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Startle reflex hyporeactivity in Parkinson's disease: an emotion-specific or arousal-modulated deficit?

K.M. Miller, PhD¹, M.S. Okun, MD², M. Marsiske, PhD¹, E.B. Fennell, PhD¹, and D. Bowers, PhD¹

¹ Department of Clinical & Health Psychology, College of Public Health and Health Professions, University of Florida

² Department of Neurology, College of Medicine, University of Florida

Abstract

We previously reported that patients with Parkinson's disease (PD) demonstrate reduced psychophysiologic reactivity to unpleasant pictures as indexed by diminished startle eyeblink magnitude (Bowers et al., 2006). In the present study, we tested the hypothesis that this hyporeactivity was primarily driven by diminished reactivity to fear-eliciting stimuli as opposed to other types of aversive pictures. This hypothesis was based on previous evidence suggesting amygdalar abnormalities in PD patients coupled with the known role of the amygdala in fear processing. To test this hypothesis, 24 patients with Parkinson's disease and 24 controls viewed standardized sets of emotional pictures that depicted fear, disgust (mutilations, contaminations), pleasant, and neutral contents. Startle eyeblinks were elicited while subjects viewed these emotional pictures. Results did not support the hypothesis of a specific deficit to fear pictures. Instead, the PD patients had reduced reactivity to mutilation pictures relative to other types of negative pictures in the context of normal subjective ratings. Further analyses revealed that controls displayed a pattern of increased startle eyeblink magnitude for "high arousal" versus "low arousal" negative pictures, regardless of picture category, whereas startle eyeblink magnitude in the PD group did not vary by arousal level. These results suggest that previous findings of decreased aversion-modulated startle is driven by reduced reactivity to highly arousing negative stimuli rather than to a specific category (i.e., fear or disgust) of emotion stimuli.

Keywords

basal ganglia; emotion; neurophysiology; neurological disorders; neurodegenerative disorders

INTRODUCTION

Parkinson's disease (PD) was originally conceptualized as a progressive disorder of motor function, although many of the original symptoms were non-motor in nature (Parkinson, 1817). It is now widely recognized that neuropsychiatric symptoms are prevalent and can be disturbing to patients and families as well as disabling to basic aspects of quality of life.

Corresponding author: Kimberly M. Miller VA Northern California Health Care System Mental Health Unit (116) 150 Muir Road Martinez, CA 94553 phone # 925-372-2000 x 6431 fax # 925-372-2830 E-mail: Kimberly.Miller9@va.gov.

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Disturbances of mood and motivation are commonly encountered and may include depression, anxiety, and apathy (Fahn, 2003; McDonald, Richard, & DeLong, 2003; Slaughter, Slaughter, Nichols, Holmes, & Martens, 2001). Additionally, patients with PD may show impaired ability to communicate emotion through various nonverbal signals such as facial expression and prosody (Blonder, Gur, & Gur, 1989; Borod et al., 1990; Buck & Duffy, 1980; Jacobs, Shuren, Bowers, & Heilman, 1995; Smith, Smith, & Ellgring, 1996). Impairment in identification and discrimination of emotional faces, prosody, and scenes has also been reported (Blonder et al., 1989; Jacobs et al., 1995; Scott, Caird, & Williams, 1984; Sprengelmeyer et al., 2003). These findings raise the possibility of impairments in emotional reactivity (how an individual responds physiologically, subjectively, or overtly to an emotion-eliciting stimulus).

Reduced facial expressivity and prosody in PD may create a situation in which it is difficult to determine if patients are actually experiencing diminished emotions. Some researchers have found that although PD patients are not as facially or prosodically expressive as their healthy counterparts, they typically report subjective feelings that are comparable in intensity when viewing emotion-eliciting pictures (Bowers et al., 2006a; Simons, Pasqualini, Reddy, & Wood, 2004; Smith et al., 1996). However, self-report ratings such as these are potentially unreliable because they are subject to demand characteristics, meaning that the participant may simply respond in the fashion that he believes is expected of him.

Recently, our laboratory examined emotional reactivity in PD through a method that does not rely on facial expression, prosody, or self-report: emotional modulation of the startle eyeblink reflex (Bowers et al., 2006b). This paradigm rests on the well-documented principle that the size of the eyeblink elicited by an acoustic probe (e.g. a loud noise) is directly modulated by an individual's emotional state (Bradley, 2000; Lang, 1995). In general, startle eyeblink magnitude is increased when an individual views unpleasant pictures, and decreased during viewing of pleasant pictures. The enhancement of startle has been viewed as a "priming" effect, whereby the protective withdrawal reflex is primed during unpleasant emotional states and inhibited during pleasant emotional states (Bradley, 2000; Lang, 1995). We recently reported (Bowers et al., 2006b) that PD patients exhibited significantly smaller startle eyeblink magnitudes than controls while viewing unpleasant, aversive pictures (e.g., snakes, mutilations, violent scenes). In contrast, startle eyeblink magnitudes during viewing of pleasant pictures (e.g., babies, romantic couples) were comparable to that of controls. We interpreted these data to suggest that PD patients may have a deficit in "translating" an aversive motivational state into a physiologic response.

The neural basis of reduced startle eyeblink response to aversive pictures in PD is unknown. One structure that may play a key role is the amygdala. The amygdala has consistently been implicated in the appraisal of fearful stimuli and response to threatening situations. Monkeys with lesions of the amygdala do not display normal fear reactions to threatening stimuli, such as snakes (Amaral, 2003; Klüver & Bucy, 1939). In humans, lesions of the amygdala have been associated with behavioral placidity, diminished physiologic reactivity, and impairments in recognizing fearful faces (Calder et al., 1996; Young et al., 1995). Electrical stimulation of the amygdala elicits many of the behaviors used to define the state of "fear," such as tachycardia, increased galvanic skin response, corticosteroid release, and increased startle (Davis, 1992).

Recent evidence points to neuropathological changes in many brain areas in PD, including limbic structures such as the amygdala, nucleus of the stria terminalis, entorhinal cortex, hippocampus, and anterior cingulate. Areas receiving projections from the amygdala, such as the locus coeruleus, tuberomammillary nucleus, basal forebrain, ventral tegmentum, and raphe nuclei are also frequently damaged. These limbic changes occur within the context of damage to motor systems (e.g. the loss of dopamine in substantia nigra that characterizes PD),

components of the hypothalamus, as well as other structures involved in regulation of autonomic functions (e.g. bulbar and spinal autonomic nuclei (Braak & Braak, 2000). Focusing on the limbic system specifically, post-mortem studies show severe cytoskeletal damage, Lewy bodies, and reduced volume in the amygdalae of PD patients (Braak & Braak, 2000; Harding, Stimson, Henderson, & Halliday, 2002). Ouchi et al. (1999) found a 30-45% reduction of dopamine agonist binding in the amygdalae of PD patients. Furthermore, levels of dopamine were found to modulate the amygdala's response in PD patients in a neuroimaging study involving matching fearful faces (Tessitore et al., 2002). This suggests that the low levels of dopamine characterizing PD may affect the amygdala's functional integrity. Given the amygdala's role in the fear response, these findings raise the possibility that amygdala dysfunction in PD may lead to impaired appraisal of or reactions to fear-eliciting stimuli.

The current study builds upon our previous study by examining whether reduced startle eyeblink reactivity in PD is specific to a particular category of unpleasant emotion (i.e., fear) or more broadly occurs in response to any aversive emotion. Many different emotions can create an aversive motivational state, such as disgust, fear, threat, or horror; in turn, these emotions can be elicited by a variety of different picture stimuli (e.g. contaminated food, mutilated bodies, snakes, a man holding a gun). Based on evidence that the amygdala appears to play a specific role in the processing of fear-eliciting stimuli, coupled with the prior findings of amygdala abnormalities in PD, we hypothesized that our previous finding of reduced physiological reactivity to aversive pictures in PD was driven by diminished reactivity to stimuli eliciting fear. Thus, the current study examines the possibility of an emotion-specific reactivity deficit in PD.

