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Emotion and ocular responses in Parkinson's Disease

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Abstract

Parkinson's disease (PD) is a neurodegenerative disease that affects motor, cognitive, and emotional functioning. Previous studies reported reduced skin conductance responses in PD patients, compared to healthy older adults when viewing emotionally arousing pictures. Attenuated skin conductance changes in PD may reflect peripheral autonomic dysfunction (e.g., reduced nerve endings at the sweat gland) or, alternatively, a more central emotional deficit. The aim of the current study was to investigate a second measure of sympathetic arousal—change in pupil dilation. Eye movements, a motor-based correlate of emotional processing, were also assessed. Results indicated that pupil dilation was significantly greater when viewing emotional, compared to neutral pictures for both PD patients and controls. On the other hand, PD patients made fewer fixations with shorter scan paths, particularly when viewing pleasant pictures. These results suggest that PD patients show normal sympathetic arousal to affective stimuli (indexed by pupil diameter), but differences in motor correlates of emotion (eye movements.)

Keywords

emotion; arousal; Parkinson's disease; pupil; eye movement

1. Introduction

Parkinson's disease is the second most common degenerative disease of the central nervous system, next to Alzheimer's disease, and affects motor, cognitive and emotional functioning. Parkinson's is most often recognized by its cardinal motor symptoms of tremor, rigidity, postural instability, and bradykinesia. Parkinson's patients tend to show motor slowing and reduced movement initiation (Bartels & Leenders, 2009; Bowers et al., 2006) and the cognitive performance of Parkinson's patients somewhat mirrors the pattern of motor functioning, with a neuropsychological profile characterized by slowed processing speed on frontal-based cognitive tasks (e.g. Schneider, 2007; Taylor & Saint-Cyr, 1995). These

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cognitive symptoms are thought to be related to dysfunction of frontal-subcortical basal ganglia circuitry.

The nature of emotional dysfunction in PD is less well characterized. Parkinson's patients experience high rates of apathy and depression and recent research suggests that apathy may be a core feature of Parkinson's disease, with estimates of apathy in PD ranging from 38% to 51% across studies (Isella et al., 2002; Starkstein et al., 2002; Pluck & Brown 2002; Sockeel et al., 2006). A recent study that compared rates of depression, apathy, and combined apathy and depression in Parkinson's disease and a comparative movement disorder population, dystonia, found that 29% of PD patients endorsed clinically significant apathy *without* depression, whereas no dystonic patients endorsed significant apathy in the absence of depression (Kirsch-Darrow, Fernandez, Marsiske, Okun, & Bowers, 2006).

Nonetheless, the specific mechanism underlying emotional dysfunction in PD remains unclear. A number of studies have reported that PD patients have abnormal recognition of facial emotion (Tessitore et al., 2002; Sprengelmeyer et al., 2003; Ariatti, Benuzzi, & Nichelli, 2008, Delaveau et al., 2009;). However, few studies have employed experimental methods using a wide range of emotional stimuli in order to investigate the nature of emotional processes in PD. Of those that have, results have been mixed. Bowers et al. (2006) found that Parkinson's patients demonstrated a blunted startle eye-blink response compared to controls while viewing unpleasant pictures (Bowers et al., 2006) and Miller et al. (2010) reported a trend such that healthy controls showed increased startle potentiation to high vs. low arousing stimuli, whereas Parkinson's patients did not. Based on these findings, Miller et al. speculated that Parkinson's patients might be hypoaroused to emotional stimuli.

This hypothesis is consistent with preliminary findings from our laboratory that Parkinson's patients show a blunted skin conductance response when viewing emotional (pleasant and unpleasant) pictures compared to healthy older adults (Bowers et al., 2008). While one interpretation of these findings is that Parkinson's patients are hypoaroused to emotional stimuli, these findings are complicated by the fact that Parkinson's patients also have damage to the peripheral autonomic nervous system, including reduced nerve endings at the sweat glands of the palm (Dabby et al., 2006). Thus, peripheral autonomic dysfunction could be an important factor mediating reduced skin conductance responses. The aim of the current study was to investigate the utility of measuring changes in pupil diameter as an alternative measure of emotional arousal in PD.

