EMOTIONAL REACTIVITY IN PARKINSON'S DISEASE: PSYCHOPHYSIOLOGICAL AND PSYCHOSOCIAL CORRELATES

By

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To my parents for teaching me the value of perseverance, self-confidence, and a sense of humor.

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Preliminary work in our laboratory suggests that patients with Parkinson's disease (PD) may demonstrate diminished physiological reactivity to threatening pictures. This may be due to the fact that the amygdala is known to exhibit pathology in PD, and is a neural structure that plays a key role in processing threat signals in the environment. Our primary aim was to further explore the possibility of reduced emotional reactivity to threatening stimuli in PD, as indexed by emotional modulation of the startle eyeblink reflex. Our secondary aim was to examine the psychosocial impact of any reactivity deficits by determining whether they are associated with depression and with the misattribution of depression by patients' spouses.

Twenty-four non-demented PD patients in the "off" medication state and 24 age- and education-matched controls viewed neutral, pleasant, disgusting (mutilations and contaminations), and threatening (human and animal attack) pictures. During this time, white noise bursts were binaurally presented to elicit startle eyeblinks. Participants also completed the Beck Depression Inventory, 2nd edition (BDI-II) and spouses completed a surrogate-report version of this measure.

Contrary to predictions, PD patients did not display reduced startle potentiation to threatening pictures depicting attack. Instead, diminished reactivity to pictures of mutilations was

found. Neither self- nor surrogate-report ratings of depression were associated with eyeblink magnitude. Additionally, spousal and PD patient depression ratings were significantly correlated, indicating that spouses do not appear to misattribute PD symptoms to depression.

We hypothesized that PD patients may have a general deficit in physiological responsivity to highly arousing negative stimuli, as opposed to an emotion-specific deficit. Mutilation pictures are particularly arousing because they represent a threat to bodily integrity; as such, it may be that mutilation pictures were the only category of pictures sufficiently arousing to detect a between-groups difference in physiological reactivity. A secondary finding suggests that spouses may serve as accurate surrogate reporters of mood when PD patients are unable to report upon their own mood. In sum, results suggest that PD patients have aberrant physiological emotional reactivity, but this does not appear to be related to spousal perceptions of mood.

CHAPTER 1
INTRODUCTION

Statement and Overview of the Problem

Parkinson's disease (PD) is a neurodegenerative disease that affects approximately half a million to one million people in the United States (McDonald, Richard, & DeLong, 2003), with 50,000 new cases diagnosed each year (National Institute of Neurological Disorders and Stroke, 2001). PD involves progressive depletion of dopaminergic neurons within the substantia nigra and is characterized by bradykinesia (slowed movements), rigidity, tremor, and postural instability. While these motor symptoms are the defining feature of Parkinson's disease, neuropsychiatric symptoms are prevalent and can be the most disturbing, disabling, and misunderstood aspects of the disease. Disturbances of mood and motivation are common and include depression, anxiety, and apathy.

In addition to neuropsychiatric symptoms, patients with Parkinson's disease have difficulty communicating emotion using nonverbal signals such as facial expression and emotional tone of voice (Blonder, Gur, & Gur, 1989; Borod et al., 1990; Buck & Duffy, 1980; Jacobs, Shuren, Bowers, & Heilman, 1995; Smith, Smith, & Ellgring, 1996). One of the prototypical clinical features of Parkinson's disease is "masked facies," a term that refers to the expressionless facial demeanor of PD patients. Diminished facial expressivity occurs relatively early on in the disease course and appears to be unrelated to depression (Katiskitis & Pilowsky, 1991; Smith et al., 1996). Findings of reduced facial expressivity in PD raise the possibility of impairments in *emotional reactivity* (how an individual responds physiologically, subjectively, or overtly). To date few studies have investigated the topic of emotional reactivity in Parkinson disease from a multicomponential framework.

Although Parkinson patients are not as facially or prosodically expressive as their healthy counterparts, they typically report subjective feelings that are comparable in intensity during tasks such as viewing emotional pictures (Bowers, Miller, Bosch, et al., 2006; Simons, Pasqualini, Reddy, & Wood, 2004; Smith et al., 1996). However, self-report ratings are potentially unreliable because they are subject to demand characteristics, meaning that the participant may simply respond in the fashion that is expected of him or her.

Our study measured emotional reactivity in Parkinson patients with a method that does not rely on facial expression, prosody (both of which are known to be affected in PD), or self-report. Instead, emotional modulation of the startle eyeblink reflex was used as an index of emotional reactivity. This paradigm rests on the well-documented principle that the size of the startle eyeblink is directly modulated by an individual's emotional state. Additionally, because the response that is being measured is near impossible to voluntarily control, it does not rely on the participant's explicit attention, training, or cooperation (Bradley, 2000).

The overall aims of our study were twofold. The primary aim was to examine whether emotional reactivity deficits in Parkinson's disease differentially affect specific emotions. A recent study in our laboratory found that PD patients demonstrated significantly reduced reactivity in response to viewing unpleasant pictures, but not pleasant or neutral pictures (Bowers, Miller, Mikos, et al., 2006). In a *post hoc* analysis, this finding was parsed apart by comparing PD patients' emotional reactivity to threat-inducing pictures (i.e., pictures suggesting imminent attack, such as a snake preparing or bite or a gun pointed at the viewer) versus other types of unpleasant pictures (i.e., mutilated bodies, a plane crash, a starving person; Miller, 2004). The threat-inducing pictures appeared to account for the diminished startle reactivity in the PD patients. The current study aimed to replicate this finding while addressing several

methodological limitations of the initial study. Namely, the present study used a larger number of pictures, an *a priori* design, and specifically compared threat -inducing pictures to another discrete emotional category of unpleasant stimuli that are similarly high in arousal level: disgust-inducing pictures. Additionally, PD patients were tested while *off* their dopaminergic medication (unlike in the previous study) so that any potentially restorative effect dopaminergic medication may have on emotional reactivity would not confound the interpretation of results.

The second aim of the present study was to examine the relationship between emotional reactivity deficits in PD patients and family members' perceptions of depressive symptomatology in the patient. This aim is fuelled by findings from previous research that diminished use of nonverbal communication signals by Parkinson patients poses significant psychosocial problems, particularly in terms of incorrect attributions of negative mood state or depression by family members and health care providers (Pentland, Pitcairn, Gray, & Riddle, 1987, 1988; Pitcairn, Clemie, Gray, & Pentland, 1990a, 1990b).

The distinct contribution of this study is its focus on measuring emotional reactivity in Parkinson's disease via a method that is not confounded by deficits in facial/vocal expression or self-report reliability issues. Furthermore, increased understanding of emotional reactivity deficits accompanying PD may prove to be clinically useful in reducing healthcare providers' and family members' attributions that the patient is apathetic, depressed, or uninterested due to lack of overt emotional reaction. Before describing the hypotheses in further detail, a brief overview of Parkinson's disease will be presented, followed by a discussion of changes in emotional functioning associated with the disease.

Motor and Cognitive Symptoms in Parkinson's Disease

Behaviorally, Parkinson's disease is characterized by motor symptoms including resting tremor, bradykinesia (slowed movement), rigidity (increased muscle tone), and akinesia

(difficulty initiating or maintaining a body movement [Hughes, Ben-Shlomo, Daniel, & Lees, 1992; Hughes, Daniel, Kilford, & Lees, 1992]). Additionally, Parkinson's patients may experience diminished facial expressivity ("masked facies"), loss of postural reflexes, and/or motoric "freezing" when attempting to walk (Fahn, 2003). These motoric symptoms are thought to be caused primarily by a depletion of dopaminergic neurons in the substantia nigra, which then affects a cascade of structures involved in the production of voluntary movement, particularly the basal ganglia. The neural circuitry involved in Parkinson's disease is shown in Figure 1-1. It has been estimated that patients with PD have a 60-85% cell loss of dopaminergic neurons in the substantia nigra (Pogarell & Oertel, 1999). As such, dopamine replacement therapy (using levodopa, a dopamine precursor that is able to cross the blood-brain barrier) is the major medical approach to treating the motor symptoms of Parkinson's (Fahn, 2003). Initially, the motor symptoms of Parkinson's disease are dramatically improved by dopaminergic therapy. Over time, however, medications become less effective and are associated with dramatic "on" and "off" medication fluctuations in symptoms. This has led to recent surgical treatments for Parkinson's disease, including the implantation of small stimulating micro-electrodes into specific brain regions within the basal ganglia (i.e., internal segment of the globus pallidus, subthalamic nucleus). The conceptual idea behind deep brain stimulation and other surgical treatments for Parkinson's disease is to change the imbalance of activation and inhibition that results from dopaminergic depletion (Benabid, 2003).

Although the motor symptoms of Parkinson's disease are the primary focus of pharmacotherapy and surgical treatments, various nonmotor symptoms (e.g., cognitive problems, dementia, psychosis, anxiety, insomnia, autonomic dysfunction, and mood disturbances) also occur and can be particularly disturbing and disabling. Common cognitive sequalae include

slowed thinking (bradyphrenia), impaired "set-shifting," reduced working memory, and forgetfulness (Cools, Barker, Sahakian, & Robbins, 2001; Dimitrov, Grafman, Soares, & Clark, 1999; Fahn, 2003; Gauntlett-Gilbert, Roberts, & Brown, 1999; van Spaendonck, Berger, Horstink, Borm, & Cools, 1995). Moreover, about is it estimated that 30-50% of Parkinson's patients eventually develop frank dementia (Jacobs, Stern, & Mayeux, 2000).