To test this hypothesis, we compared startle eyeblink magnitudes that were elicited while participants viewed fear pictures to those occurring during disgust pictures. Disgust pictures were selected because they elicit similarly high subjective arousal and valence ratings as fear pictures (Bradley, Codispoti, Cuthbert, & Lang, 2001). This allowed us to examine emotion-specific reactivity while controlling for level of arousal and unpleasantness. Disgust stimuli were subdivided into contamination pictures (e.g., vomit, spoiled food) and mutilation pictures because prior studies suggest they may elicit distinct neural responses and emotional reactions (Schienle et al., 2006; Wright, He, Shapira, Goodman, & Liu, 2004). This allowed for separate examination of startle eyeblink magnitudes for these two types of pictures. Participants rated how much fear and disgust they felt in response to each picture. It was predicted that PD patients would demonstrate reduced startle potentiation in response to pictures eliciting fear compared to healthy age-matched controls, whereas they would not differ from controls in startle eyeblink magnitudes to disgust- eliciting pictures.¹

METHOD

Participants

Participants included 24 patients with idiopathic PD who were free of dementia and 24 matched healthy controls. The PD patients were recruited from the University of Florida Movement Disorders Center and controls were recruited from the community. Diagnosis of PD was made by a fellowship-trained movement disorders neurologist according to the UK Brain Bank

¹With respect to disgust processing in PD, we are not aware of any studies that have examined emotional response to disgust-inducing stimuli; however, some authors have reported impaired ability to recognize facial expressions of disgust in PD (Kan, Kawamura, Hasegawa, Mochizuki, & Nakamura, 2002; Sprengelmeyer et al., 2003; Suzuki, Hoshino, Shigemasa, & Kawamura, 2006). While some reports indicate a disgust-specific facial recognition impairment (Suzuki et al., 2006), others suggest facial recognition deficits across a combination of different aversive facial expressions, such as disgust and anger (Sprengelmeyer et al., 2003) or fear and disgust (Kan et al., 2002). These studies raise the possibility that both fear and disgust processing could be compromised in PD; however, all these studies examined emotional facial recognition, not emotional responses to scenes as in the current report, and thus the issue of impaired emotional reactivity in PD remains open for investigation.

criteria (Hughes, Daniel, Kilford, & Lees, 1992). A summary of participant demographic variables and patient disease characteristics are presented in Table 1. As shown, the two groups did not statistically differ with respect to age, education, or gender distribution. Overall, the sample was well educated, ranged in age from 50 to 80 years ($M = 68.2$ [7.3]), and contained slightly more males than females. The PD patients were generally in the middle stages of their disease (Hoehn and Yahr stage of 2 or 3; Hoehn and Yahr, 1967) with a moderate degree of disease severity based on the Unified Parkinson Disease Rating Scale (Fahn, Elton, & Committee, 1987). These staging and severity indices were obtained within six months of the experimental task sessions.

To be included, all participants had to be free of neurologic disorder (other than PD in the Parkinson group), dementia, prior or current alcohol or substance abuse problems, and major psychiatric disturbance. Dementia was screened using the Dementia Rating Scale, second edition (DRS-2; Mattis, 2001). Participants scoring greater than 1.5 standard deviations below age- and education appropriate norms provided in the DRS-2 manual (Jurica, Leitten, & Mattis, 2001) were excluded. Visual acuity, which could affect ability to see the stimulus pictures, was not formally assessed; however, participants were instructed to wear any glasses or contacts that they typically wear while performing the picture-viewing tasks. Depression symptom severity was screened using the Beck Depression Inventory, second edition (BDI-2; Beck, 1996). Participants with scores exceeding 19 (i.e., those with moderate or severe depression symptoms; Beck, Steer, & Brown, 1996) were excluded. Seven of the PD patients were on anti-depressant medications (three on bupropion, two on escitalopram, one on sertraline, and one on venlafaxine). One PD patient on escitalopram was also on clonazepam to aid sleep. None of the controls were on any antidepressant medications. The PD patients and controls did not significantly differ with respect to scores on the DRS-2 ($t[46] = 0.33$, $p > 0.1$); means: PD = 140.92 [SD = 2.83], control = 141.13 [SD = 1.30]). However, PD patients obtained significantly higher scores than controls on the BDI-2 ($t[46] = 2.99$, $p = .005$), although both groups had mean scores in the non-depressed range (PD = 6.17 [SD = 4.76], control = 2.58 [SD = 3.45]). Three PD patients and one control had BDI-2 scores falling within the mildly depressed range, defined as scores between 14 and 19 (Beck et al., 1996). All other participants scored within the non-depressed range.

Stimulus Materials

Picture stimuli used in the psychophysiology session included 48 pictures during which a startle probe was presented and 16 “filler” trials during which no probe was presented. The 48 probe pictures were composed of 24 unpleasant pictures (further subdivided into 12 disgust and 12 fear pictures), 12 neutral pictures, and 12 pleasant pictures. Unpleasant pictures were limited to pictures intended to elicit feelings of fear and disgust because other negative emotions, such as anger and sadness, have been shown to be difficult to elicit reliably in a laboratory (Smith et al., 1996) and because disgust and fear are emotions associated with similarly high physiological arousal, as evidenced by similar emotion-modulated startle eyeblink magnitudes in normal controls (Yartz & Hawk, 2002). All pictures were drawn from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 2001a) and were chosen based on the normative study data published for the IAPS (Lang, Bradley, & Cuthbert, 2001b) and from a large study in which participants were asked to rate IAPS pictures for the discrete emotions elicited (Bradley, Codispoti, Sabatinelli, and Lang, 2001). Bradley and colleagues (2001b) found that both men and women rated pictures of contamination (e.g., dirty toilets, vomit, feces), accidents/injuries, and mutilated bodies as very high in disgust, whereas pictures of animal attacks and humans attacking one another were rated as very high in fear. Thus, these types of pictures were selected when creating the disgust and fear picture sets for the current study.

Disgust pictures were further subdivided into six mutilation pictures and six contamination pictures. This subdivision was based on neuroimaging (fMRI) findings in normal adults indicating that distinct neural responses occurred to mutilation pictures versus contamination pictures (Wright et al., 2004). In brief, both types of pictures (mutilation, contamination) resulted in insula activation; however, the mutilation pictures also caused greater activation of the occipital temporal cortex and unique activation of the right superior parietal cortex relative to the contamination pictures. This raises the possibility that contamination and disgust pictures could potentially also be associated with different patterns of psychophysiological reactivity. Subdividing the disgust pictures into mutilation and contamination pictures allowed for the examination of potential differences in emotion ratings and startle eyeblink reactivity.

The pleasant and unpleasant (i.e., fear and disgust) pictures were equivalent with regards to average arousal ratings reported by participants in the IAPS normative study (Lang et al., 2001b). With regards to valence ratings, IAPS normative ratings placed the pleasant pictures as equidistant from the “most pleasant” anchor point as the fear and disgust pictures were from the “most unpleasant” anchor point on the 1-9 rating scale (this scale is explained in more detail in Procedure section). Pleasant pictures depicted a variety of contents that received high valence ratings in the IAPS normative study (e.g. happy couples, money, a sailboat, etc.). Finally, the 12 neutral pictures had average arousal ratings that were lower than the pleasant, fear, and disgust pictures and average valence ratings that fell in the middle of the 1-9 rating scale in the IAPS normative study. Examples of neutral pictures include a chair, a fork, and a lamp. A complete listing of all picture stimuli and their associated normative valence (pleasantness) and arousal ratings can be found in Appendix I.

Procedure

Informed consent to participate in this research was obtained from all participants according to University of Florida and federal guidelines. All participants were tested in the cognitive neuroscience laboratory during two separate sessions. During the first session, participants were administered a brief battery of neuropsychological tests to screen for depression and dementia. The PD patients were tested while on their normal dopaminergic medications so that test performance would approximate their typical daily level of cognitive and motoric functioning. Testing patients off medication would likely have resulted in slowed information processing speed (“bradyphrenia”) in addition to slowed motor speed, which would not be representative of their typical functioning when they are on dopaminergic medication. Measures included the Dementia Rating Scale, second edition (DRS-2; Mattis, 2001) and the Beck Depression Inventory, second edition (BDI-2; Beck, 1996). The second session took place within two weeks of session one and consisted of the experimental psychophysiology procedure. Prior to this session, all PD patients underwent an overnight, minimum of 12 hours dopaminergic medication wash-out and thus were tested when “off” their normal dopaminergic medications. The rationale for this wash-out is that it is unknown how dopaminergic medications may affect emotional reactivity at the physiological level. Since a key aim of the study was to characterize any emotional reactivity deficits found in PD, it was essential to withhold any medication that might alleviate or mask potential emotional reactivity deficits, as it is possible dopamine could have a restorative effect.