Investigations of pupillary changes have concluded that pupil constriction, including the initial light reflex following onset of visual stimulation, is predominantly controlled via parasympathetic input to the sphincter muscle from the Edinger Westphal nucleus. On the other hand, pupil dilation is predominantly controlled via sympathetic input to the dilator muscle from the thoracic cell columns in the spinal cord. Pupil dilation can result from either direct sympathetic input, which is modulated by noradrenergic brain stem nuclei, the hypothalamus, and the central nucleus of the amygdala, or from the inhibition of parasympathetic input to the sphincter muscle, primarily mediated by the reticular formation, locus coeruleus and other direct and indirect cortical pathways (Lowenstein, 1955; Steinhauer, Siegle, Condray, and Pless, 2004; Gilzenrat, Nieuwenhuis, Jepma, & Cohen, 2010).

While a number of studies have explored the neural mechanisms underlying cognitive effects on the pupil (e.g. Steinhauer, Siegle, Condray, & Pless, 2004; Steinhauer, Condray, & Kasparak, 2000), less attention in the last decade has been directed towards elucidating the exact mechanisms underlying the effect of emotional arousal on the pupil. Early studies

by Hess and Polt in the '60s reported bidirectional effects on pupil dilation depending on the pleasantness of the emotional stimulus. These findings were difficult to replicate, perhaps due to imprecise measurement, lack of statistical analyses, and small numbers of stimuli and participants (see Bradley et al., 2010).

More recently, Bradley and colleagues (Bradley, Miccoli, Escrig, & Lang, 2008) utilized a wide range of standardized emotional picture stimuli and found that, rather than bidirectional effects, pupil dilation was significantly greater when participants viewed both pleasant and unpleasant pictures, compared to neutral pictures. Following the initial parasympathetically-mediated light reflex, pupil changes covaried with skin conductance responses in these healthy college students, prompting the conclusion that pupil dilation is an index of sympathetic activation during emotional picture processing. This response may be driven by enhanced sympathetic input to the pupil via modulatory input from the central nucleus of the amygdala and the hypothalamus (see Ranson and Clark, 1959 as cited in White and Depue, 1999). Bradley, Houbova, Miccoli, Costa, & Lang, (2010) also found that healthy adults make a greater number of voluntary visual fixations, and with longer scan paths, when viewing pictures with emotional, compared to neutral content. These differences were interpreted as reflecting increased information seeking in a motivationally relevant context, as a prelude to selecting/initiating an appropriate defensive or appetitive action.

The current study measured both pupil diameter and ocular movements as indices of emotional processing in PD patients and healthy older adults during affective picture processing. Prior studies have reported a variety of saccadic deficits in Parkinson's disease. For instance, one study concluded that PD patients show normal voluntary saccade movements but impaired reflexive movements (Yoshida, Yamada, Matsuzaki, 2002) whereas another found the opposite results (Briand, Strallow, Hening, Poizner, & Sereno, 1999). Studies have also found that PD patients show hyper-reflexive saccades (van Koningsbruggen, Pender, Machado, & Rafal, 2009; Fielding, Georgiou-Karistianis, & White, 2006). Finally, a recent study (Clark, Neargarder, & Cronin-Golomb, 2010) found no difference in number or duration of visual fixations for PD patients when viewing emotional faces.

Previous investigations of pupil motility in PD have consistently found that Parkinson's patients show a reduced amplitude of the initial light reflex (Beaumont, Harris, Leendertz, & Phillipson, 1987; Harris, 1991; Miceli et al., 1991; Granholm et al., 2003), but no differences in the maximum dilation during dark adaptation (Miceli et al., 1991) or in response to tropicamide, an acetylcholine antagonist which blocks the parasympathetic input to the sphincter muscle (Granholm et al., 2003). Therefore, while the parasympathetically mediated initial light reflex may be compromised in PD, there is no significant evidence that sympathetic input to the pupil is jeopardized by PD. In the current study, visual parameters were selected to elicit a measurable light reflex following picture onset. We expected that PD patients would show attenuation of this parasympathetically mediated reflex, in line with previous studies. Because effects of emotional arousal on pupil dilation are likely to be mediated by sympathetic nervous system activity (Bradley et al., 2008), measuring pupil diameter following the light reflex during emotional picture viewing provides an index of the integrity of sympathetic activation in emotional processing in PD.

Because previous studies have hypothesized that disrupted emotional processing in PD may be related to amygdalar dysfunction (Tessitore et al., 2002; Bowers et al., 2006) one hypothesis is that PD patients will show reduced emotional reactivity when viewing emotional stimuli for both pupil dilation and eye movements. An alternative hypothesis is that, if emotional dysfunction in PD is driven by disruption of higher cortical circuitry with

the basal ganglia, then PD patients and controls might exhibit similar sympathetic arousal, measured by pupil dilation, whereas group differences would be most pronounced in the motor system, as indexed by eye movements.