Myriad studies have investigated the pattern of motoric and cognitive deficits found in Parkinson's disease. Fewer have delved into the domain of emotional changes that accompany Parkinson's disease, the focus of the current study. In the following section, the literature concerning emotional changes in PD is reviewed.

Emotional Processing in Parkinson's Disease

Emotional processing can be broadly conceptualized as encompassing four domains: mood (subjective emotional experience), perception, expression, and physiology. Research to date suggests that PD patients may exhibit difficulties in at least three of these domains, each of which are considered in turn below.

Mood Disturbance

Depression is a significant problem in Parkinson's disease, with one- third to one- half of all patients suffering from a depression syndrome (Cummings, 1992; Dooneief et al., 1992; McDonald et al., 2003; Slaughter, Slaughter, Nichols, Holmes, & Martens, 2001). In addition to decreasing quality of life, depression and other psychiatric disturbance in Parkinson patients appear to exacerbate motoric symptoms (Cummings, 1992). Accumulating evidence over the years suggests that depression in PD may be secondary to the underlying neuroanatomical degeneration, rather than simply a reaction to psychosocial stress and disability, although the latter may clearly play a role as well. The incidence of depression is correlated with changes in central serotonergic function and neurodegeneration of specific dopaminergic-, serotonergic-,

and noradrenergic- mediated cortical and subcortical pathways (Burn, 2002; German et al., 1992; Mayberg et al., 1990; Remy, Doder, Lees, Turjanski, & Brooks, 2005).

Other common psychiatric disturbances in Parkinson's disease are anxiety and apathy (Fahn, 2003). Apathy refers to diminished emotional reactivity to both positive and negative events, lack of motivation to engage in goal-directed behavior or cognition, and a subjective sense of indifference (Marin, 1991). Approximately 40 to 50% of Parkinson's patients have been described as meeting criteria for apathy, based on assessment through various apathy rating scales (Isella et al., 2002; Kirsch-Darrow, Fernandez, Marsiske, Okun, & Bowers, 2006; Starkstein et al., 1992), with higher levels of apathy in Parkinson's patients relative to equally disabled patients with severe osteoarthritis (Pluck & Brown, 2002). Those patients with high levels of apathy are not more likely to be depressed or anxious than those with the lowest levels of apathy (Kirsch-Darrow et al., 2006; Pluck & Brown, 2002). Like depression, it has been argued that apathy is more likely a direct consequence of disease-related physiological changes than a psychological reaction or adaptation to disability (Brown & Pluck, 2000; Pluck & Brown, 2002).

Emotional Expression

In addition to mood disturbances, patients with Parkinson's disease also have impaired ability to communicate emotion using various nonverbal signals such as facial expression (the "masked facies" of Parkinson's disease) and prosody (Blonder et al., 1989; Borod et al., 1990; Buck & Duffy, 1980; Jacobs et al.; Smith et al., 1996). Diminished facial expressivity occurs relatively early in the disease course and has been found to be unrelated to depression (Katiskitis & Pilowsky, 1991; Smith et al., 1996). Recent studies from our laboratory using sophisticated computer imaging techniques have found that the facial movements in Parkinson's disease are actually smaller in amplitude, slower to initiate, occur less frequently, and correlate with other

motor symptoms of Parkinson's disease such as bradykinesia (Bowers, Miller, Bosch, et al., 2006). Diminished use of nonverbal communication signals by Parkinson patients can create a host of psychosocial problems, ranging from misdiagnosis of depression to the misattribution of negative emotion states by family members and health care providers. These problems will be discussed in greater detail in subsequent sections.

Perception of Emotion

Research literature regarding the perception of emotional information (faces, scenes, prosody) in PD is inconsistent at best. Some investigators have found that individuals with Parkinson's disease are impaired when asked to identify emotional faces, emotional prosody, or emotional scenes (Blonder et al., 1989; Jacobs et al., 1995; Scott, Caird & Williams, 1984; Sprengelmeyer et al., 2003). Others, however, have not documented differences between Parkinson's disease patients and healthy controls (Adolphs, Schul, & Tranel, 1998; Madeley, Ellis, & Mindham, 1995). Some possibilities that may account for these discrepancies are methodological inconsistencies regarding the severity of Parkinson's disease, whether patients are tested on versus off medications, and the extent of co-existing cognitive impairment or mood disturbance.

Recently, a particular interest has emerged with respect to the possibility that Parkinson's patients may have specific difficulties with processing of negatively-valenced emotions such as fear and/or disgust relative to other emotions. Some researchers have found that PD patients appear to be more impaired at recognizing aversive facial expressions (i.e., anger, disgust, fear) than other expressions. For example, Kan, Kawamura, Hasegawa, Mochizuki, & Nakamura (2002) found that PD patients were selectively impaired at recognizing fear and disgust facial expressions. However, not all researchers have found impairments in recognition of emotional facial expressions (Adolphs, et al., 1998; Madeley et al., 1995).

Physiological Reactivity

A fourth domain within the multicomponential framework of emotion processing is physiological reactivity, which can be studied in the laboratory via measuring subjects' physiological reactivity to emotional materials. There are several methods commonly used in the measurement of psychophysiologic reactivity. One method is skin conductance response (SCR) to emotional stimuli. This is accomplished by applying electrodes that essentially measure "palm sweat" on the inside of the hands. In general, the larger the SCR, the greater the physiological arousal the subject has experienced in response to the emotional stimulus. Although measurement of SCR can be useful, it has limitations. First, individuals vary considerably in how their SCR to emotional stimuli habituates over time. Some individuals habituate after a few trials, whereas others do not appear to habituate much at all. Secondly, 15-20% of healthy people are "nonresponders;" that is, they to do not exhibit a discernable difference in SCR to varying types of emotional stimuli (Bradley, 2000; O'Gorman, 1990). Finally, excess motor activity (such as tremor in the hands) can dramatically interfere with skin conductance recordings (Bradley, 2000). For these reasons, SCR data do not always produce consistent results, may not detect subtle between-groups differences in physiological responding, and may not be the most appropriate physiologic measure for patients with a movement disorder.

Another widely used index of emotional reactivity is emotional modulation of the startle eyeblink response (Lang, Bradley, & Cuthbert, 1990; Vrana, Spence, & Lang, 1988). This index takes advantage of the reflexive eyeblink that naturally occurs in response to an abrupt, jarring stimulus. In essence, a priming effect occurs whereby negatively-valenced stimuli augment the size of the eyeblink and positively-valenced stimuli decrease the size of the eyeblink. It is this measure that served as the index of emotional reactivity in the present study and is described in

detail in a later section. However, first the potential mechanisms for the emotional processing deficits just reviewed will be discussed.

Mechanisms of Emotional Changes

There are at least two mechanisms that may affect emotional processing in Parkinson's disease. First, research suggests that PD patients experience changes (decreased neurotransmitter production or reduced binding) to several neurotransmitters involved in emotion. It has been proposed that the emotional changes observed in PD patients may be a consequence of the loss of nigro-striatal dopamine and/or the loss of mesolimbic and mesocortical dopamine, which in turn may affect serotonin and norepinephrine-producing regions of the brain (the dorsal raphe nuclei and the locus coeruleus, respectively). Secondly, evidence of pathological changes to the structural integrity of key limbic structures has been found in the brains of individuals with Parkinson's disease. Both of these mechanisms are discussed in turn below.

Changes to Neurotransmitters Implicated in Emotion

It is thought that some of the emotional changes found in PD may be in part linked to limbic circuitry subserved by the neurotransmitter dopamine. There are three main systems through which dopamine depletion may affect emotional processing in PD by disrupting *modulation* of these systems: the striato-thalamo-cortico loops, the mesolimbic circuit, and the mesocortical circuit. Beginning with the first of these, Alexander, DeLong, & Strick (1986) proposed a network of five parallel striato-thalamo-cortical circuits that allow frontal cortical activity to be modulated by ascending input from the basal ganglia/thalamus through direct and indirect pathways. Two of these circuits involve key limbic areas such as the orbitofrontal cortex (OFC), the anterior cingulate cortex (ACC), and the nucleus accumbens. General schematas of these two circuits are shown in Figure 1-2.

Outside of these striato-thalamo-cortical circuits, the dopamine-mediated mesolimbic pathway is implicated in emotional processing as well. The ventral tegmental area has dopaminergic connections to the ventral striatum (which consists of the nucleus accumbens and olfactory tubercle) of the basal ganglia. Changes in dopaminergic input to the ventral striatum can then affect the associated striato-thalamo-cortical circuits, and thus depletion of dopamine may affect the ability of limbic structures to influence frontal cortical activity. Finally, the mesocortical circuit connects the ventral tegmental area to the cortex, and provides yet another way in which dopamine depletion may affect emotional functioning. Cortical dopamine release modulates the descending cortico-striatal fibers, potentially influencing the activity of the striato-thalamo-cortico circuits (Brown & Pluck, 2000).

With respect to mood changes in PD, Mayberg et al. (1990) found reduced metabolic activity in the inferior-orbitofrontal cortex and caudate of depressed PD patients, with severity of depression having an inverse relationship with orbitofrontal metabolism. This suggests that depression in PD is associated with dysfunction of these areas. Mayberg and colleagues have proposed the following explanation of how serotonin is affected by loss of dopamine: dopaminergic efferents from the ventral tegmental area project to the OFC (mesocortical) which then project to limbic structures such as the dorsal raphe nuclei, where serotonin is produced. In this way, disruption to the meso-cortico-limbic dopamine circuitry may affect the serotonergic cell bodies in the dorsal raphe.