In preparation for the psychophysiology procedure, surface Ag-AgCl electrodes were positioned under the participants' left and right eyes to record electromyographic (EMG) activity from the orbicularis oculi muscle. Participants sat in a straight-backed cushioned chair with armrests located in a sound-attenuated and electrically shielded 12'×12' room. The room was lit via a light on a dimmer switch that was set to the same level (40 watts) across all participants to ensure standardized lighting. The experimenter came into the room and read a standardized script of instructions to the participant explaining how to make valence and

arousal ratings. As part of these instructions, participants were told to look at each picture the entire time it was presented on the monitor. After the participant indicated an understanding of instructions, the experimenter left the room and viewed the participant via videomonitor for the remainder of the psychophysiology procedure. Startle eyeblink responses were elicited by a single 50 ms burst of white noise (95 db, instantaneous rise time) delivered binaurally through Telephonics stereo headphones. The session began with 12 probes delivered in the absence of any other stimulus (unprimed startles), followed by two sample picture trials to familiarize participants with the procedure. The sample pictures consisted of one pleasant picture (a bunny) and one unpleasant picture (a snake) to ensure the participant understood how to use the valence and arousal rating scales, described in further detail below.

Picture stimuli for the emotion-modulated startle task were displayed on a 21-inch computer monitor located two feet in front of the participant. Participants were presented with 64 pictures that included 48 startle probe trials and 16 “filler” trials, during which no startle probe was presented. The 64 pictures were arranged in four blocks of 16 pictures each. Pictures were arranged in pseudorandom order with the constraint that pictures from the same category (e.g. “fear”) could appear no more than twice in a row in order to minimize the possibility of mood induction effects. Each block consisted of 12 startle probe trials plus four interspersed filler trials. The 12 startle probe trials consisted of three pleasant pictures, three neutral pictures, three fear pictures, and three disgust pictures. Two different picture orders were created by repositioning the pictures so that pictures occurring in the first half of Order 1 were presented in the second half of Order 2. Pictures were not only shifted by half, but also re-ordered pseudorandomly, again with the constraint that no more than two pictures from any one category appear in a row. Administration of the two orders was counterbalanced across participants and groups in order to minimize potential effects of order of presentation.

During each trial, a picture was presented on the computer monitor for six seconds. During this time, a single 50 ms white noise burst (i.e., startle probe of instantaneous rise time, 95 db) was randomly presented at one of three time intervals following picture onset (4200, 5000, or 5800 ms). Startle probe onset was counterbalanced across the different picture categories. The use of three different time points after picture onset was designed to prevent participants from developing expectancy of the startle probe. After the presentation of each picture, participants completed subjective ratings as described below.

Valence and arousal ratings of pictures

Participants made verbal ratings of valence and arousal using the Self Assessment Manikin (SAM) that appeared on the computer screen immediately after the picture was shown. Progression to the next picture was self-paced so that participants could take as long as needed to make their ratings. After they verbally indicated their ratings, there was a variable 10-15 second inter-trial interval before the onset on the next trial. The ratings of valence and arousal were obtained so that participants' subjective emotional experiences could be compared to their objective physiologic response. SAM is a graphic display depicting a cartoon figure that varies along the dimensions of valence and arousal (Greenwald, Cook, & Lang, 1989). For valence, different versions of the cartoon figure depict the cartoon's level of pleasantness. The scale goes from highly unpleasant to neutral to highly pleasant. Each figure has a number (1-9) associated with it. For arousal, different versions of the cartoon figure are shown ranging from sleepy/calm/bored to neutral to highly excited or energized, again ranging from 1-9. Participants were asked to rate their reactions to each picture immediately after viewing it by referring to the SAM rating scale. Please refer to Appendix II for the full script of instructions given to participants prior to the psychophysiology experiment, including how to make SAM ratings.

Basic emotion ratings of pictures: Post-experimental session

Following completion of the entire psychophysiology experiment, each participant again viewed the 48 primary picture stimuli on an Apple iBook laptop and was asked to make additional ratings. Participants rated how much happiness, fear, disgust, and sadness they felt while viewing each picture using a 1-9 rating scale, ranging from feeling no emotion at all (“1”) to strongly feeling the emotion (“9”). For example, if a participant felt none of the target emotions in response to a particular picture, he would rate each emotion as a “1. Although sadness was not a target emotion, it was included in the ratings in anticipation that some types of pictures may elicit mixed emotions including sadness. Participants were instructed not to “think back” to how they felt during the psychophysiology procedure, but rather rate their current feelings while viewing the pictures. These post hoc basic emotion ratings served as a manipulation check to determine if the targeted emotion (i.e., “disgust” for the contamination and mutilation pictures, “fear” for the fear pictures, “happiness” for the pleasant pictures) was produced. The pictures were presented in a different order than during the psychophysiology experiment, and two alternate orders were created. Administration of these two orders was counterbalanced across diagnostic group and sex.

Psychophysiology Data Reduction

Data from each participant were visually examined and trials with clear artifacts (e.g., eyeblink movements before probe onset) were rejected. Additionally, trials in which the participant turned away from the stimulus picture or closed his eyes (observed by the experimenter watching the participant on a videomonitor) were discarded. This occurred only a total of five times across the control group and four times across the PD group, and thus represented less than one percent of all trials. Data reduction was completed using a custom software program for data condensing. Latency and amplitude of the peak response within 20 ms to 120 ms after probe onset were determined. Trials with a peak latency outside of this 20 ms to 120 ms latency range were discarded, as visual analysis of data from these participants as well as prior work in our laboratory suggest that peaks occurring outside of this time window typically reflect blinks that were unrelated to the startle probe itself (i.e., artifacts or natural blinks occurring either before or after presentation of the probe). This 120ms time window for detection of peak amplitude is also employed by other laboratories (e.g. see Funayama, Grillon, Davis, and Phelps, 2001). Trials with a peak amplitude more than three standard deviations above or below each participant's mean magnitude for a given picture category were also excluded. Raw scores were converted into T-scores (mean of 50, standard deviation of 10) for each participant's left and right eyes separately. This serves to reduce inter-subject variability by essentially using each participant's own raw scores as their “baseline” so that relative amounts of deviation from their average blink size can be examined without the problem of large variations in raw blink sizes across participants. Because preliminary analyses revealed no significant differences between right and left eye startle eyeblinks, these two values were averaged and a composite startle eyeblink score was used in subsequent analyses. When data from one eye were invalid, only the valid eye was used.² Only participants who had at least two valid trials for each picture category were retained for subsequent analyses.

Data Analysis

The primary aim of this report is to test the hypothesis that PD patients would demonstrate reduced emotional reactivity, as indexed by emotional modulation of startle, specific to fear-eliciting pictures. To test this prediction, data were subjected to a 2 Group (PD, control) $\times$ 5 A Priori Picture Category (pleasant, neutral, fear, disgust- contamination, disgust-mutilation)

²Laboratories commonly record from only one eye (e.g. Bradley et al., 2001a,b use left eye), and according to Berg and Balaban (1999), “which eye is selected is a matter of convenience and preference” (pp. 36). We opted to record from both eyes so that in situations when data from only one eye were valid, the other eye could be used, thereby maximizing the number of usable trials for analysis.

repeated measures Analysis of Variance (ANOVA) with startle eyeblink magnitude T-scores as the dependent variable. A main effect of picture category and a group-by-picture-category interaction was predicted. The interaction was decomposed by five planned one-way ANOVAs (one for each a priori picture category) with group as the between-participants factor. Bonferroni-corrected post hoc t-tests were used to further examine significant effects.