2. Material and Methods

2.1 Participants

Fifteen nondemented Parkinson's patients and fifteen healthy older adults participated in the current study. After data collection, one patient and three controls were excluded due to loss of pupil discrimination for over 25% of trials, resulting in a final N of 14 PD patients and 12 healthy controls. Parkinson's patients were recruited from the University of Florida Movement Disorders Clinic and had all been previously examined by a movement disorders specialist and met brain bank criteria for idiopathic Parkinson's disease (Hughes, Daniel, Kilford, & Lees, 1992). Patients were tested while continuing to take Parkinson's medications. The control group was recruited from the community and from spouses of PD patients. Participants were characterized as nondemented (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 (e.g., pallidotomy, deep-brain stimulation for treatment of PD symptoms.)

Table 1 displays the demographic and clinical characteristics of the PD and control group. Overall, participants were well educated and predominantly male (17 men and 9 women), ranging in age from 57 to 81 years; the PD group was slightly younger than the control group (PD mean=69.4 years; control mean=74.4 years, $p=.06$). Yate's continuity corrected X^2 for differences in gender ratio between the groups was nonsignificant ($p=.78$).

With respect to antidepressant usage, 7 out of the 14 PD patients (compared to 2 out of the 12 controls) were currently taking antidepressant medications¹. Yate's continuity corrected X^2 for antidepressant usage ratio between the PD and control groups was not statistically significant ($p=.17$). Although the chi-square test indicated that the difference in ratio of antidepressant usage was not statistically significant, it is unclear whether or not antidepressants affect pupil motility or the emotion-modulated pupillary response. Prior studies have shown that norepinephrine reuptake inhibitors, in particular, can increase resting pupil diameter and reduce the amplitude of the pupillary light reflex (Phillips, Bitsios, Szabadi, & Bradshaw, 2000; Siepmann, Ziemssen, Mueck-Weymann, & Siepmann, 2007). However, only one patient was currently taking an SNRI and there were no differences between the groups in terms of their baseline pupil diameter (see Results.) It is also unlikely that light reflex differences between PD patients and controls are related to antidepressant usage, as previous studies have shown a blunted light reflex in PD patients, including one that examined newly diagnosed PD patients who were not yet taking any medications (Micieli et al., 1991).

The only significant difference between the groups was in Mini Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) scores, such that the PD group scored an average of 1.2 points lower than the control group ($t(24) = 2.23$, $p < .05$). Although the PD group scored marginally higher than the Control group on the Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996), ($t(24) = 2.11$, $p = .05$), the BDI score of the PD group (mean of 8.1) fell well below the recommended cut-off of 14 for depressive symptoms in PD by the task force for the Movement Disorders Society (Leentjens, Verhey, Luijckx, & Troost, 2000).

¹Of the PD patients, 4 were taking SSRI's, 1 was on an MAO-I, 1 was on an SNRI, and 1 was on Welbutrin. Of the controls, one was taking Welbutrin and one was taking a tricyclic antidepressant.

The PD patients ranged from moderate to severe 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 et al., 1987). The UPDRS and Hoehn–Yahr staging took place within 6 months of the experimental protocol.

2.2 Stimuli

Forty-two pictures² were selected from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 2008). These pictures consisted of 14 unpleasant pictures (mean pleasure/arousal = 2.4, 6.4), including mutilations, threatening animals, human violence, etc. There were 14 neutral pictures (mean pleasure/arousal = 5.0, 3.0), including buildings, office scenes, furniture, etc. The 14 pleasant pictures (mean pleasure/arousal = 7.4, 5.9) included babies, couples, food, sports activities, etc. Unpleasant and pleasant stimuli were significantly more arousing than the neutral stimuli, based on the IAPS normative arousal ratings (Lang et al., 2008; $t=14.7$, $p<.001$ for unpleasant and $t=3.4$, $p<.001$ for pleasant). Normative arousal ratings did not significantly differ between pleasant and unpleasant picture categories ($t=2.04$, $p=.143$). Pictures were landscape (1024 × 768) in orientation and were displayed in 16-bit grayscale. The mean luminosity of the selected pictures was modified using Adobe Photoshop (version 5.0.2; Adobe Systems Inc., San Jose, CA) following the methods of Bradley et al. (2008), in order to equate the mean and distribution of luminosity values for the pleasant (mean=105.3), neutral (mean=101.3), and unpleasant pictures (mean=102.4) ($F(2,39) = .90$, $p=.42$; Levene's statistic (2,39)=1.32, $p=.29$).

