic symptoms, etc.), and had no history of brain surgery, such as deep-brain stimulation for treatment of PD symptoms.

Following data collection, seven patients and two controls were excluded due to having less than seventy percent acceptable trials for EEG analysis, usually due to excessive movements, closing of the eyes, or high electrode impedances that were unable to be reduced to less than 70 k-Ω prior to data acquisition. The final sample consisted of 17 PD patients and 16 healthy controls.

Table 1 lists the demographic and clinical characteristics of the analyzed PD and control groups. Overall, participants were well-educated and predominantly male, as is characteristic of Parkinson's patients (which affects more males than females). The PD group was significantly younger than the control group (PD mean = 59.9 years; control mean = 70.6 years, $p < .01$); thus, age was included as a covariate in subsequent statistical analyses. The groups did not significantly differ in years of education.

The PD patients ranged from mild to moderate in disease severity, according to standard staging and severity criteria including the Hoehn-Yahr classification (Hoehn and Yahr, 1967) and the motor score of the Unified Parkinson Disease Rating Scale (UPDRS; Fahn and Elton, 1987). The UPDRS and Hoehn-Yahr staging were performed separately by neurologists at the Center for Movement Disorders and Neurorestoration and took place within 6 months of the experimental protocol, performed at the Cognitive Neuroscience Laboratory, McKnight Brain Institute. All patients exhibited bilateral disease symptoms (Hoehn-Yahr stages 2–3).

Compared to the control group, the PD patients endorsed significantly more symptoms of apathy (apathy scale; Marin, 1991; $t(22.1) = 3.20$, $p < .01$) and depression (Beck depression inventory-II; Beck, Steer & Carbin, 1988; $t(28) = 4.69$, $p < .01$). Of the 17 PD patients, six were currently taking antidepressant medications (compared to none for controls). Yate's continuity corrected X^2 for antidepressant usage ratio between the PD and control groups was significant ($p = .01$), showing that antidepressants were significantly more common among PDs than controls. Thus, patients currently taking antidepressants were compared to those not taking antidepressants in statistical analyses to investigate whether effects might be related to antidepressant usage.

2.2. Stimuli

Seventy-two pictures were selected from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 2008) that included 24 unpleasant pictures, including mutilations, threatening animals, human violence, etc.; 24 neutral pictures including neutral faces, scenes, household items, etc.; and 24 pleasant pictures, including romantic couples, food, sports activities, etc. Pleasant and unpleasant pictures were comparable in terms of normative arousal ratings. Each picture was shown in two separate blocks, for a total of 48 unpleasant, 48 neutral, and 48 pleasant trials.

2.3. Apparatus

Picture presentation was controlled by a PC running E-Prime software (Psychology Software Tools, Inc., Sharpsburg, PA). Pictures were displayed to participants on a 1024 × 768 monitor. The EEG was collected using a 64-channel

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