Data analysis of valence, arousal, and discrete emotion ratings followed this same general analysis pattern. Thus, subjective ratings of valence and arousal were analyzed through two separate 2 (Group) $\times$ 5 (A Priori Picture Category: pleasant, neutral, fear, disgust-contamination, and disgust-mutilation) repeated measures ANOVAs. Post-hoc basic emotion ratings were analyzed through a series of four 2 (Group) $\times$ 5 (A Priori Picture Category: neutral, pleasant, fear disgust-contamination, disgust-mutilation) repeated measures ANOVAs (one for each post hoc basic emotion rating: happiness, disgust, fear, and sadness). Pearson's bivariate correlations were used to examine the relationship between arousal ratings and emotion-modulated startle eyeblink magnitudes.

RESULTS

Psychophysiology Data

Unprimed startle eyeblink—An initial analysis examined whether the PD patients and controls differed in terms of their basic “unprimed” startle eyeblink responses. This was done by analyzing the 12 initial unprimed baseline startle trials (i.e., no picture presented). Results of independent t-tests showed no group differences in peak startle eyeblink magnitude (means: PD = 5.38 mV [SD = 4.45], control = 6.59 mV [SD = 6.78]; $t[46] = .73$, $p > .1$). Similarly, there was no difference in baseline startle latency (means: PD = 72.86ms [SD = 11.64], control = 74.19ms [SD = 8.26]; $t[46] = .45$, $p > .1$).

Emotion-modulated startle eyeblink

Discarded trials: The total percentage of discarded trials was 9.9%. Discarded trials were based on eye movement artifact (determined by visual inspection; 5.1% of all discarded trials), peak latency out of range (2.8%), peak amplitude out of range (1.5%), and no peak maximum amplitude found (0.6%). A 2 (Group) $\times$ 2 (Stimulus Presentation Order) $\times$ 5 (A Priori Picture Category: pleasant, neutral, fear, disgust-contamination, disgust-mutilation) repeated measures ANOVA with number of discarded trials as the dependent variable did not yield any significant main effects or interactions (all p 's $> .1$).

Latency: A 2 (Group) $\times$ 2 (Stimulus Presentation Order) $\times$ 5 (A Priori Picture Category: pleasant, neutral, fear, disgust-contamination, disgust-mutilation) repeated measures ANOVA was conducted to determine whether latency was affected by any of these variables. Results revealed no significant main effects or interactions (all p 's $> .1$). Thus, the latency to peak magnitude did not appear to vary as a function of group, stimulus presentation order, or a priori picture category.

Magnitude: An initial analysis was conducted in order to determine whether stimulus presentation order or startle probe onset latency (4200 ms, 4800 ms, 5000 ms) resulted in different findings. For both PD patients and controls, no significant main effects or interactions were found (all p 's $> .6$). Thus, the remaining analyses were collapsed across the three different startle probe onset latencies and two presentation orders.

Primary analysis: Relationship between Emotion Categories and Startle Eyeblink

Magnitude: Mean startle eyeblink magnitudes for each group for pleasant, neutral, fear, disgust-contamination, and disgust-mutilation pictures are shown in Figure 1. A repeated

measures ANOVA yielded a significant main effect of A Priori Picture Category ($F[4,184] = 9.18, p < .001, \eta^2_p = .17$) and a Group $\times$ A Priori Picture Category interaction ($F[4,184] = 2.49, p < .05, \eta^2_p = .05$). Bonferroni-corrected post hoc comparisons indicated that the main effect of A Priori Picture Category was driven by the fear pictures, which were associated with significantly larger startle magnitudes (collapsing across both groups) than those for all other picture categories (all p 's $< .02$). No other comparisons were significant. When results were examined for controls and PD patients separately, controls showed significantly larger startle eyeblink magnitudes to fear pictures compared to neutral and pleasant pictures (p 's $< .05$). Additionally, startle eyeblink magnitudes to mutilation pictures tended to be larger compared to pleasant pictures, but this comparison was no longer significant after Bonferroni corrections were made ($p = .1$). In contrast, PD patients showed significantly larger startle eyeblink magnitudes for fear pictures compared to neutral, pleasant, and mutilation pictures (p 's $< .05$).

The Group $\times$ A Priori Picture Category interaction was decomposed by conducting five separate univariate ANOVAs (one for each a priori picture category) with Group as the between-participants factor. Only the comparison for the mutilation pictures was significant ($F[1, 46] = 6.66, p < .02, \eta^2_p = .13$), with controls showing significantly larger startle eyeblink magnitudes than PD patients (means: PD = 48.34 [SD = 3.91], control = 51.09 [SD = 3.47]). Thus, the prediction that startle eyeblink magnitudes in response to fear pictures would be reduced in PD patients compared to controls was not supported; instead, mutilation pictures resulted in attenuated startle eyeblink magnitude in the PD group.

Behavioral Data

Subjective ratings of pictures by Parkinson and control groups

Valence and Arousal Ratings: First, we examined subjective ratings of valence and arousal that participants made on a trial-by-trial basis during the psychophysiology task. For valence ratings, results yielded a significant main effect of A Priori Picture Category ($F[4,184] = 49.24, p < .001, \eta^2_p = .52$). The effect of Group was nonsignificant [$F(1,46) = .34, p > .1$], as was the Group $\times$ A Priori Picture Category interaction [$F(4,184) = .07, p > .1$]. Bonferroni-corrected post hoc comparisons collapsing across the two groups revealed that pleasant pictures were rated as significantly more pleasant than all other picture types (all p 's $< .001$). Neutral pictures were rated as significantly more pleasant than contamination, mutilation, and fear pictures (all p 's $< .001$). Looking at just the unpleasant picture categories (fear, disgust- contamination, and disgust- mutilation pictures), the mutilation pictures were rated as significantly more pleasant than the fear pictures ($p < .05$). No other comparisons were significant.

For arousal ratings, results once again yielded a significant main effect of A Priori Picture Category ($F[4,184] = 56.00, p < .001, \eta^2_p = .55$), and no other significant effects or interactions (all p 's $> .1$). Bonferroni-corrected post hoc comparisons collapsing across the two groups revealed that the neutral pictures were rated as significantly less arousing than all other picture types (p 's $< .001$). No other comparisons were significant, indicating that pleasant, fear, disgust- contamination, and disgust- mutilation pictures were perceived as equally arousing by participants. Table 2 shows mean valence and arousal ratings for each picture category by group.

Basic Emotion Ratings: Next, we examined post hoc basic emotion ratings made by all participants after the psychophysiology portion of the experiment. As previously described, each participant rated each picture in terms of how happy, disgusted, fearful, and sad he felt while viewing the pictures a second time after completion of the psychophysiology trials. These ratings served as a manipulation check to ensure that the pictures did in fact evoke the emotions they were intended to elicit. A series of four 2 (Group) $\times$ 5 (A Priori Picture Category: neutral, pleasant, fear, disgust- contamination, disgust- mutilation) repeated measures ANOVAs were

conducted (one for each post hoc basic emotion rating: happiness, disgust, fear, and sadness). Post hoc emotion ratings by group and a priori picture category are shown in Table 3. For happiness ratings, results yielded a main effect of A Priori Picture Category ($F[4,184] = 463.02$, $p < .001$, $\eta^2_p = .91$), with no other significant effects. Bonferroni-corrected pairwise comparisons collapsing across the two groups revealed that pleasant pictures had significantly higher happiness ratings than all other types of pictures (all p 's $< .001$). Additionally, neutral pictures had significantly higher happiness ratings than fear, mutilation, and contamination pictures, while fear pictures had significantly higher happiness ratings than mutilation pictures (p 's $< .001$).

For disgust ratings, the repeated measures ANOVA showed a main effect of A Priori Picture Category ($F[4,184] = 274.23$, $p < .001$, $\eta^2_p = .86$) as well as an A Priori Picture Category $\times$ Group interaction ($F[4,184] = 3.19$, $p < .02$, $\eta^2_p = .07$). Bonferroni-corrected pairwise comparisons collapsing across the two groups revealed that both mutilation and contamination pictures were rated as significantly more disgusting than all other picture types (p 's $< .001$), whereas mutilation and contamination pictures did not differ from one another in subjective disgust ratings. Both the neutral and pleasant pictures were rated as significantly less disgusting than fear, contamination, and mutilation pictures (all p 's $< .001$). The Group $\times$ A Priori Picture Category interaction was decomposed by conducting five separate univariate ANOVAs (one for each a priori picture category) with Group as the between-subjects factor. Only the comparison for fear pictures was significant ($F[1, 46] = 7.93$, $p < .01$), $\eta^2_p = .15$), with PD patients rating these pictures as eliciting more disgust compared to controls (means: PD = 5.55 [SD = 1.99], control = 4.81 [SD = 1.94]).