2.3 Apparatus

Picture presentation was controlled by an IBM-compatible computer running Presentation software (Neurobehavioral Systems, San Francisco, CA). Pictures were displayed on a 1024 × 768 (19-in.) monitor (Samsung SyncMaster 191T) located in the experimental room, set at a distance of 114 cm (45 inches) from where the participant was seated, subtending 19 × 14 degrees of visual angle.

Pupil diameter and eye movements were recorded from the right eye of each participant using an ASL EYE-TRAC 6000 eyetracker system (Applied Science Laboratories, Bedford, MA), which allows free movement of the head and consists of a video camera and an infrared light source pointed at the participant's eye. A magnetic sensor, attached to a headband, tracked and adjusted for head movement. The recording video camera was located in a wood box in front of the subject, and a red translucent screen obscured it from view. Pupil diameter and eye position were sampled at 60 Hz for 3 seconds prior to picture onset, for 6 seconds during picture onset, and 3 seconds following picture offset.

2.4 Procedures

Upon arrival at the laboratory, each participant signed a consent form and was subsequently administered the MMSE. He or she was then seated in a chair in a small, sound attenuated, dimly lit room. Ambient light intensity was the same for every experimental session. The magnetic headband for tracking head movements was placed on the participant's head and eye movements were calibrated using a procedure which requested that the participant fixate a series of 9 dots arrayed in different spatial locations. The participant was then told that he or she would be viewing a series of pictures. The participant was told not to look away or

²The IAPS numbers for pictures used in this study are: pleasant: 2080, 4220, 4607, 4641, 4660, 4680, 5470, 7330, 8030, 8080, 8200, 8370, 2160, 8280; neutral: 2190, 2200, 5500, 7000, 7010, 7030, 7090, 7130, 7170, 7500, 7550, 7700, 6150, 7190; unpleasant: 1090, 1301, 2120, 3000, 3010, 3100, 3130, 3530, 6230, 6370, 9040, 9050, 7380, 9810

close his or her eyes, but rather to continue viewing the picture the entire time it was on the screen.

On each trial, a grayscale slide and a centered black fixation cross were displayed for 3 seconds before picture presentation. This was followed by the presentation of an IAPS picture for 6 seconds, followed by a variable inter-trial interval ranging from 4.5 to 8.5 seconds. The IAPS pictures were presented in blocks of six, with two pictures from each condition (pleasant, neutral, unpleasant) in each block. Each participant saw the picture set in the same order.

When the participant finished viewing the pictures, the headband was removed and the participant completed a series of mood questionnaires. Finally, the participant rated each picture he/she saw along the dimensions of valence and arousal using the Self Assessment Manikin (Bradley and Lang, 1994), a graphic figure using a 1 to 9 rating scale. For hedonic valence, ratings ranged from unpleasant (1) to neutral (5) to pleasant (9). For arousal, ratings ranged from calm (1) to neutral (5) to very excited (9).

2.5 Data reduction and analysis

Data from four participants were excluded because pupil discrimination failed to be achieved for more than 25% of trials (1 PD and 3 controls; resulting in a final N of 14 PD patients and 12 controls. For each trial, samples where the pupil was obscured due to blinks were identified (using an algorithm with multiple criteria provided by the Applied Science Laboratories File Analysis Program, ASL Results, version 1.11.02.) and linear interpolation was used to estimate pupil size. Regions of data loss that did not meet criteria for a blink were considered discrimination loss and omitted from the data.

Pupil diameter during picture viewing was first deviated from a 1 s baseline prior to picture onset. Based on the resulting waveform (see Figure 1), an initial light reflex during picture viewing was scored as the maximum pupil constriction in a window from 0 to 2 seconds after picture onset. Because of group differences in the magnitude of the initial light reflex (see Results), pupil dilation during picture processing (unpleasant, neutral, pleasant) was expressed as a change from the trough of the light reflex. Thus, pupil diameter in response to each picture type (unpleasant, neutral, and pleasant) was calculated as the mean change from the light reflex in a window from 2.5 to 6 seconds after picture onset.