Dysfunction of dopaminergic pathways may potentially disrupt noradrenergic cells in a similar way. In a recent PET study, Remy et al. (2005) used a tracer that binds with strong affinity to epinephrine and dopamine transporters, but with much weaker affinity to serotonin transporters. They found that non-depressed PD patients had significantly higher binding of this

tracer in the locus coeruleus, mediodorsal thalamus, ventral striatum, ACC, and right amygdala. These authors pointed out the locus coeruleus sends noradreneric projections to the ventral striatum. Thus, a loss of dopamine to the ACC/MOFC "limbic loop" may indirectly affect norephinephrine cells in the same way that serotonin is proposed to be affected.

In sum, depletion of dopamine in PD (in both the Alexander loops and the mesolimbic and mesocortical loops) may in turn affect norepinephrine and serotonin through connected circuitry. Changes in the dopaminergic, noradrenergic, and serotonergic systems may then lead to changes in mood and emotional processing.

Limbic System Neuropathology

Recently, several investigators have found evidence of neuropathological changes to limbic structures in Parkinson patients. In a post-mortem study, Harding and colleagues (Harding, Stimson, Henderson, & Halliday, 2002) found a 20% reduction in amygdalar volume of PD patients compared to normal controls, in addition to the presence of Lewy bodies in many subjects' amygdali. Ouchi and colleagues (1999) found a 30-45% reduction of dopamine agonist binding in the amygdali of PD patients, as well as a 48% reduction in dopamine agonist binding in the orbitofrontal cortex, another key limbic region. They speculated this might be due to a loss of pre-synaptic dopamine terminals in these regions. A histological study of brains of deceased PD patients (Braak & Braak, 2000) found cytoskeletal damage to neurons in the amygdala, anterior cingulate cortex, raphe nucleus and locus coeruleus.

Evidence of pathology of the amygdala is particularly relevant to the current study. The amygdala is a small, almond-shaped structure located in the anterior temporal lobe. It has consistently been implicated in the recognition of fearful stimuli and the response to fearful or 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).

The fact that the amygdala has been shown to exhibit neuropathology in PD brings up the issue as to whether Parkinson's patients might have a diminished emotional reactivity to threatening stimuli, or difficulty interpreting expressions of fear in others. Although researchers have investigated the ability of PD patients to recognize fearful faces, no published study to date has examined physiologic reactions to fear-evoking stimuli. However, preliminary work suggests that PD patients may show diminished emotional reactivity specific to threat-inducing materials (Miller, 2004). With regards to the facial recognition literature, Kan et al. (2002) found that PD patients were selectively impaired at recognizing fear and disgust facial expressions; however, neither Adolphs et al. (1998), Madeley et al. (1995), nor Pell and Leonard (2005) found consistent impairments in PD patients' ability to recognize emotional facial expressions. Importantly, these studies involved recognition of *faces* as opposed to viewing *emotion-eliciting pictures*, as will be the case in the current study. In an fMRI experiment using threat-inducing pictures from the International Affective Picture System (which will be used in the current study), Hariri, Mattay, Tessitore, Fera, & Weinberger (2003) found a significant bilateral amygdala BOLD response when healthy subjects were asked to simply match a threatening picture to a picture identical to it. This suggests that amygdala is involved in processing of threat-inducing pictures, although it is unknown whether pathology to its structure would result in deficits in emotional processing and emotional reactivity specifically. Tessitore et al. (2002)

reported that viewing of facial expressions of fear was associated with robust bilateral amygdala response in healthy subjects, but absent in PD patients who had been withdrawn from levodopa. Administration of levodopa partially restored amygdala BOLD response, but not to the degree present in healthy subjects. This raises the possibility that the loss of dopamine characterizing PD may affect processing of emotional materials by neural circuitry that includes the amygdala, and bolsters the argument for the withdrawal of all dopaminergic medications from PD participants in the current study. Recently, Yoshimura, Kawamura, Masaoka, & Homma (2005) reported an absence of event-related potentials from the amygdali of PD patients while viewing fearful faces. Thus, the literature clearly suggests abnormal amygdala responsivity in PD patients during the processing of fear- or threat- inducing stimuli.

Emotional Modulation of the Startle Eyeblink Response

The current study employs emotional modulation of the startle eyeblink response as a means through which to measure emotional reactivity. In order to understand the mechanism of the phenomenon of emotional modulation of the startle eyeblink response, it is first necessary to describe the basic startle reflex and how it is neurally mediated. In mammals, an automatic startle response occurs at the abrupt onset of a stimulus, such as a jarring noise or flash of light. This response is protective for the organism and is characterized by limb and trunk movements of the body, as well as a reflexive eyeblink (Bradley & Vrana, 1993). In humans, the eyeblink has been used to measure the startle reflex response because it is the most reliable, easily recorded, and quickest component of the startle response.

A variety of studies over the past decade have documented that the size of the startle eyeblink is directly modulated by an individual's emotional state. In humans, startle response magnitude (as indexed by reflexive eyeblink) is augmented when an individual is involved in an emotionally aversive task. Conversely, startle responses are attenuated during more pleasant

tasks. This valence modulation of startle is observed across a variety of tasks involving picture viewing, imagining emotional situations, and anticipation of shock (Bradley, 2000; Bradley, Codispoti, Cuthbert, & Lang, 2001; Lang et al., 1990). 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.

The neural circuitry of startle and its modulation has been exquisitely detailed in studies by Davis and colleagues using a rodent model (Davis, 1992; Davis, Gendelman, Tischler, & Gendelman, 1982). In brief, the basic startle circuitry is mediated entirely at the level of brainstem. However, startle responses can be directly modulated (i.e., potentiated or inhibited) by input from the central nucleus of the amygdala via its projection to the brainstem. Electrical stimulation of the amygdala in rats facilitates startle (Rosen & Davis, 1988), while lesions of the amygdala diminish fear-potentiated and shock-sensitized startle responses but leave basic startle intact (Hitchcock & Davis, 1991; Hitchcock, Sananes, & Davis, 1989). Thus, dysfunction of the amygdala does not eliminate the basic startle response *per se*. Rather, it eliminates potentiation of startle reactivity during aversive emotional states. In humans, for example, temporal lobe ablations involving the amygdala are associated with reduced startle modulation during viewing of aversive pictures or while listening to negative sentences (Bowers et al., 2001).

The use of the startle response as an index of emotional reactivity in a Parkinson's sample has several advantages. First, because it does not require a *voluntary* motor response (as measurements of facial expressivity or vocal prosody do), it eliminates the confounding problem that the movements being used as an index of expressivity may be affected by the motor symptoms of PD. Secondly, measurement of physiological reaction does not depend on self-report (as many paper-and-pencil measures of mood and emotion do), and thus the demand

characteristics associated with it are minimal since the eyeblink response is difficult to voluntarily control (Bradley, 2000).

Basic Startle in Parkinson's Disease

Relevant to the present study is the question of whether PD patients might have a basic defect in startle eyeblink reactivity *per se*. Conceivably, Parkinson's patients could have motor abnormalities that reduce or minimize the size of the eyeblink response. This, in turn, would result in reduced startle eyeblink magnitudes in response to negative emotional pictures, giving rise to the impression of diminished emotional reactivity to unpleasant stimuli. However, two studies have reported that while the latency of startle is slightly delayed in PD, the magnitude or size of the basic startle eyeblink response to acoustic stimuli does not differ significantly between PD patients and controls (Kofler et al., 2001; Vidailhet, Rothwell, Thompson, Lees, & Marsden, 1992). Similarly, we recently found no significant difference in startle magnitude between PD patients and age-matched controls tested in our laboratory (Bowers, Miller, Mikos, et al., 2006). Taken together, these findings suggest that Parkinson patients do NOT have a basic defect in basic startle reactivity, as indexed by size of the eyeblink response.

Psychosocial Effects of Emotional Changes in Parkinson's Disease

As described, Parkinson's disease is characterized by overt affective changes including a reduction in facial and vocal expressivity. These changes have the potential to effect the perception and treatment of PD patients by those closest to them, and are the focus of the second aim of the current study. In an investigation directed at testing the observation that PD patients tend to be interpreted as "cold" or "unfeeling," Pentland et al. (1987, 1988) found that when silent video footage of PD patients was shown to health professionals, the patients were rated as being significantly more hostile, anxious, suspicious, unhappy, and bored than controls with heart disease. In a follow-up study, tape recordings of interviews with PD patients and heart

disease controls were presented to naïve listeners and produced similar findings (Pitcairn et al., 1990b). In both these studies there was no measurable difference between the two subject groups with regard to affect or personality measures, and none of the patients were suffering from depression. These authors suggested that the non-verbal behavior of PD patients, characterized by upper body rigidity and a lack of hand movement, contributes greatly to the misattribution of depression. To date, no study has examined the effect of emotional changes on *family members'* perceptions of the PD patient. Thus, the second specific aim of the current study is to obtain spousal ratings of perception of depression symptoms in their relative with PD and compare these to the PD patients' self-report ratings of depression. This will allow for investigation of whether emotional reactivity deficits are associated with greater *misperception* of depression in PD patients by family members.

Preliminary Findings

Bowers, Miller, Mikos, et al. (2006) recently completed a study of emotional modulation of startle in 23 PD patients while on dopaminergic medication and 17 age-matched controls. All participants were presented with 44 pictures from the International Affective Picture System (Lang, Bradley, & Cuthbert, 2001a), with one-third of the pictures being unpleasant in valence, one-third being pleasant, and one-third neutral. Data analysis revealed a significant Emotion Category x Group interaction ($F(1,33)= 4.60$, $p<.05$), with PD patients exhibiting significantly smaller eyeblink magnitudes than controls while viewing unpleasant pictures. In contrast, eyeblink magnitudes during viewing of pleasant pictures were comparable to that of controls. These data suggest that PD patients may have a selective deficit in emotional reactivity to unpleasant stimuli.