Turning to fear ratings, results yielded a main effect of A Priori Picture Category ($F[4,184] = 162.57$, $p < .001$, $\eta^2_p = .78$); no other effects were significant. Bonferroni-corrected pairwise comparisons showed that neutral pictures were rated as significantly less fear-evoking than all other picture categories, whereas fear pictures were rated as significantly more fear-evoking than all other picture types (p 's $< .001$). Additionally, mutilation pictures were associated with significantly higher fear ratings than neutral, pleasant, and contamination pictures (p 's $< .001$).

In sum, each a priori picture category was effective in evoking the intended emotional reaction. Overall, the self-report data suggest that group differences in their subjective valence, arousal, or basic emotion ratings cannot account for the reduced startle eyeblink magnitude to mutilation pictures observed in PD patients.

A dimensional approach: Relationship between arousal level of negative pictures and startle eyeblink—Another possible explanation for the reduced reactivity to mutilation pictures by the PD patients is that it was driven by diminished psychophysiologic reactivity to high-arousal, aversive stimuli. One argument against this possibility is that our relatively small study sample did not rate mutilations as more arousing than other types of negative pictures at a statistically significant level. However, in a larger study with 95 healthy subjects, Bradley et al. (2001a) found that mutilation pictures were among the most arousing of all negative picture contents as measured by subjective arousal ratings and skin conductance responses. To examine this possibility, we ranked all negative pictures in the current study by arousal ratings from the IAPS normative study (Lang et al., 2001b) and selected the top one-third to create a “high arousal” group of pictures (IAPS numbers: 3500, 6260, 6313, 3400, 1120, 6510, 3060, 3000) and the bottom one-third to create a “low arousal” group (IAPS numbers: 9373, 1274, 7359, 9300, 6415, 9301, 6242, 6243). The middle one-third of pictures were not included in this analysis. Ratings from the IAPS normative study were chosen since our study design was balanced for arousal and valence ratings across the pleasant, neutral, fear, and disgust a priori emotion categories using these ratings. Levene's test indicated homogeneity of variance by group and arousal level. A 2 (Group) $\times$ 2 (Arousal Level) repeated measures

ANOVA yielded a trend towards a significant main effect of Arousal Level ($F[1, 46] = 3.20$, $p = .08$, $\eta^2_p = .07$), with the high arousal negative pictures ($X = 51.66[2.94]$) associated with larger startle eyeblink magnitudes than low arousal negative pictures ($X = 50.67[2.44]$). The effect of group was nonsignificant ($p > 0.1$). The Group $\times$ Arousal level interaction was significant ($F[1, 46] = 6.41$, $p = .015$, $\eta^2_p = .12$), and is depicted in Figure 2. Whereas the control group showed larger startle eyeblink magnitudes to the high arousal negative pictures ($X = 52.43[3.50]$) than low arousal pictures ($X = 50.03[2.44]$), the PD group did not. Instead, they displayed no difference in startle reactivity between high and low arousal negative pictures (means: high arousal = $50.90[2.05]$, low arousal = $51.31[3.63]$). Post-hoc t-tests indicated that controls and PD patients did not differ with respect to startle eyeblink magnitudes to the low arousal pictures ($t[46] = 1.43$, $p > .1$); however, the PD group showed a trend towards smaller startle eyeblink magnitudes than the control group to the high arousal pictures ($t[46] = 1.85$, $p = 0.07$). To clarify whether this arousal effect was specific to negative pictures, or held true for the positive pictures as well, we repeated the same analysis using the top one-third pleasant pictures with the highest normative arousal ratings (IAPS numbers: 5621, 5629, 8370, 8501) and the bottom one-third pleasant pictures with the lowest normative arousal ratings (IAPS numbers: 5260, 4653, 4599, 4626).³ The main effect of Arousal Level was nonsignificant ($F[1, 46] = 0.28$, $p = 0.60$) as was the interaction effect ($F[1, 46] = 0.99$, $p = 0.33$), indicating that for both groups, normative arousal ratings of the pleasant pictures did not appear to significantly modulate emotion-modulated startle eyeblink magnitudes.

Overall, these results indicate that arousal level of the negative pictures modulated startle eyeblink magnitudes in the control group, but not the PD group. To determine the relationship between this finding and our prior finding of decreased startle eyeblink magnitude to mutilation pictures in the PD group, we examined the composition of the “high arousal” pictures. The eight high arousal pictures contained five fear pictures (out of a total of 12 fear pictures used in the study, thus 41% of the total fear pictures) and three mutilation pictures (out of a total of seven mutilation pictures used in the study, 43% of the total mutilation pictures). The five fear pictures had an average normative arousal rating of 6.95 ($SD = 0.03$) and the three mutilation pictures had an average normative arousal rating of 7.12 ($SD = 0.22$). This difference was not statistically significant ($t[1] = 1.89$, $p = 0.30$); however, the mutilation pictures had a greater range and larger standard deviation (range: 6.91–7.34) than the fear pictures (range: 6.93 – 6.99). Additionally, two of the mutilation pictures had the highest arousal ratings out of all 8 of the “high arousal” pictures. This suggests that as a group, mutilation pictures and fear pictures were matched for arousal based on their mean, but at the individual picture level the mutilation pictures had a greater proportion of pictures with higher arousal ratings than the fear pictures. Thus, the mutilation pictures with particularly high arousal levels may have driven the overall effect of reduced startle eyeblink magnitudes in the PD group.

Relationship between subjective arousal ratings and startle eyeblink magnitude

—To further investigate the relationship between arousal level and emotion-modulated startle eyeblink magnitude, bivariate correlations between subjective arousal ratings and objective startle eyeblink magnitudes were conducted for each group separately by picture category (neutral, pleasant, disgust-contamination, disgust-mutilation, and fear). No correlations were significant (all p 's $> .1$).

Influence of depression, antidepressants, and disease severity and duration on startle eyeblink magnitude—Next, the relationship between BDI-2 scores and startle eyeblink magnitudes in response to each a priori picture category was examined through a

³Because the stimulus set contained fewer positive than negative pictures, this analysis contained fewer pictures than the corresponding analysis with negative pictures.

series of five separate linear regressions (one for each a priori picture category: neutral, pleasant, fear, disgust- contamination, disgust- mutilation). BDI-2 scores, diagnostic group, and the BDI-2 $\times$ diagnostic group interaction term were entered simultaneously as the independent variables and startle eyeblink magnitude T-scores served as the dependent variable. None of the resulting regression models were statistically significant.

Because antidepressants or anxiolytics may dampen startle reactivity in healthy individuals (Davis & Gallagher, 1988; Harmer, Shelley, Cowen, & Goodwin, 2006), the influence of these medications on startle reactivity was also examined. To do so, the seven PD patients on antidepressants and/or anxiolytics were removed from the sample and a 2 (Group) $\times$ 5 (A priori picture category) repeated measures ANOVA was conducted with the data from this smaller sample. The pattern of results mirrored that of the larger sample. Thus, diminished reactivity to mutilation pictures by PD patients was maintained when excluding patients on antidepressants and anxiolytics.

To determine whether disease duration or severity were associated with the finding of decreased startle reactivity to mutilation pictures in the PD patients, the variables “years with PD” and “UPDRS Motor score” were entered as independent variables simultaneously into a regression model with startle eyeblink T-score to disgust- mutilation pictures as the dependent variable. The overall model was not significant, indicating that neither of these disease-related variables account for a significant portion of the variance in startle eyeblink magnitudes ($F_{[2,21]} = 47.02$, $p = .22$; $R^2 = 0.13$, adjusted $R^2 = 0.05$.)