For each trial, visual fixations were determined during picture viewing using ASL EyeAnal software in which a fixation was defined as the eye remaining within 1 degree of visual angle for at least 100 ms. For each trial, the reduction software indicated the number of fixations, the duration of each fixation, and the distance (i.e., visual angle in degrees) between successive fixations ("saccade length"). The saccade length across fixations was summed for each trial to compute the scan path.

3. Results

3.1 Pupil Dilation

Figure 1 shows the average change in pupil diameter from a one second pre-picture baseline for each group, across the six-second interval of picture viewing (across all trial types.) There were no significant difference in terms of baseline pupil diameter between PD patients (mean=4.76 mm) and control participants (mean=4.45 mm), $t(24)=-.68$, $p=.50$.

On the other hand, as illustrated in Figure 1, an independent samples t-test indicated that the initial light reflex occurring following picture onset was significantly smaller in the PD

group (mean = -.16, SD = .12), compared to the control group (mean = -.36, SD = .12) ($t(24) = 4.08$, $p < .001$).

Figure 2 shows the change (from the initial light reflex) in pupil diameter when viewing pleasant, neutral and unpleasant pictures for Parkinson patients and healthy controls. A Group (2) x Picture Emotionality (3) mixed analysis of variance (MANOVA) was conducted using pupil change as the dependent variable; Pillai's Trace F approximations are reported. Results of the MANOVA yielded a significant main effect of picture emotionality ($F(2,23) = 4.30$, $p < .05$, $\eta_p^2 = .27$). Follow-up comparisons indicated that both unpleasant and pleasant pictures elicited significantly greater pupil dilation compared to neutral pictures (t 's (24) = 2.90 and 2.62, respectively, p 's $< .05$). There was no significant difference in the pupillary response to pleasant and unpleasant images ($t(24) = .7$, $p = .48$). Importantly, PD patients and healthy controls both evidenced similar emotional reactivity (Group X Picture Emotionality $F < 1$, $p = .52$), with larger increases in pupil diameter when viewing emotional, compared to neutral, pictures. A main effect of group in this analysis simply indicated a generally larger increase in pupil size for healthy controls ($F(1,24) = 6.20$, $p < .05$) primarily due to the larger light reflex in this group.

Effects of Parkinson disease severity and mood symptoms on the emotion-modulated pupillary response were assessed by calculating the difference in pupil dilation when viewing emotional pictures (pleasant and unpleasant) and neutral pictures. There was no significant relationship between the emotion-modulated pupillary response and indices of Parkinson disease severity (Spearman rank correlations for Hoehn-Yahr stage "on" $r = -.14$, $p = .70$, LED $r = -.07$, $p = .84$; UPDRS "on" $r = .03$, $p = .93$; disease duration $r = -.45$, $p = .11$) or measures of emotional functioning (Apathy Scale $r = .15$, $p = .61$; Beck Depression Inventory $r = -.27$, $p = .36$; STAI trait $r = -.07$, $p = .81$). Additionally, Parkinson disease severity variables did not significantly correlate with the magnitude of the light-reflex across all picture-viewing trials (UPDRS "on" $r = -.01$, $p = .98$; HY "on" $r = -.06$, $p = .87$; LED $r = .50$, $p = .12$, disease duration $r = .20$, $p = .49$).

3.2 Eye Movements

Figure 3 illustrates the average number of fixations when viewing unpleasant, neutral, and pleasant pictures. The dependent variables were suitable for multivariate analysis as the data were univariate normal (i.e., both dependent variables had skewness and kurtosis estimates less than one) and the *Box-M* test for the homogeneity of variance-covariance matrices across design cells was nonsignificant. Pillai's Trace F-estimates are reported.

A mixed 2 (Parkinson, Control) by 3 (unpleasant, neutral, pleasant) MANOVA indicated that picture emotionality affected the number of discrete fixations ($F(2,22) = 6.30$, $p < .01$, $\eta_p^2 = .36$). Bonferroni post-hoc tests showed that, across the two groups, more fixations were made when viewing emotional compared to neutral pictures, ($t(23) = 3.60$, $p < .01$ for unpleasant, $t(23) = 2.62$, $p < .05$ for pleasant). A significant main effect of Group indicated that Parkinson's patients made fewer fixations than healthy controls ($F(1,23) = 4.64$, $p < .05$). These effects were qualified by a significant Group by Picture Emotionality interaction ($F(2,22) = 3.50$, $p < .05$). Whereas Parkinson's patients made significantly fewer fixations than healthy controls when viewing pleasant ($p = .01$) or neutral ($p < .05$) pictures, PD patients made a similar number of fixations as controls when viewing unpleasant pictures ($p = .24$).