To determine whether certain types of unpleasant pictures were more contributory to diminished startle reactivity than others, a *post hoc* exploratory analysis was conducting by

categorizing the unpleasant pictures into "threatening" versus "other" types of unpleasant pictures (Miller, 2004). This *post hoc* division was partially determined by the fact that the stimulus set contained several pictures designed to induce feelings of fear or threat (i.e., a gun pointed at the subject, a dog with fangs open ready to bite), but fewer pictures representative of other negative emotions (i.e., disgust, sadness, etc.). Again, the Emotion Category x Group interaction was significant ($F(1, 28)= 5.31$, $p<.05$), with Parkinson's patients displaying smaller eyeblinks than controls in response to the threat-inducing slides (Figure 1-3). However, this exploratory analysis had several limitations, including the fact that the analyses were *post hoc* in nature and the total number of "threat" pictures was small. Thus, the current study was designed to better control for these limitations. This was done by using a larger number of unpleasant pictures, an *a priori* design, and by specifically comparing threat-inducing pictures to another discrete emotional category of unpleasant stimuli that are similarly high in arousal level: disgust-inducing pictures. This allowed for an examination of whether the deficits previously observed in PD patients were due to aversive stimuli in general, stimuli that are extremely arousing or upsetting, or stimuli that are threatening in nature. Additionally, PD patients underwent an overnight (12-hour) anti-parkinsonian medication wash-out so that presence of symptom-alleviating medication would not confound the interpretation of emotional reactivity results.

Specific Aims

Although much research has pointed to emotional *expressivity* deficits in Parkinson's disease, few studies have examined possible emotional *reactivity* deficits in PD. Preliminary work suggests that Parkinson patients may demonstrate a significantly diminished reactivity to threatening or fear-inducing emotional materials, compared to their healthy counterparts. This may be due to the fact that the amygdala has been known to exhibit pathology in PD, and is a

neural structure that plays a key role in processing and interpreting threat signals in the environment. As such, the present study has the following specific aims:

Specific Aim 1

The first aim tested the hypothesis that Parkinson patients would demonstrate reduced emotional reactivity, as indexed by emotional modulation of startle, to threatening pictures. This aim was based on the view that the amygdala appears to play a specific role in the processing of threat-inducing stimuli coupled with prior findings of amygdala atrophy in Parkinson's disease. Therefore, startle eyeblink magnitudes while viewing threat-inducing pictures were directly compared against eyeblink magnitudes while viewing another category of similarly arousing and unpleasant stimuli (i.e., disgust pictures). It was predicted that PD patients would demonstrate reduced startle potentiation in response to threat-inducing stimuli compared to healthy age-matched controls, whereas they would not differ from controls in eyeblink magnitudes to disgust pictures. This aim examined the possibility of an emotion-specific reactivity deficit in PD.

Specific Aim 2

The second aim was to explore the relationship between emotional reactivity deficits in Parkinson's disease and spousal- and self-report measures of mood. This aim consisted of two key aspects. The first involved determining whether emotional reactivity deficits are correlated with depressive symptomatology. Based on prior work, it was predicted that depression and startle eyeblink magnitudes would not be significantly associated (Bowers, Miller, Mikos, et al., 2006). This prediction was further supported by Allen, Trinder, & Brennan's (1999) study, which found that severe depression affected emotional modulation of startle eyeblink, whereas mild to moderate depression did not. The second aspect involved examination of spousal ratings of perception of depression for both PD patients and controls. A greater discrepancy between self and spousal ratings of depression for PD patients than for controls was predicted. Specifically, it

was predicted that spouses of PD patients would perceive their significant other as being more depressed than they truly are. Ostensibly, this would be due to their misattributing symptoms of PD (e.g., masked facies) to depression. Finally, the relationship between discrepancy in self- versus spousal- depression ratings and emotion-modulated startle eyeblink magnitude was examined to determine whether misattribution of mood state by others is associated with reduced physiological emotional reactivity.

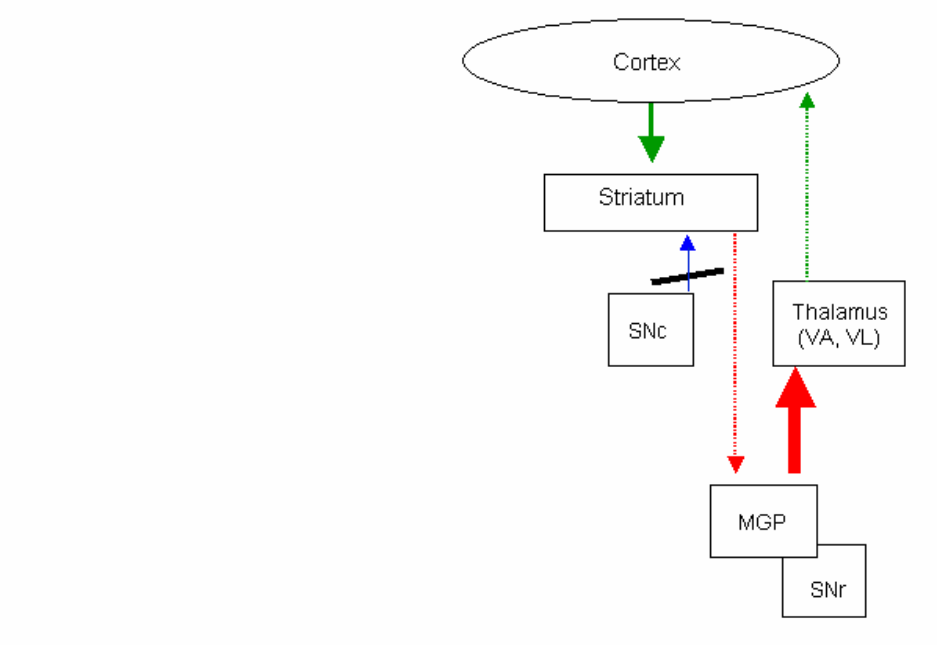

Figure 1-1. Simplified direct loop in the PD patient's dysfunctional motor system. The striatum receives excitatory projections from the cortex, but input from the SNc is impaired due to a reduction of dopamine. This results in the striatum not receiving enough excitatory input to exert its inhibitory influence over the MGP and SNr. The MGP and SNr, free of inhibition from the striatum, provide inhibitory influence over the thalamus, thus preventing the thalamus from providing excitatory output to the cortex. The inhibition of the thalamus and lack of cortical activation results in poverty of movement. (SNc = substantia nigra pars compacta, MGP = medial globus pallidus, SNr = substantia nigra pars reticularis, VA= ventral anterior nucleus, VL= ventral lateral nucleus).

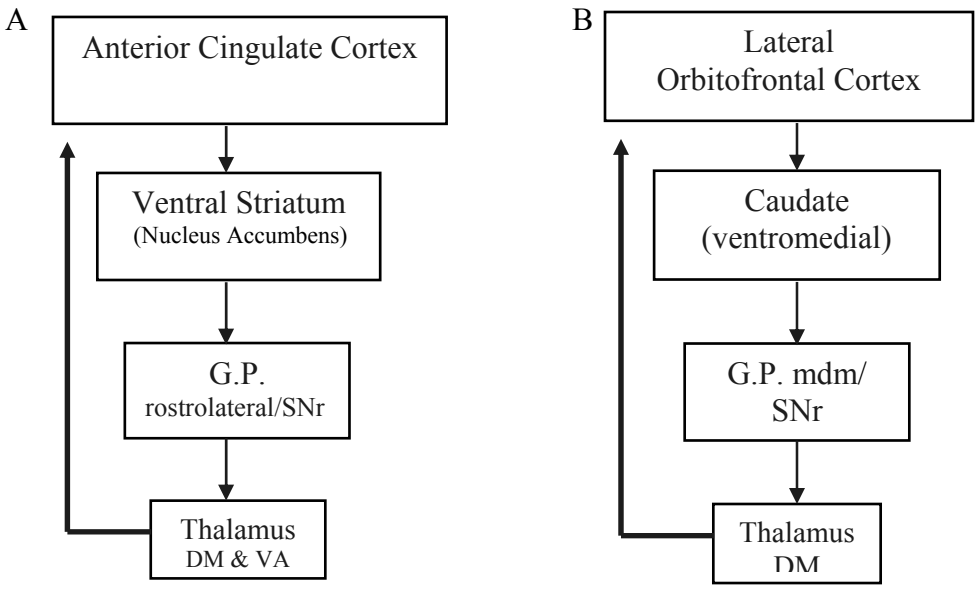

Figure 1-2. Two hypothesized striato-thalamo-cortical loops involved in emotion. A) ACC loop. B) OFC loop. (G.P.= globus pallidus, SNr = substantia nigra pars reticularis, mdm = medial dorsomedial nucleus, DM= dorsomedial nucleus, VA= ventral anterior nucleus).