DISCUSSION

The primary aim of this study was to examine the possibility of an emotion-specific reactivity deficit to fear pictures in PD patients, as indexed by startle eyeblink magnitude. In a previous study, we found diminished startle reactivity to aversive pictures in PD patients (Bowers et al., 2006b). Due to the composition of the pictures in the “aversive” category, we were unable to determine whether this effect was driven by certain emotion categories of unpleasant stimuli (i.e., fear vs. disgust). Based on evidence that the amygdala appears to play a specific role in the processing of fear-eliciting stimuli (Amaral, 2003; Calder et al., 1996; Klüver & Bucy, 1939; Young et al., 1995), along with prior findings of structural and functional amygdala abnormalities in PD (Braak & Braak, 2000; Harding, Stimson, Henderson, & Halliday, 2002; Ouchi et al., 1999), the current study tested the hypothesis that reduced reactivity to aversive pictures may be more specifically due to reduced reactivity to fear stimuli. This hypothesis was not supported by the current findings. Instead, PD patients demonstrated significantly smaller startle eyeblink magnitudes to a specific subcategory of aversive pictures, mutilations. Startle eyeblink magnitudes to contamination pictures as well as to fear, pleasant, and neutral picture categories did not differ from controls.

What might be the basis for this mutilation-specific hyporeactivity? There are several potential explanations. First, the PD group might find the mutilation pictures less unpleasant, less arousing, or less disgusting compared to controls. This could be due to visuoperception problems, resulting in misperception of pictures, or due to misappraisal of the emotional meaning behind the pictures. These concerns were addressed by examining the valence and arousal ratings made by each participant during the psychophysiology experiment, as well as the post hoc basic emotion ratings made afterwards. The two groups did not significantly differ with regards to their valence or arousal ratings for mutilation pictures or for any of the a priori picture categories (neutral, pleasant, fear, disgust- contamination, disgust- mutilation). Additionally, in their post hoc ratings of degree of happiness, disgust, fear, and sadness associated with mutilation pictures, PD patients' ratings were comparable to controls. This is consistent with prior research showing that PD patients typically report subjective feelings that

are comparable to those reported by controls during tasks such as viewing emotional video clips (Simons et al., 2004; Smith et al., 1996). Taken together, these findings suggest that the lack of startle potentiation to mutilation pictures is not due to decreased subjective ratings of unpleasantness or arousal from the standpoint of a dimensional model of emotion, or due to inaccurate subjective *appraisal* from a discrete categorical approach to emotion.

A second possibility is that PD patients have a deficit in translating their aversive motivational state into a physiological response. To elaborate, Lang (1995) described emotions as action dispositions associated with a physiological, behavioral, and affective response. According to this model, emotions are driven by two opponent motivational systems. Activation of the appetitive system is associated with behavioral approach as well as attenuation of the startle reflex. Activation of the aversive system is characterized by protective withdrawal/avoidance and increased startle reflex. We previously suggested that perhaps PD patients are able to correctly appraise the emotional significance of a stimulus, but are unable “translate” activation of the aversive motivational system into a physiological response (Bowers et al., 2006b). We suggested this may be attributable to faulty communication between the amygdala and prefrontal cortex due to low levels of dopamine in PD. This hypothesis was based on a series of animal studies providing evidence that dopamine modulates prefrontal cortex -controlled inhibition and disinhibition of the amygdala in response to stress-inducing stimuli (Amaral, Price, Pitkanen, & Carmichael, 1992; Inglis & Moghaddam, 1999; Rosenkranz & Grace, 1999). Typically, the amygdala is under inhibitory control from the prefrontal cortex (Rosenkranz & Grace, 1999, 2002). In response to sensory-driven stress (e.g., viewing an aversive picture), dopamine is released in the basolateral amygdala (Inglis & Moghaddam, 1999) causing a chain of neural events resulting in suppression of the prefrontal cortex's inhibition of the amygdala (Marowsky, Yanagawa, Obata, & Vogt, 2005). According to Bowers et al. (2006b), one can speculate that in PD dopaminergic depletion would reduce the extent to which this amygdala disinhibition would occur in response to a highly-arousing, stress-evoking stimulus. Because the amygdala projects to basic startle circuitry within the brainstem as well as the hypothalamus, which mediates sympathetic nervous system arousal (Amaral et al., 1992) the net effect would potentially be to reduce physiologic reactivity, as indexed by measures such as emotion-modulated startle eyeblink or skin conductance response.

An explanation for reduced reactivity specifically to mutilation pictures that is consistent with this theory is that the mutilation pictures used in the study were actually more arousing (and thus activated the aversive motivational system to a greater degree) than were the fear and contamination pictures used in the study. Participants in our sample did not rate the mutilation pictures as significantly higher in arousal than other aversive pictures; however, in a large-scale study, Bradley et al. (2001a) found that mutilation and animal attack pictures were associated with significantly higher skin conductance response (another measure of physiological arousal) and arousal ratings compared to other unpleasant pictures (such as pictures of vehicular accidents or contaminations). It is possible that reduced startle eyeblink magnitude to mutilation pictures may be due to the fact that the mutilation pictures in our study, or perhaps a subset of these mutilation pictures, were the only type of aversive pictures sufficiently arousing to detect a deficit in physiological reactivity in PD patients. At first glance this explanation may appear counterintuitive, as the PD group showed robust startle potentiation to fear pictures, suggesting intact physiological response to arousing negative stimuli. However, when we examined the normative IAPS ratings for the pictures included in the current study, we found that although fear and mutilation pictures had similar mean arousal ratings, at the individual picture level the mutilation picture category had a greater proportion of pictures with very high arousal ratings. The top two negative pictures with the highest arousal ratings were mutilations. Similarly, in our previous study, four of the top five negative pictures with the highest arousal ratings were mutilations (Bowers et al., 2006b). Thus, it is plausible that these highly arousing pictures, which fall into the “mutilation” category, may have driven

the effect of reduced startle eyeblink magnitude in the PD group by bringing down the group mean eyeblink magnitude for mutilation pictures. Unfortunately, it is impossible to discern if this effect is due to the specific mutilation pictures used in our study (and thus represents an artifact of study design and not a mutilation-specific effect), or if the content of mutilation pictures is intrinsically more arousing than other pictures due to their very nature. It would be possible to address this issue through a replication study in which the top few negative pictures with the highest arousal ratings are not mutilations. In either case, our theory that reduced startle eyeblink magnitude in PD is mediated by arousal level of the pictures is supported by an analysis in which we compared startle eyeblink magnitudes for the eight negative pictures with the highest normative arousal ratings versus the eight negative pictures with the lowest arousal ratings. In the control group, arousal level modulated the startle reflex, with the most arousing pictures resulting in larger startle eyeblinks. In contrast, arousal level did not modulate startle response in PD patients. They showed similar startle eyeblink magnitudes to both low arousal and high arousal pictures. As studies have implicated the amygdala in learning and memory of highly arousing positive as well as negative stimuli (see McGaugh, 2004 for a review of this literature), we followed up on this analysis by examining the groups' pattern of eyeblink magnitudes to the pleasant pictures with the highest and lowest normative arousal ratings. For both controls and PD patients, normative arousal ratings did not appear to modulate eyeblink magnitudes. It is possible that this analysis did not reach statistical significance because there were a fewer number of positive than negative pictures in our stimulus set, or because of the fact that the range of normative arousal ratings was smaller for the positive pictures than for the negative pictures. Keeping in mind these limitations, our findings suggest that PD patients and controls respond similarly to positive picture stimuli, but PD patients show a reactivity deficit to *certain* highly arousing negative pictures. In further support of an arousal-driven reactivity deficit to aversive stimuli, we recently reported findings with respect to skin conductance response (SCR) in PD patients that mirror these startle reflex results (Bowers et al., 2008). Generally, viewing arousing emotional stimuli is associated with an increase in SCR. While controls showed the expected increase in SCR during viewing of emotional pictures, PD patients showed no modulation of SCR. Taken together, these findings support the hypothesis of a deficit in translating a motivational state into a physiological response in PD. The high-low arousal analysis in the present study supports a threshold model in which highly arousing and aversive stimuli (such as the mutilation pictures) are needed to detect differences in physiological reactivity between controls and PD patients, whereas less arousing stimuli may not be sufficient to detect this difference. In considering this hypothesis, it is important to point out that the PD group did show normal startle modulation to the fear pictures, suggesting that there is not a complete disconnect between translating an aversive motivational state into a physiological response in these patients. In accounting for this discrepant response to the fear pictures versus the mutilation pictures, one possibility is that some intrinsic aspect of mutilation stimuli makes them particularly threatening to the viewer (discussed in further detail below), thus activating the prefrontal-amygdala circuitry to a greater extent than the a priori "fear" pictures and revealing the subtle dysfunction of this circuitry.