A similar MANOVA was conducted to explore the effect of picture emotionality on the average scan path when viewing pleasant, neutral, and unpleasant pictures (Figure 3). In general, scan paths were longer when viewing emotional pictures (both pleasant and unpleasant, p values $< .001$) compared to neutral ($F(2,22) = 16.09$, $p < .001$, $\eta_p^2 = .59$). Overall, Parkinson patients exhibited shorter scan paths, compared to healthy controls, ($F(1,23)$

=11.34, $p < .01$, $\eta_p^2 = .33$). A marginal interaction ($F(2,22) = 2.89$, $p = .08$, $\eta_p^2 = .21$) suggested shorter scan paths for Parkinson's patients when viewing pleasant, compared to unpleasant, pictures ($p = .01$), whereas controls showed equivalent scan paths when viewing pleasant and unpleasant pictures ($p = .92$).³

3.3 Ratings of Affective Pictures

3.3.1 Arousal—Table 2 displays the mean arousal and valence ratings made by the PD and control groups. A Group (2) x Picture Emotionality (3) mixed ANOVA indicated a main effect of emotionality on arousal ratings, $F(1.4,32.1) = 35.63$, $p < .001$, $\eta_p^2 = .61$. Planned contrasts demonstrated that emotional pictures (both pleasant and unpleasant) were rated as more arousing than neutral pictures, $F_s(1,23) = 38.28$ and 48.24 for unpleasant and pleasant, respectively, p values $< .001$. There were no significant differences in average subjective ratings of arousal between groups ($p = .40$) nor was there a significant Group x Picture Emotionality interaction ($p = .49$).

3.3.2 Valence—The same mixed ANOVA model was conducted to examine subjective valence ratings between groups, using Greenhouse-Geisser F approximations. The analysis yielded a main effect of valence, $F(1.3,30.0) = 155.35$, $p < .001$, $\eta_p^2 = .87$. Planned contrasts demonstrated unpleasant images were rated as less pleasant than neutral images, $F(1,23) = 119.31$, $p < .001$, and pleasant images were rated as more pleasant than neutral images, $F(1,23) = 119.78$, $p < .001$. There was no significant difference in average subjective ratings of valence between groups ($p = .73$), nor was there a significant Group x Valence interaction ($p = .83$).

4. Discussion

Both Parkinson's patients and healthy controls showed increased pupil dilation while viewing emotional (pleasant or unpleasant) compared to neutral pictures. These data suggest intact sympathetic arousal when viewing emotional pictures in PD patients, and replicate the pattern of pupillary reactions observed when healthy young adults view emotional and neutral pictures (e.g. Bradley et al., 2008). These data suggest that previously reported SCR blunting (Bowers et al., 2008) may be related to peripheral autonomic dysfunction in PD rather than to central hypoarousal. Instead, the current data suggest that Parkinson's patients show appropriate differential sympathetic arousal when viewing emotionally arousing cues when the pupil is used to index sympathetic nervous system activity.

The initial light reflex following picture onset was significantly smaller in Parkinson's patients than in controls, replicating previous findings (Beaumont et al., 1987; Harris, 1991; Micieli et al., 1991; Granholm et al., 2003). Dysfunction of the light reflex may be linked to hyporeactivity of dopamine retinal cells, pathology in the Edinger Westphal nucleus itself, or pathology along the peripheral pathway to the pupil, possibly in the ciliary ganglion (Granholm et al., 2003). Regardless of the specific mechanism, this finding provides evidence that the parasympathetic pathway to the pupil may be jeopardized in PD, and lends additional support to the interpretation that emotion-modulation of the pupillary response is sympathetically driven (Bradley et al., 2008), given that this response was preserved in PD.

³Pupil diameter was computed based on the horizontal diameter of the pupil. The effect of horizontal eye displacement on pupil size is small unless the rotation angle is large. In our study, the computation indicates that pupil diameter would remain approximately 99% of its current value at the maximum horizontal displacement of the eye. Nonetheless, separate analyses were conducted that involved correcting pupil size for horizontal gaze position. The effect of emotionality and group on pupil dilation did not change after correcting for the eye's horizontal gaze position.