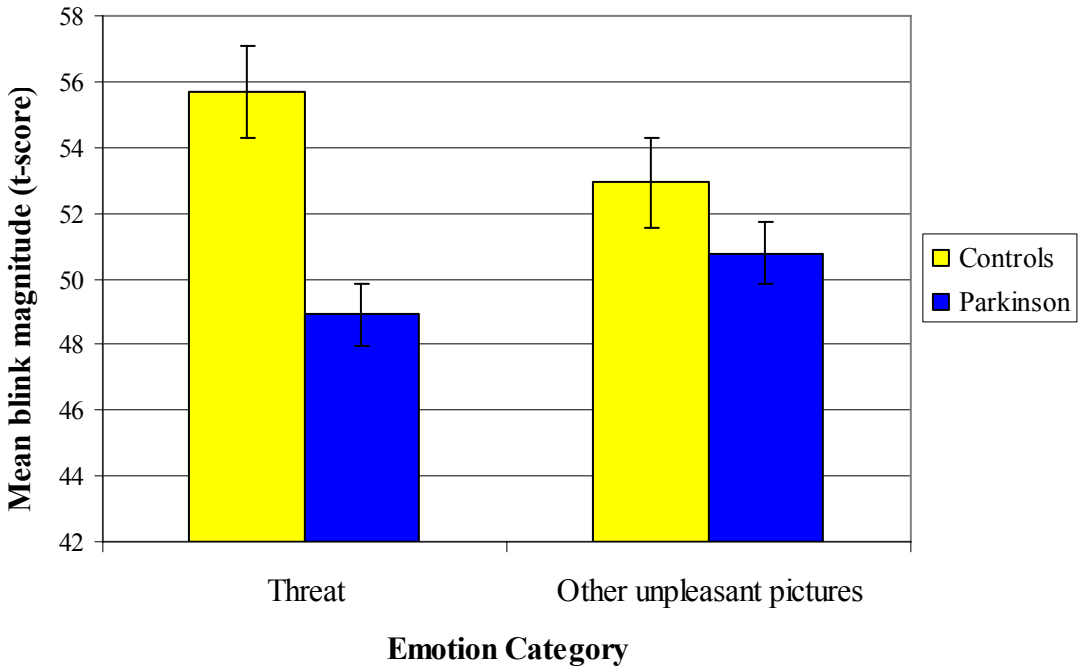

Figure 1-3. Preliminary findings of emotion-modulated startle eyeblink magnitude in PD patients and controls. PD patients showed significantly smaller eyeblink magnitudes in response to "threat" pictures. Error bars indicate standard errors of means.

CHAPTER 2
MATERIALS AND METHODS

Overview

All participants came to the laboratory on two separate occasions, spaced no more than two weeks apart. The first session was a screening session, during which cognitive and mood measures were administered and a medical and psychiatric history was taken. The second session consisted of the psychophysiology experiment and emotion ratings. Additionally, participants with significant others were given the Surrogate BDI-II to take home for their partner to complete.

Participants

All study participants were between 50 and 85 years old. Parkinson patients were recruited from the Movement Disorders Center at the University of Florida as well as from ongoing studies within the Cognitive Neuroscience laboratory. Controls were recruited via flyers posted in the community and in newspapers, as well as from a list of participants from prior experiments who had indicated an interest in being contacted for future studies. Informed consent to participate in this research was obtained following University of Florida IRB guidelines.

Exclusion criteria for the control group included

- History of head injury, neurological disease, learning disability, substance abuse, or major psychiatric disorder
- Current use of psychotropic medications
- Current medical illness that could potentially affect cognition (e.g., cancer or HIV)
- Less than nine years of formal education
- Possible dementia or disturbance in cognition. This was determined by a score greater than 1.5 standard deviations below age- and education-appropriate norms (i.e., below 7th percentile) on either the Dementia Rating Scale, 2nd Edition (DRS-II) total score ***or*** on the delayed recall portions of California Verbal Learning Test, 2nd Edition (CVLT-II) and

Logical Memory II total recall score from the Wechsler Memory Scales, 3rd Edition (WMS-III)

- Significant depression symptomatology. This was determined by a score > 19 (the cut score for moderate depression recommended by Beck, Steer, and Brown, 1996) on the Beck Depression Inventory, 2nd Edition. Previous research has found that individuals with severe levels of depression symptoms have a different pattern of startle modulation relative to healthy controls (Allen et al., 1999; Kaviani et al., 2004). As such, high levels of depression symptoms may affect startle modulation.

All Parkinson patients included in the study were diagnosed by a fellowship-trained movement disorders neurologist. Parkinson patients were subject to the same exclusion criteria as controls. The only exception was that PD patients were not excluded if they were currently taking antidepressants or anti-anxiety medications. Additional exclusion criteria specific to the PD group included

- Evidence of secondary or atypical parkinsonism (as suggested by history of stroke, exposure to toxins or neuroleptics, history of encephalitis, neurological signs or upper motor neuron disease, cerebellar involvement, or lack of response to levodopa therapy)
- Presence of a co-morbid movement disorder
- Unstable medication regime resulting in severe dyskinesias or freezing
- Hoehn and Yahr stage greater than three (due to safety concerns in the off-medication condition
- Prior neurosurgical treatments including deep brain stimulation or lesion surgery.

The initial sample of participants consisted of 28 Parkinson patients and 27 healthy controls. Three PD patients were excluded after the screening session due to BDI-II scores over 19, indicating moderate-to-severe depression. One was excluded for double vision due to its potential influence on perception of affective pictures. One control was excluded due to diagnosis of ADHD and learning disorder revealed during the screening session, and one due to substance abuse and apparent intoxication during the screening session. Another control decided

against participating in the experimental session due to sensitivity to seeing blood. Thus, a total of 24 PD patients and 24 controls completed all study procedures.

Session 1 (Screening): Materials and Procedures

During the screening session, all participants were administered the Dementia Rating Scale, 2nd Edition (DRS-II; Mattis, 2001), the California Verbal Learning Test, 2nd Edition (CVLT-II; Delis, Kramer, Kaplan, & Ober, 2000), the Wechsler Memory Scales, 3rd Edition (WMS-III) Logical Memory I and II subtests (Wechsler, 1997), the Boston Naming Test (BNT; Kaplan, Goodglass, and Weintraub, 2001), and the Beck Depression Inventory, 2nd Edition (BDI-II; Beck, 1996). The PD patients were tested while on their normal dopaminergic medications so that test performance would estimate their typical level of cognitive and motoric functioning. Measures administered are described briefly below. At the completion of Session 1, participants with a spouse were asked to bring home a copy of the Surrogate BDI-II for their spouse to complete and bring or mail back to the laboratory.

The Dementia Rating Scale, 2nd Edition is a screening measure for dementia that yields a total score, as well as subscale scores in the domains of attention, initiation/ perseveration, construction, conceptualization, and memory. The authors report a test-retest reliability of .97 and a split-half reliability of .90 (Jurica, Leitten, & Mattis, 2001). The DRS-II has been validated for use on various neurological populations, including patients with Parkinson's disease. For screening purposes, total raw scores were converted to age- and education-corrected MOANS (Mayo Older American Normative Studies; Lucas et al., 1998) scaled scores, then percentiles, to determine study eligibility.

The California Verbal Learning Test, 2nd Edition is a verbal memory task that involves repeated presentations of a list of sixteen words. The words can be grouped into semantic categories, allowing for assessment of voluntary and cued use of strategy in learning. The test

includes both immediate and delayed recall of list material. Test-retest and split-half reliabilities for subscores of the various CVLT-II indices are generally above .80 (Delis et al., 2000).

The Wechsler Memory Scales, 3rd Edition (WMS-III) Logical Memory I and II subtests assess ability to recall information presented in narrative format. Two stories are read by an examiner, and immediate and delayed recall for story details are tested. The second story is presented twice, allowing for analysis of learning slope. Test-retest and split-half reliabilities for Logical Memory I total recall and Logical Memory II total recall subscores are above .80 (Wechsler, 1997).

The Boston Naming Test, 2nd Edition (BNT) is a confrontation naming task consisting of 60 ink drawings varying in degree of familiarity (Kaplan et al., 2001). The test has been shown to effectively elicit naming impairments in aphasic patients, and has been found to be significantly correlated with tests of verbal knowledge and reading ability (Lezak, Howieson, and Loring, 2004).

The Beck Depression Inventory, 2nd Edition (BDI-II) is a self-report questionnaire presented in multiple choice format designed to measure presence and degree of symptoms of depression. It consists of twenty-one items, each scored from 0 to 3. This widely used measure of depression symptomatology has internal consistency and test-retest reliability both above .9 (Beck, Steer, and Brown, 1996). The BDI-II manual recommends the following cut score guidelines: 0-13 minimal depression, 14-19 mild depression, 20-28 moderate depression, and 29 and above severe depression (Beck et al., 1996).

The Surrogate BDI- II is a measure created explicitly for use in the current study. It is identical to the BDI-II, with the exception that the word "I" was replaced by "my family member." Both control and PD participants with spouses were asked to bring home this

questionnaire to give to their spouse. The questionnaire was accompanied by a letter that included instructions and a description of the purpose of the questionnaire. This letter, as well as the Surrogate BDI-II, was approved by the University of Florida IRB. The Surrogate BDI-II included the following instructions for spouses: "This questionnaire consists of 21 groups of statements. Please read each group of statements carefully and choose the one statement from each group that best describes **your evaluation** of how your family member has been thinking, feeling, or acting over the past **TWO WEEKS**, including today. For some statements, you may not know how s/he has been feeling or thinking; this is okay, just make your best guess. If several statements in the group seem to apply equally well, circle the highest number for the group." The spouse was asked to complete the questionnaire on the same day that their partner participated in the experiment so that self- and surrogate BDI-II scores would refer to the same time period.

Although the concept of a Surrogate BDI-II has not been previously used with a PD population, Logsdon and Teri (1995) have used a surrogate version of the BDI (first edition) in which caregivers reported depressive symptoms in patients with Alzheimer's disease. They reported that coefficient alpha levels were comparable to levels reported for the traditional self-report format and concluded that the BDI was appropriate for surrogate reporting of depression symptoms.