Surprisingly, we found no correlation between subjective arousal ratings and objective startle eyeblink magnitudes in the control or PD groups. One explanation for lack of significant correlations may be restricted range or small sample size. Another possibility is that participants may have been responding to demand characteristics when making their subjective ratings. For example, participants may have rated a picture of a snake high in arousal simply because they thought it was intended to evoke high arousal, not because they actually felt this way. A final possibility that must be considered is that participants did not understand exactly what was meant by rating "arousal;" although all participants were given sample pictures to rate prior to the start of the study and all made reasonable arousal ratings. However, the concept of "arousal level" is arguably more difficult to understand than is the concept of valence ratings.

The reason underlying the emotional intensity as well as the motivational relevance of the mutilation pictures is unknown; however, our results suggest these stimuli strongly activate the aversive motivational system. In considering how an individual's appraisal of a stimulus affects their physiological response to it, Springer, Rosas, McGetrick, & Bowers (2007) recently pointed out that an experimenter's a priori categorization of a stimulus (e.g. "fear" or "disgust") may be less important than its functional impact upon the viewer. For example, studies employing IAPS pictures stimuli often include a "fear" stimulus set that places "victim" pictures (in which one person is directly victimizing another person in the picture by pointing a gun at them or hitting them, etc.) in the same category as "direct threat" pictures (in which a gun or other weapon is pointed directly at the viewer); however, Bernat, Patrick, Benning, & Tellegen (2006) have shown that emotion-modulated startle eyeblink magnitudes are larger for the "direct threat" pictures. This suggests that subtle nuances within the picture contents themselves may affect how participants appraise, and consequently respond to, a stimulus. Along this line of reasoning, we can speculate that from an evolutionary standpoint that it might be highly arousing and aversive to see a mutilated person. Because mutilation pictures depict a destruction of bodily integrity, seeing an injured/mutilated conspecific may signal "direct threat" to one's own bodily integrity.

There are several limitations to the current study that should be acknowledged. First, the patient sample may not be representative of the typical person with PD. The sample was highly educated (average of 16 years of education), although it is unlikely that educational status influenced the emotion-modulated startle eyeblink, which it is thought to be an automatic reaction (Bradley, 2000).

The sample also had an imbalance of men and women (14 men and 10 women per group). Although preliminary analyses including "sex" as an independent variable revealed no significant effect of sex for any of the key study aims, the study was not designed to be sufficiently powered to examine sex differences. In a large study of sex differences in physiologic reactivity examining men and women's responses to a wide variety of picture contents, Bradley et al. (2001b) reported that women tended to respond with greater defensive activation (i.e. larger emotion-modulated *startle* eyeblink, more cardiac deceleration, increased facial EMG activity changes) compared to men when viewing unpleasant pictures. This raises the possibility that sex may interact with startle potentiation to the fear, contamination, or mutilation pictures.

The present study is also limited by the fact that participants were limited to PD patients in Hoehn and Yahr stage 2 or 3, and the majority of patients had on-medication UPDRS motor scores falling in the 20s (range: 4-41). Although startle eyeblink magnitudes were not significantly associated with UPDRS motor score, this finding is limited by the fact that persons with severe PD were not included in the study. It is possible that a linear relationship between disease severity and startle eyeblink magnitude exists (as was found by Bowers et al., 2006b), but was not detected because of the restricted range in the current study. As the disease progresses, we would expect further pathological changes to the amygdala, which may increase the magnitude of any emotional reactivity deficits. Future studies should include patients with a broader range of disease severity in order to more fully examine the impact of disease progression upon emotion-modulated startle. Finally, there are some methodological limitations to our study that should be acknowledged. A formal assessment of visuoperception was not conducted, and it is possible that poor visuoperception could affect participants' ability to correctly perceive the stimulus pictures. In terms of participants' emotion ratings, two different rating scales of subjective emotional reaction were used in the study, which may have potentially been confusing to participants. Additionally, the post-experimental emotion ratings included "disgust," "fear," "happiness," and "sadness," even though sadness was not a target emotion, and it is possible that having these as the only emotion rating options could have

biased participants' towards a particular response set (e.g. “angry” and “surprised” were not provided).

In conclusion, our data do not support the hypothesis of an emotion-specific reactivity deficit to PD. Instead, our results suggest PD patients display diminished reactivity to highly arousing aversive stimuli, regardless of the specific emotions experienced. We previously suggested this may be due to impairment in translating their motivational state into a physiological response. Based on the data from the current study, we expanded upon our earlier theory by suggesting a threshold model in which only highly arousing negative stimuli, such as mutilation pictures, are sufficient to detect this impairment. Future studies should investigate whether this hyporeactivity is caused by peripheral autonomic nervous system changes in PD, such as Lewy bodies within the sympathetic ganglion, or central nervous system dysfunction. Our results add to the growing literature indicating that PD is not simply a movement disorder, but a disease that also affects emotional and physiological responses.

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Appendix

APPENDIX I

International Affective Picture System (IAPS) Normative Valence and Arousal Ratings

Picture Category	IAPS #	Picture Description	Valence ^a	Arousal ^a
Neutral	7100	firehydrant	5.24 (1.20)	2.89 (1.70)
	7235	chair	4.96 (1.18)	2.83 (2.00)
	7080	fork	5.27 (1.09)	2.32 (1.84)
	7050	hairdryer	4.93 (0.81)	2.75 (1.80)
	7020	fan	4.97 (1.04)	2.17 (1.71)
	7211	clock	4.81 (1.78)	4.20 (2.40)
	7035	mug	4.98 (0.96)	2.66 (1.82)
	7038	shoes	4.82 (1.2)	3.01 (1.96)
	7950	tissue	4.94 (1.21)	2.28 (1.81)
	7150	umbrella	4.72 (1.00)	2.61 (1.76)
	7175	lamp	4.87 (1.00)	1.72 (1.26)
	7233	plate	5.09 (1.46)	2.77 (1.92)
		<i>Average</i>	<i>4.97 (1.16)</i>	<i>2.68 (1.83)</i>
Pleasant	8501	money	7.91 (1.66)	6.44 (2.29)
	8034	snowskier	7.06 (1.53)	6.30 (2.16)
	5260	waterfall	7.34 (1.74)	5.71 (2.53)