Although there were no differences between PD patients and controls in pupillary increases when viewing emotional stimuli, there were some notable differences between Parkinson's patients and controls in eye movements. Overall, PD patients made fewer fixations during picture viewing and exhibited shorter scan paths. Aberrant eye movements for PD patients, compared to their healthy counterparts, are not unexpected, since the basal ganglia have distinct connections with the frontal eye fields, which are responsible for voluntary eye movements. Furthermore, these ocular differences are consistent with the slowed motor and cognitive functioning that is characteristic of PD patients. Moreover, previous research has reported that PD patients have impaired volitional saccades (c.f. Briand et al., 1999).

When viewing emotional pictures, both groups made more fixations, and overall scan paths were also longer while participants viewed emotional pictures. These data replicate the ocular patterns observed in healthy adults which may reflect increased information-seeking for emotionally salient cues (Bradley et al., 2010). Differences between Parkinson's patients and controls in eye movement patterns were most pronounced when Parkinson's patients viewed pleasant pictures. Thus, for unpleasant pictures, PD patients and controls did not differ in either the number of fixations or scan path length. When viewing pleasant pictures, however, PD patients made significantly fewer fixations and exhibited shorter scan paths compared to controls, suggesting aberrant physiological correlates of appetitive picture processing specifically at the level of motivated behavior.

Increased pupil dilation to arousing stimuli is likely driven by amygdalar input to the hypothalamus, which drives increased sympathetic innervation of the pupil (see White and Depue, 1999), and thus occurs relatively independently of basal ganglia circuitry. The precise mechanism that drives emotion-modulated ocular movements is unclear, but undoubtedly relies on basal ganglia circuitry, given its reciprocal connections to the frontal eye fields mediating voluntary eye movements (Alexander, Delong, & Strick, 1986) and the purported role of basal ganglia-prefrontal circuitry in voluntary, goal-directed behavior (Brown & Pluck, 2000; Levy & Dubois, 2006). This is consistent with our finding that ocular movements during emotional picture viewing were more compromised in PD than pupil dilation, as pronounced disruption in basal ganglia circuitry is inherent to the disease.

Thus, it is relevant to consider these findings within the framework of potential mechanisms underlying emotional abnormalities in Parkinson's disease. A number of studies have interpreted emotional abnormalities in PD patients as reflecting amygdalar dysfunction (e.g. Tessitore et al., 2002; Bowers et al., 2006). Indeed, PD patients have been shown to have amygdalar atrophy and lewy-body deposition post-mortem (Braak et al., 1994; Harding, Stimson, Henderson, & Halliday, 2002). However, the current results suggest that emotional deficits in PD may relate to dysfunction in the same fronto-subcortical loops that give rise to many of the motor and cognitive symptoms of Parkinson's disease. While the current study was not explicitly designed to measure emotional responsivity in apathetic PD patients, the results are consistent with recent conceptualizations of the development of apathy in PD as being a progressive reduction of signal to noise ratio transmitted from the basal ganglia to the prefrontal cortices, which begins in the dorsal striatum (and evolves to the ventral striatum as well), resulting in reduced voluntary goal-directed behaviors (Levy & Dubois, 2006; Levy & Czernecki, 2006).

Furthermore, finding selectively aberrant eye movements when viewing pleasant stimuli may suggest that the appetitive behavior system is specifically impaired in Parkinson's disease. Thus, emotional dysfunction in PD may more accurately be characterized by anhedonic (non pleasure-seeking) behavioral tendencies. Interestingly, a recent study showed that apathetic Parkinson's patients demonstrated reduced pleasure/reward seeking behavior compared to non-apathetic PD patients, while there was no difference between the

groups in behaviors that reflect the avoidance of punishment (BIS/BAS; Jordan, Ferencz, McKently, Okun, & Bowers, 2010).

It should be noted that the Parkinson patients in this study were tested while continuing to take dopaminergic medications, and thus it is unclear how patients might respond in a hypodopaminergic state. Patients were purposefully tested while taking dopaminergic medication, as this state of affairs better represents daily functioning. Moreover, although patients gain improvement in motor function while taking these medications, they continue to experience emotional symptoms. In fact, it has been shown that apathy positively correlates with levodopa equivalent dosage (Isella et al., 2002). This is likely because dopamine differentially affects motor, limbic, and cognitive functions and, in theory, each function requires a unique dopaminergic dosage in order to achieve optimal functioning (Cools, 2006; Rowe et al., 2008). Ideally, future studies will test patients both on and off their dopaminergic medications in order to understand the relative influence of dopamine on emotional reactivity.