Session 2 (Psychophysiology): Materials and Procedures

Medication Wash-Out for Parkinson Patients

Parkinson participants were asked to withhold all anti-Parkinson medications for at least twelve hours prior to participating in Session 2. This is because it is unknown how anti-Parkinson medications may affect emotional reactivity at the physiological level. Because one aim of the study was to characterize any emotional reactivity deficits found in Parkinson's

disease, it was essential that any medication that might alleviate or mask potential deficits be withheld during study participation. The half-life of the most potent PD medication, levodopa, is about 60-90 minutes, whereas the most commonly used dopamine agonists, pramipexole and ropinirole, have a half-life between 3-8 hours. Thus, participants with PD were asked to withhold all dopa medications overnight for a period of at least 12 hours. Based on these half-lives, it is reasonable to expect that a 12-hour time span would normally place the PD participant in the "off" medication state.

Picture Stimuli

The picture stimuli used in the psychophysiology portion of the study consisted of 48 primary pictures (24 unpleasant (further subdivided into 12 disgust and 12 threat), 12 neutral, and 12 pleasant). Unpleasant pictures were limited to pictures intended to elicit feelings of disgust and threat/fear because other negative emotions, such as anger and sadness, have been shown to be difficult to elicit reliably (Smith et al., 1996) and because disgust and fear are emotions associated with similarly high physiological arousal. Pictures were drawn from the International Affective Picture System (IAPS; Lang et al., 2001a) and were chosen based on the normative study data published for the IAPS (Lang, Bradley, & Cuthbert, 2001b) and a study in which 135 subjects were asked to rate IAPS pictures in terms of the discrete emotions the pictures elicited (Bradley, Codispotti, Sabatinelli, & Lang, 2001). The latter study found that both men and women rated pictures of contamination (e.g., dirty toilets, vomit, feces), accidents/injuries, and mutilated bodies as primarily very high in disgust, whereas pictures of animal attacks and humans attacking one another were rated as primarily very high in fear (Bradley, Codispotti, Sabatinelli, et al., 2001). Thus, these types of pictures were selected when creating the disgust and threat picture sets for the current study.

The disgust pictures were further subdivided into 6 mutilation pictures and 6 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, He, Shapira, Goodman, and Liu, 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. Subdividing the disgust pictures into mutilation and contamination pictures allowed for the examination of potential differences in emotion ratings and startle eyeblink reactivity for these two types of stimuli.

The pleasant and unpleasant (i.e., threat and disgust) pictures were equivalent with regards to average arousal ratings reported by participants in Lang et al.'s (2001b) IAPS normative study. With regards to valence ratings, normative ratings placed the pleasant pictures as equidistant from the "most pleasant" anchor point as the threat and disgust pictures were from the "most unpleasant" anchor point on the 1-9 rating scale. The neutral pictures had an average valence rating that fell in the middle of the rating scale and an average arousal rating that was lower than the pleasant, threat, and disgust pictures. A complete listing of all picture stimuli and their associated normative valence and arousal ratings can be found in Appendix A.

Pictures were presented in a fixed, pseudo-random order, with the constraint that no more than two trials of the same picture type could occur in a row. 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. Administration of the two orders was counterbalanced to minimize potential effects of order of presentation.

Psychophysiology Procedure

Upon arrival at the laboratory, surface Ag-AgCl electrodes filled with an isotonic electrolyte were positioned under the participants' left and right eyes to record electromyographic (EMG) activity from the orbicularis oculi muscle. Electrode placement followed recommendations by Fridlund & Cacioppo (1986). Participants were then asked to sit in a comfortable chair, located in a sound-attenuated and electrically shielded 12'x12' room. Participants were told that throughout of the experiment they could communicate with the experimenter via an intercom. Startle eyeblink responses were elicited by a single 50 ms burst of white noise (95 db, instantaneous rise time) produced by a Colbourn S81-02 module and delivered binaurally through Telephonics (TD-591c) stereo headphones. The session began with twelve probes delivered in the absence of any other stimulus (blank startles). These initial probes were designed to ensure appropriate elicitation of the startle responses, correct any potential problems with electrodes' functioning or placement, and assess group differences in blank startle characteristics.

Picture stimuli for the emotion-modulated startle task were displayed on a 21-inch computer monitor located directly two feet in front of the participant. After the participant was familiarized with the procedure (including use of the emotion rating scale, described below) and practiced using the rating scale with four sample pictures, the experiment commenced. Participants were presented with 64 pictures that included 48 startle probe trails and 16 "filler" trials, during which no startle probe was presented. The 64 pictures were arranged in four blocks of 16 pictures each. Each block consisted of 12 startle probe trials plus 4 interspersed filler trials. This ratio of startle to no-startle probe trials (approximately 75% of trials associated with a startle probe) is consistent with the majority of past studies examining emotional modulation of

the startle reflex using picture stimuli (Bradley, 2000; Cuthbert, Bradley, & Lang, 1996; Vrana et al., 1988).

Each picture was presented on the computer monitor for six seconds. During this time, a white noise burst (startle probe) 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. This was followed by a variable 10-15 second inter-trial interval before the onset on the next trial.

Valence and Arousal Ratings of Pictures

Approximately 8 to 12 seconds following the presentation of each picture, the Self Assessment Manikin (SAM) appeared on the computer screen. SAM is a graphic display depicting a cartoon figure that varies along the dimensions of valence and arousal (Greenwald, Cook, & Lang, 1989; Lang, 1980). 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, each figure has a number associated with it, ranging from 1-9. During the experiment, participants were asked to rate their reactions to each picture immediately after viewing it by referring to the SAM rating scale. Participants spoke their ratings aloud, and ratings were transmitted via intercom to an examiner in another room, who recorded all responses. Participants were given as long as needed to make their ratings.

Post Hoc Ratings of Basic Emotions

Following completion of the entire psychophysiology experiment, electrodes were removed and each participant was reshown the 48 primary picture stimuli on an Apple iBook laptop and 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. 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 threat pictures, "happiness" for the pleasant pictures) was produced at both the group and the individual level.

Participants were told that this rating scale was different from the one using during the psychophysiology experiment, and that their ratings with this new scale would not correspond to ratings with the previous scale. The rating scale was depicted visually as a vertical line labeled with the numbers one through nine. The number "1" was accompanied by the text "I did not feel any of this emotion at all," the number "5" was accompanied by the text "I moderately felt this emotion," and the number "9" was accompanied by the text "I strongly felt this emotion." Participants advanced through the pictures by pressing a touchpad, and were instructed to move through the pictures at their own pace. Participants wrote down their ratings on a separate response sheet.

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 group and sex.

Psychophysiology Data Reduction

The raw EMG signal was amplified (30,000 gain) and frequencies below 90 Hz and above 1000 Hz were filtered using Colbourn bioamplifiers. The raw signal was then rectified and integrated using a Colbourn Contour Following Integrator with a nominal time constant of 100

milliseconds. Digital sampling at 1000 Hz began 50 ms before presentation of the acoustic startle probe and continued for 250 ms after startle probe offset. Data from each participant were visually examined, and trials with clear artifacts (e.g., eyeblink movements before probe onset) were rejected. Subsequent 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 the specified latency range were discarded, as were trials with a peak amplitude more than 3 standard deviations above or below each participant's mean magnitude for a given picture category. In order to minimize the effects of inter-subject variability in overall magnitude, raw scores were converted into T-scores (mean of 50, standard deviation of 10) for each participant's left and right eyes separately. For each picture category, average T-scores were computed using all valid trials from both eyes. When data from one eye were invalid, only the valid eye was used. Only participants who had at least two valid trials for each picture category were retained for subsequent analyses.

Primary Statistical Analyses

Prior to proceeding with the analyses outlined below, data were checked to ensure assumptions of univariate normality were met. Significance tests were two-tailed and set at the conventional levels for significance ($p < .05$). When *post ho*c t-tests were used to further examine significant effects, Bonferroni correction for multiple comparisons was employed. All analyses were performed using SPSS for Windows statistical software (Version 13.0, Lead Technologies, Inc., Chicago, IL). The statistical analyses used to test primary study predictions are described below.

Specific Aim 1

It was predicted that Parkinson patients would demonstrate reduced emotional reactivity, as indexed by emotional modulation of startle, specific to threatening pictures. To test this

prediction, data were subjected to 2 Group (PDs, controls) x 5 *A Priori* Picture Category (pleasant, neutral, threat, disgust- contamination, disgust-mutilation) repeated measures Analysis of Variance (ANOVA) with 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-subjects factor.

Specific Aim 2

A secondary aim of the study was to explore the relationship between emotional reactivity deficits in Parkinson's disease and self-report measures as well as spousal-report measures of mood. First, the relationship between self-reported depression and eyeblink magnitudes was examined through five separate linear regressions (one for each picture category: neutral, pleasant, threat, disgust- contamination, and disgust- mutilation). BDI-II scores, diagnostic group, and the BDI-II x diagnostic group interaction term were entered simultaneously as the independent variables. Eyeblink magnitude T-scores served as the dependent variable. Based on previous literature (Allen et al., 1999; Bowers, Miller, Mikos, et al., 2006), it was predicted that BDI-II scores and eyeblink magnitude would *not* have a significant linear relationship.