Picture Category	IAPS #	Picture Description	Valence ^a	Arousal ^a
	4599	romantic couple	7.12 (1.48)	5.69 (1.94)
	8370	rafting	7.77 (1.29)	6.73 (2.24)
	4653	couple	6.56 (1.65)	5.83 (2.07)
	4626	wedding	7.6 (1.66)	5.78 (2.42)
	8170	sailboat	7.63 (1.34)	6.12 (2.30)
	5621	skydivers	7.57 (1.42)	6.99 (1.95)
	5629	hiker	7.03 (1.55)	6.55 (2.11)
	8470	gymnast	7.74 (1.53)	6.14 (2.19)
	8200	waterskier	7.54 (1.37)	6.35 (1.98)
		<i>Average</i>	<i>7.41 (1.52)</i>	<i>6.22 (2.18)</i>
Fear	6313	knife attack	1.98 (1.38)	6.94 (2.23)
	3500	gun pointed at man	2.21 (1.34)	6.99 (1.68)
	6510	masked man	2.46 (1.58)	6.96 (2.23)
	6242	gang with gun	2.69 (1.59)	5.43 (1.93)
	6260	aimed gun	2.44 (1.54)	6.93 (1.98)
	6821	gang attacking car	2.38 (1.72)	6.29 (2.19)
	6243	man pointing gun	2.33 (1.49)	5.99 (2.23)
	1120	snake	3.49 (1.93)	6.93 (2.20)
	1052	snake	3.5 (1.87)	6.52 (2.02)
	1525	attackdog	3.09 (1.72)	6.51 (2.25)
	1932	shark attack	3.85 (2.11)	6.47 (2.09)
	1300	dog with teeth bared	3.55 (1.78)	6.79 (1.84)
		<i>Average</i>	<i>2.83 (1.67)</i>	<i>6.56 (2.07)</i>
Disgust	3000	mutilated face	1.59 (1.35)	7.34 (2.27)
	3071	mutilated body	1.88 (1.39)	6.86 (2.05)
	3110	burn victim	1.79 (1.30)	6.70 (2.16)
	3400	severed hand	2.35 (1.90)	6.91 (2.22)
	3150	bloody chopped fingers	2.26 (1.57)	6.55 (2.20)
	3060	mutilated body	1.79 (1.56)	7.12 (2.09)
	6415	dead bloody tiger	2.21 (1.51)	6.2 (2.31)
	9300	dirty toilet	2.26 (1.76)	6.00 (2.41)
	7359	bug on pie	3.38 (1.75)	5.07 (2.09)
	9301	dirty toilet	2.26 (1.56)	5.28 (2.46)
	9373	vomit	3.38 (1.48)	5.01 (2.16)
	1274	roaches	3.17 (1.53)	5.39 (2.39)
		<i>Average</i>	<i>2.36 (1.56)</i>	<i>6.20 (2.23)</i>

Note: Values are expressed as mean (SD). Valence ratings are on a 1-9 scale, with 9 being most pleasant. Arousal ratings are on a 1-9 scale, with 9 being most arousing.

^aFrom Lang et al., 2001b

APPENDIX II

Instructions to Participants for Psychophysiology Task

In this study, you will be looking at pictures such as this one and then rate how you felt while you looked at the picture. We want to know how pleasant or unpleasant you found the picture, and we also want to know how arousing or exciting the picture was to you. In other words, we want you to make two judgments about the picture - how pleasant/unpleasant it was and how arousing it was to you.

You'll start the study by sitting quietly, and then a picture will come on the monitor for a few moments. You should look at the picture the entire time it is on the screen. The picture will go off and after a few moments a rating slide will be shown. You will make your ratings once the rating scale comes on.

This next picture has a figure that we call SAM. You will use this figure to make your ratings. The first rating is how pleasant or unpleasant the picture made you feel. Look at SAM on the left side of the screen. He ranges from being extremely happy, pleased, satisfied, contented at one end of the scale. At the other end of the scale, he is very unhappy, unsatisfied, annoyed, sad, distressed. In the very middle of the scale, SAM is neutral and indifferent. So, SAM ranges from feeling extremely pleasant to neutral to extremely unpleasant. After viewing the picture, we want you to rate how pleasant or unpleasant you found the picture to be. Use the SAM scale and select the number that corresponds to your reaction. So, a number 1 would mean that you felt extremely unpleasant, whereas a number 9 would mean you felt extremely pleasant. You can use numbers in between as well. Do you have any questions? How would you rate the picture you just saw?

The second rating is how excited or calm you felt while looking at the picture. Look at the SAM figure on the right side of the screen. He ranges from being extremely aroused, excited, frenzied, alert and ready to go at one end of the scale. At the other end of the scale, he is sleepy, sluggish, dull, calm. In the middle of the scale, SAM is more average in arousal level. So, SAM ranges from feeling extremely excited and aroused to more average in energy level to extremely sluggish. After viewing the picture, we want to rate how arousing you found the picture to be. Use the SAM scale and select the number that corresponds to your reaction. A number 1 would mean that you felt sluggish, whereas a number 9 would mean you felt extremely aroused and energized. Do you have any questions? How would you rate the picture you just saw?

Ok, let me clarify that the two ratings you made can be distinct. Some pictures can be high in arousal and high in pleasantness, whereas others might be high in pleasantness yet low in arousal. For example, some people might find pictures of babies very pleasant but low in arousal, whereas a picture of a gruesome murder might be very negative and very arousing. Do you understand?

Let me briefly summarize the procedure for each trial now. A picture will be presented on the screen, and you should look at it the entire time it is on the screen. The picture will go off and a few moments later the rating slide will appear. At that point, you will rate how you felt viewing the picture using the SAM figure. Tell us out loud your ratings for how pleasant-unpleasant you found the picture, and also how arousing you found the picture. We can hear you over the intercom. After you make your ratings, please relax quietly until the next picture is presented

without closing your eyes. Additionally, sporadically throughout the experiment, you may hear brief bursts of white noise through the headphones that I will place on your head. Do not be concerned with these sounds, just continue with the task. Do you have any questions?

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Figure 1.

Figure 2.

Table 1

Demographic and clinical characteristics by group

Characteristic	Parkinson (N= 24)	Control (N= 24)	Statistical test
Age (years)	68.00 (6.92)	68.38 (7.73)	$t(46) = .18$
Sex ratio (men: women)	14:10	14:10	$\chi^2(1) = 0$
Education (yrs)	16.21 (3.16)	16.33 (2.88)	$t(46) = .14$
Disease duration (yrs)	5.54 (3.63)	—	
Hoehn and Yahr stage ^a	2.27 (0.42)	—	
UPDRS Motor ^a	23.46 (8.49)	—	
Levodopa equivalent dose (mg)	682.43 (323.26)	—	

Note: Values are expressed as mean (SD). UPDRS Motor = motor scale of the Unified Parkinson Disease Rating Scale

^a Scores obtained in the “on” medication state

Table 2Valence and arousal ratings of affective pictures by *a priori* picture category and group

<i>A Priori</i> Picture Category	Valence		Arousal	
	Parkinson	Control	Parkinson	Control
Neutral	4.71 (0.68)	4.61 (0.65)	3.93 (1.79)	3.36 (1.67)
Pleasant	6.07 (1.72)	5.96 (1.70)	6.67 (0.99)	6.41 (0.90)
Fear	2.60 (1.17)	2.62 (1.29)	6.79 (1.54)	6.53 (1.56)
Disgust- contamination	2.68 (0.95)	2.43 (0.90)	6.46 (1.47)	6.36 (1.36)
Disgust- mutilation	3.04 (2.02)	3.07 (2.15)	6.92 (1.59)	6.74 (1.56)

Note: Values are expressed as mean (SD). Valence ratings are on a 1-9 scale, with 9 being most pleasant. Arousal ratings are on a 1-9 scale, with 9 being most arousing. No between- groups differences for valence or arousal were found.

Table 3

Post hoc basic emotion ratings by group

<i>Post hoc</i> emotion	Group	<i>A priori</i> picture category				
		Neutral	Pleasant	Fear	Disgust- contam.	Disgust- mutil.
Happy	Parkinson	2.48 (1.33)	7.03 (1.05)	1.20 (0.27)	1.53 (0.82)	1.07 (0.21)
	Control	2.44 (1.57)	6.89 (1.34)	1.20 (0.55)	1.27 (0.66)	1.12 (0.47)
Disgust	Parkinson	1.32 (0.66)	1.21 (0.73)	5.55 (1.99)	6.78 (1.56)	6.85 (1.88)
	Control	1.09 (0.18)	1.03 (0.09)	4.08 (1.62)	6.88 (1.65)	6.59 (2.13)
Fear	Parkinson	1.18 (0.37)	2.27 (1.07)	6.81 (2.04)	2.38 (1.83)	4.55 (2.82)
	Control	1.04 (0.13)	1.92 (1.12)	6.83 (1.74)	1.83 (0.92)	3.74 (1.99)
Sad	Parkinson	1.25 (0.43)	1.14 (0.50)	3.44 (2.07)	2.59 (1.92)	5.27 (2.63)
	Control	1.08 (0.18)	1.12 (0.35)	3.40 (1.90)	2.38 (1.71)	5.98 (1.99)

Note: Values are expressed as mean (SD). *Post hoc* basic emotion ratings were all based on a 1-9 scale in which 1 indicates no emotion was felt and 9 indicates the emotion was strongly felt. Disgust-contam. = contamination pictures; Disgust-mutil. = mutilation pictures.