In summary, the results of the current study indicate that PD patients' sympathetic arousal response to motivationally relevant stimuli, measured by pupil dilation, is intact, whereas behavioral correlates of emotion, measured by voluntary eye movements, were disrupted, lending preliminary evidence that PD patients demonstrate preserved emotional arousal in the presence of reduced emotional behavior, perhaps due to dysfunction of higher cortical mechanisms responsible for motivated behavior in PD. Future research should focus on the mechanisms underlying impaired motivated behavior in Parkinson's disease.

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Research Highlights

- Previous study showed muted skin conductance response in Parkinson's patients.
- Skin conductance may be affected by peripheral autonomic dysfunction in PD.
- Pupil dilation was used as an alternative measure of emotional arousal in PD.
- Eye movements served as index of motivated behavior.
- PD group showed normal arousal but abnormal eye movements to emotional pictures.

Figure 1. Change in pupil diameter (from a 1 s pre-picture baseline) illustrates that Parkinson patients, compared to healthy older adults, show an attenuated light reflex following presentation of a visual stimulus.

Figure 2.

Changes in pupil diameter (from the trough of the initial light reflex) increase similarly when viewing pleasant and unpleasant, compared to neutral, pictures for both Parkinson patients and healthy older adults.

Figure 3.

Top: Parkinson patients make overall fewer fixations during picture viewing than healthy older adults. Bottom: Scan path length is generally shorter for Parkinson patients, compared to healthy older adults. Error bars represent +/- 1 standard error.

Table 1

Demographic and clinical characteristics of Parkinson's and healthy older adult groups.

	Parkinson's Group (N=14)	Control Group (N=12)	P-Value
Gender (M / F)	10 / 4	7 / 5	0.78
Antidepressant (Y / N)	7 / 7	2 / 10	0.17
Age	69.4 (8.4)	74.4 (3.9)	0.06
Education (years)	18.4 (3.6)	16.5 (3.8)	0.19
Mini Mental State Exam (MMSE)	28.2 (1.7)	29.4 (0.9)	0.04*
Beck Depression Inventory (BDI)	8.1 (6.2)	3.8 (4.0)	0.05*
Apathy Scale (AS)	8.2 (4.9)	7.2 (3.4)	0.54
State Anxiety (STAI-Y1)	29.1 (11.9)	29.0 (11.5)	0.98
Trait Anxiety (STAI-Y2)	30.8 (11.3)	32.9 (12.1)	0.65
Disease duration	7.4 (3.5)	-	-
Levodopa Equivalent Dosage (LED)	737.1 (537.9)	-	-
UPDRS "On" Meds	25.1 (6.9)	-	-
Hoehn-Yahr (HY) Stage "On" Meds ^a	2.3 (0.4)	-	-

Note: Categorical variables are presented as ratios; quantitative variables are presented as Mean (Standard Deviation). Variables marked with an asterisk (*) denote significant group differences at $\alpha=.05$.

^a7 patients were HY stage 2, 1 was HY stage 2.5, 2 were HY stage 3. 4 patients did not have HY data available within 6 mos. of testing

Table 2

Picture ratings and change in pupil diameter (deviated from the trough of the initial light reflex) and standard deviation when viewing unpleasant, neutral, and pleasant pictures for Parkinson patients and healthy controls.

	Unpleasant	Neutral	Pleasant
Pleasure Ratings[/]			
Parkinson	2.57 (1.1)	5.22 (.57)	7.11 (.52)
Control	2.63 (1.1)	5.39 (.67)	7.06 (1.0)
Arousal Ratings[/]			
Parkinson	6.17 (1.5)	3.19 (1.3)	5.78 (1.2)
Control	5.48 (2.3)	3.11 (2.1)	5.01 (2.4)
Change in Pupil Diameter (mm)			
Parkinson	.24 (.12)	.15 (.09)	.24 (.11)
Control	.35 (.16)	.27 (.09)	.35 (.15)

[/]Pleasure ratings are based on 1-9 Self Assessment Manikin (SAM) scale (Bradley and Lang, 2004) where 9 is the highest pleasantness. Arousal Ratings are based on a 1-9 SAM scale where 9 is the highest arousal rating.