Next, Surrogate BDI-II data were analyzed via repeated measures ANOVA with diagnosis as a between-subjects factor and self-report/ Surrogate BDI-II score as a two-level within-subjects factor. Because not all participants had a spouse or partner, the sample size for this analysis consisted of 21 PD patients and their partners and 18 controls and their partners. We were interested in the main effect of self-/ surrogate BDI-II scores to determine whether a discrepancy exists between ratings of depression completed by oneself versus a spouse. Additionally, the diagnosis x self/spousal-report interaction allowed for examination of the prediction that the difference between self- and surrogate BDI-II ratings would be greater for the

PD group compared to the control group (i.e., a significant diagnosis x self/spousal-report interaction). It was predicted that spouses of PD patients would perceive them as being more depressed than they truly are, due to misattribution of PD symptoms (e.g., masked facies) to depression.

The relationship between BDI-II scores, Surrogate BDI-II scores, group membership, and startle eyeblink magnitudes was examined using five separate linear regressions (one per *a priori* picture category) to determine the contribution these variables may have to total eyeblink magnitude variance. BDI-II self-report scores, Surrogate BDI-II scores, diagnostic group, and the BDI-II x Surrogate BDI-II interaction term were simultaneously entered into the regression equation as independent variables. There were no specific *a priori* predictions as to whether Surrogate BDI-II scores or the discrepancy between self- and spousal- report level of depression (represented by the BDI-II x Surrogate BDI-II interaction term) would contribute to eyeblink magnitude variance.

CHAPTER 3
RESULTS

Participant Characteristics

A summary of participant demographic variables and patient disease characteristics are presented in Table 3-1. 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, 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]) and all were on L-DOPA and/or dopamine agonists. Seven of the PD patients were on anti-depressant medications (three on Wellbutrin, two on Lexapro, one on Zoloft, and one on Effexor). One PD patient on Lexapro was also taking on clozepam to aid in sleep at night. None of the controls were on any psychotropic medications.

Cognitive and Mood Measures

Parkinson patients and controls did not significantly differ with respect to Dementia Rating Scale-II, Boston Naming Test, California Verbal Learning Test-II, or Wechsler Memory Scales-II Logical Memory I and II scores. In contrast, Parkinson patients obtained significantly higher scores than controls on the BDI-II ($t[46] = 2.99$, $p = .005$), 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-II 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. Group means and standard deviations for cognitive and mood measures are shown in Table 3-2.

Baseline 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 twelve initial unprimed baseline trials (i.e., no picture presented). Results of independent t-tests showed no group differences in peak eyeblink magnitude (controls = 6.59 mV [SD = 6.78], PD = 5.38 mV [SD = 4.45]; $t[46] = .73$, $p > .1$). Similarly, there was no difference in baseline startle latency (controls = 74.19ms [SD = 8.26], PD = 72.86ms [SD = 11.64]; $t[46] = .45$, $p > .1$). Thus, the PD patients displayed unprimed startle eyeblink responses that were similar in both size and latency to those of the control group.

Emotion-Modulated Startle Eyeblink

Discarded Trials

The total percentage of discarded trials was 9.9%. Discarding was 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) x 2 (Stimulus Presentation Order) x 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) x 2 (Stimulus Presentation Order) x 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 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 the two stimulus presentation orders resulted in different findings. This involved a 2 (Group) x 2 (Stimulus Presentation Order) x 5 (*A Priori* Picture Category: pleasant, neutral, fear, disgust-contamination, disgust- mutilation) repeated measures ANOVA with startle magnitude (T-score) as the dependent variable. No significant main effect or interactions with stimulus presentation order were found, and thus for the remaining analyses the two orders were combined to increase power.

The role of startle probe onset latency was also examined to determine whether startle magnitude was influenced by the timing of probe presentation. A 3 (Probe Onset Latency: 4200 ms, 5000 ms, 5800 ms) x 3 (Valence: pleasant, neutral, unpleasant) repeated measures ANOVA was conducted for the controls and PD patients separately. For both groups, no significant main effect of startle probe onset latency or interaction with valence was found (all p's > .6). Additionally, a 3 (Latency) x 3 (Valence) x 2 (Group) repeated measures ANOVA revealed no significant interactions (all p's > .1). Thus, the remaining analyses are collapsed across the three different startle probe onset latencies.

Verification of typical pattern of startle modulation

Before examining the primary aim of the study, emotion-modulated startle eyeblink magnitudes were checked to verify that the typical pattern of emotion modulation did in fact occur. Typically, magnitudes for pleasant pictures are smaller compared to neutral pictures, whereas magnitudes for unpleasant pictures are larger. To examine whether this pattern held true for the current study, the threat, disgust- contamination, and disgust- mutilation pictures were collapsed into a general "unpleasant" category. Eyeblink magnitude t-scores were then subjected to 2 (Group) x 3 (Valence: pleasant, neutral, unpleasant) repeated measures ANOVA. Results

revealed a significant main effect of valence ($F[2,92] = 9.37$, $p < .001$, $\eta^2_p = .17$). No other effects were significant. Bonferroni-corrected *post hoc* comparisons indicated that the pleasant pictures were associated with significantly smaller eyeblink magnitudes than both neutral and unpleasant pictures ($p < .05$). The comparison between unpleasant pictures and neutral pictures was not statistically significant; however, mean eyeblink magnitudes were larger for unpleasant pictures than neutral pictures. These results indicate that the typical pattern of emotional modulation was observed for both controls as well as PD patients. Mean eyeblink magnitudes by group and valence are shown in Figure 3-1.

Primary analysis

To examine the hypothesis that PD patients would should display decreased startle eyeblink magnitude to threat pictures, a 2 (Group) x 5 (*A Priori* Picture Category: pleasant, neutral, threat, disgust- contamination, disgust- mutilation) repeated measures ANOVA was conducted. This yielded a significant main effect of *A Priori* Picture Category ($F[4,184] = 9.18$, $p < .001$, $\eta^2_p = .17$) and a Group x *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 threat pictures, which were associated with significantly larger startle magnitudes (collapsing across both groups) than those for the neutral, pleasant, disgust- contamination, and disgust- mutilation pictures (all p's $< .02$). No other comparisons were significant. When results were examined for controls and PD patients separately, controls showed significantly larger eyeblink magnitudes to threat pictures compared to neutral and pleasant pictures (p's $< .05$). Additionally, eyeblink magnitudes to mutilation pictures magnitudes 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 eyeblink magnitudes for threat pictures compared to neutral, pleasant, and mutilation pictures (p's < .05).

The Group x *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 disgust- mutilation pictures was significant (F[1, 46] = 6.66, p < .02), η^2_p = .13), with controls showing significantly larger startle eyeblink magnitudes than PD patients (means: PD = 48.34 [SD = 3.91], controls = 51.09 [SD = 3.47]). Thus, the prediction that eyeblink magnitudes in response to threat pictures would be reduced in PD patients compared to controls was not supported; instead, it was the disgust-mutilation pictures that resulted in attenuated startle eyeblink magnitude in the PD group. Mean eyeblink magnitudes for each group for pleasant, neutral, threat, disgust- contamination, and disgust-mutilation pictures are shown in Figure 3-2.

Habituation Pattern

To follow-up on the finding of decreased startle eyeblink magnitude in the PD group in response to the disgust- mutilation pictures, each group's eyeblink magnitudes to mutilation pictures was examined on a trial-by-trial basis. The purpose of this analysis was to determine if group differences in eyeblink magnitudes can be accounted for by differential patterns of habituation to the mutilation stimuli. For example, one possibility is that controls and PD patients initially showed similar eyeblink magnitudes to the pictures, but PD patients habituated more quickly. To examine this possibility, a 2 (Group) x 7 (Trial Number) repeated measures ANOVA was conducted for the mutilation pictures. Overall, both groups showed habituation of startle eyeblink magnitude over time (F[11, 506] = 4.55, p < .001), η^2_p = .09), as is typically found with this paradigm. However, the Group x Trial Number interaction was nonsignificant (F[11, 506] =

0.88, $p > .5$). This indicates that differences in eyeblink magnitude habituation do not explain the group difference in responsivity to mutilation pictures.

Valence and Arousal Ratings

One explanation for the attenuated startle eyeblink magnitude observed in the PD group in response to the disgust- mutilation pictures may be that these pictures were considered less aversive or less arousing by the patients. Thus, subjective ratings of valence and arousal were analyzed through two separate 2 (Group) x 5 (*A Priori* Picture Category: pleasant, neutral, threat, disgust- contamination, and disgust- mutilation) repeated measures ANOVAs. 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 x Emotion 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 threat pictures (all p's < .001). Looking at just the unpleasant picture categories (threat, disgust- contamination, and disgust- mutilation pictures), the mutilation pictures were rated as significantly more pleasant than the threat 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, threat, disgust- contamination, and disgust- mutilation pictures were perceived as equally arousing by subjects. Table 3-3 shows mean valence and arousal ratings for each emotion category by group.

In summary, PD patients did not rate the mutilation pictures as being less unpleasant or less arousing than controls; thus, these self-report ratings cannot explain the finding of reduced eyeblink magnitude to mutilation pictures in Parkinson group.

Post Hoc Basic Emotion Ratings

An alternate explanation is that mutilation pictures were not effective in evoking a strong disgust reaction in the PD group, or perhaps even a strong negative reaction of any type. Because emotion-modulated startle potentiation is dependent on participants experiencing the pictures as aversive, this could explain the PD patients' diminished eyeblink magnitudes to mutilation pictures. To explore this possibility, the *post hoc* basic emotion ratings made by all participants after the psychophysiology portion of the experiment were examined. As previously described, each participant rated each picture in terms of how happy, disgusted, fearful, and sad he or she felt while viewing the picture. These ratings served as a manipulation check to ensure that the pictures did in fact evoke the emotions they were intended to. Specifically, it was expected that contamination and mutilation pictures would be associated with the highest "disgust" ratings, threatening pictures would be associated with the highest "fear" ratings, and pleasant pictures would be associated with the highest "happiness" ratings.

First, a 2 (Group) x 2 (Stimulus Presentation Order) x 5 (*A Priori* Picture Category) x 4 (*Post hoc* Basic Emotion) repeated measures ANOVA was conducted to confirm that order of stimulus presentation during the *post hoc* rating portion of the experiment did not effect results. The main effect and interactions with presentation order were all non-significant. As such, data from the two presentation orders were combined. Next, a series of four 2 (Group) x 5 (*A Priori* Picture Category: neutral, pleasant, threat, 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 3-4. For the 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 threat, mutilation, and contamination pictures, while threat pictures had significantly higher happiness ratings than mutilation pictures ($p's < .001$).

For disgust ratings, the repeated measures AVOVA 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 x 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 threat, contamination, and mutilation pictures (all p's < .001). The Group x *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 threat 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], controls = 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 threat 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 summary, each a *priori* picture category was effective in evoking the intended emotional reaction. Participants rated pleasant pictures as significantly higher in happiness than all other pictures types, mutilation and contamination pictures as significantly higher in disgust compared to all other picture types, and threat pictures as significantly higher in fear compared to all other picture types. While PD patents rated the threatening pictures as higher in disgust compared to controls, no group differences were found with respect to degree of happiness, disgust, fear, or sadness in response to the mutilation pictures. Overall, the self-report data suggest that group differences in valence, arousal, or basic emotional reactions cannot account for the reduced eyeblink magnitude to mutilation pictures observed in PD patients.

Arousal Level as Measured by Skin Conductance Response

A potential problem with self-report data is that it is possible that participants rated pictures based on how they thought they were *expected* to respond, as opposed to based on how they truly felt. Recently, studies from two different laboratories reported that PD patients rated highly arousing negative pictures as less arousing than controls (Bowers, Miller, Mikos, et al, 2006; Wieser et al., 2006); however, this was not observed in the present study. Thus, it is important to consider the possibility that demand characteristics may have played a role in self-report ratings.

One way to address concerns about the veracity of subjective ratings of arousal level is to examine an objective index of physiological arousal. For this reason, a *post hoc* analysis of skin conductance response (SCR) was conducted. SCR is an index of sympathetic arousal that is

difficult to consciously control. Changes in SCR are relatively independent of valence; thus, an increase in SCR is typically observed in response to any type of highly arousing picture, whether it is positive or negative in valence(Bradley, 2000). In a large study using pictures from the International Affective Picture System, Bradley, Codispoti, Cuthbert, et al. (2001) found that erotica, mutilations, and human and animal attacks were associated with the largest SCR.

With regards to the present study, an examination of SCR to mutilation pictures for controls and PD patients is of particular interest. A finding of reduced SCR to these pictures in the PD patients compared to controls would suggest that the PD group did not find the mutilation pictures as arousing as controls. This, in turn, could account for the reduced eyeblink magnitudes observed in the PD patients in response to this category of pictures, since both valence and arousal play a role in emotion-modulated startle eyeblink response.

Before conducting this key analysis of interest, the general pattern of SCR to pleasant, neutral, and unpleasant pictures was examined. For a full description of the SCR data collection and reduction procedures, please refer to Appendix B. Threat, disgust- contamination, and disgust- mutilation pictures were collapsed into a general "unpleasant" category. SCR data were then subjected to 2 (Group) x 3 (Valence: pleasant, neutral, unpleasant) repeated measures ANOVA. Results revealed no significant effects or interactions, although the main effect of valence approached significance ($F[2,92] = 2.79$, $p = 0.06$, $\eta^2_p = .06$). Group means for each valence category are depicted in Figure 3-3. Although not statistically significant, the pattern of SCR in controls versus PDs was of theoretical interest, and thus t-tests comparing neutral to pleasant pictures as well as neutral to unpleasant pictures were conducted for each group. For the control group, both pleasant and unpleasant pictures resulted in significantly greater SCR compared to neutral pictures (pleasant vs. neutral: $t(23) = 2.63$, $p < .02$; unpleasant vs. neutral:

$t(23) = 2.94$, $p < .01$). In contrast, neither pleasant nor unpleasant pictures differed significantly from neutral pictures for the Parkinson group (p's > .3).

Next, a 2 (Group) x 5 (*A Priori* Picture Category: pleasant, neutral, threat, disgust-contamination, disgust- mutilation) repeated measures ANOVA was conducted so that pictures within the unpleasant pictures subcategory could be examined separately. As would be expected based on the non-significant results of the previous repeated measures ANOVA, no significant effects were found; however, examination of the observed power suggested this analysis was insufficiently powered to investigate differences within this many different picture categories (power = .28). Means and standard deviations for control and PD skin conductance response to each pictures category are shown in Table 3-4.

In sum, the control group displayed a typical pattern of emotion-modulated skin conductance response, with larger SCR to pleasant and unpleasant pictures compared to neutral pictures, whereas PD patients did not show any modulation. The analysis that included the different unpleasant picture subcategories (threat, disgust- contamination, disgust- mutilation) did not reveal any significant group difference, although it was hindered by low power. These results do not support the idea that PD patients found mutilation pictures less arousing than controls; however, they do suggest that PD patients show an absence of emotion-modulated skin conductance response overall.

Re-Examination of Eyeblink Magnitude via Idiographic Analysis

Although previous analyses indicated that *a priori* picture categorizations were consistent with overall *post hoc* basic discrete emotion ratings at the group level (i.e., pictures generally evoked the intended emotion), inter-subject differences in emotional reactions to pictures could potentially influence eyeblink magnitudes at an individual level. As an example, a picture of a man hiking atop a mountain that is designed to be pleasant in valence may actually evoke

feelings of fear for an individual who is scared of heights. Similarly, although pictures of animal attacks were intended to evoke fear, some animal-lovers reported feelings of happiness for these pictures. For this reason, eyeblink magnitude data were reanalyzed via an idiographic approach based on the *post hoc* basic emotion ratings (happy, fear, disgust, and sad) made by each participant.

Individual Categorization of Pictures

For each participant, *post hoc* ratings for each picture were examined and the picture was categorized in terms of the basic emotion with the highest rating (e.g., if a picture of a mutilation had a higher disgust rating compared to happiness, fear, and sadness ratings, the picture would be categorized as eliciting disgust for that participant).

Pictures with ratings less than a "4" (on a 1-9 scale, with 9 indicating highest emotional intensity) on all of the basic emotions were categorized as "neutral," since they were rated as eliciting very little of any emotion. Pictures with similarly high ratings on two contradictory emotions (e.g., happy and disgust or happy and fear) were excluded due to difficulty in appropriately categorizing these pictures.

Initial inspection of ratings revealed that many participants frequently rated aversive pictures (e.g., the *a priori* fear and disgust pictures) as similarly high in disgust and fear. Thus, pictures with less than a 2-point difference in ratings of disgust and fear were categorized as "general aversive" for purposes of idiographic analysis. Initial inspection of ratings also showed that participants rarely rated a picture as higher in "sadness" than any other basic emotion; instead, sadness typically co-occurred with either a high disgust or fear rating, or both. For this reason, sadness was considered to be a "secondary" emotion, at least within the context of the present study, and when a high sadness rating occurred the picture was categorized under the "primary" emotion (disgust, fear, or general aversive) that also received a high rating. Thus,

"sad" was not used as a discrete category within the idiographic analysis of eyeblink magnitude data. The basic emotions examined with respect to eyeblink magnitude were neutral, happy, fear, and disgust, as well as "general aversive."

Emotion-Modulated Startle Eyeblink Magnitude

Next, mean eyeblink T-scores for the neutral, happy, fear, disgust, and general aversive categories were calculated for each participant. These T-scores were then subjected to a 2 (Group) x 5 (*Post hoc* Emotion Category) repeated measures ANOVA. Results yielded a significant main effect of *Post hoc* Emotion Category ($F[4,184] = 4.83$, $p < .001$, $\eta^2_p = .10$). The Group x *Post hoc* Emotion Category interaction was nonsignificant ($F[4,184] = 0.38$, $p > .01$). Bonferroni-corrected pairwise comparisons collapsing across groups indicated that eyeblink magnitudes in response to pictures categorized as "fear" and "general aversive" were significantly larger than for "happy" pictures ($p < .001$ for fear vs. happy; $p < .05$ for general aversive vs. happy). No other pairwise comparisons were significant. Mean eyeblink magnitudes for each group based on *post hoc* basic emotion categorization are shown in Figure 3-5.

In summary, the idiographic analysis based on *post hoc* basic emotion categorization yielded similar results as the *a priori* categorization analysis with respect to the main effect: for both methods of analysis, fear-evoking pictures were associated with a significantly larger startle eyeblink magnitude than happy pictures. This held true for both the PD and control groups. Thus, the prediction that PD patients would show reduced eyeblink magnitude to pictures rated highest in fear was not confirmed. Additionally, the idiographic analysis showed that pictures that were rated as very high in both disgust and fear (the "general aversive" pictures) were also associated with significantly larger startle eyeblink magnitude than happy pictures. In contrast, the idiographic analysis did not yield a significant Group x Emotion Category interaction like the *a priori* categorization analysis.

Influence of Trait Positive and Negative Affectivity and Trait Anxiety on Startle Eyeblink Magnitude

One potential explanation for the observed differences in eyeblink magnitudes to mutilation pictures between PD patients and controls may be that the individuals within the two groups systematically differed on certain personality traits. Recent research suggests that individual personality differences may influence emotion-modulated startle. Specifically, some studies have found that people with extremely low levels of trait anxiety, neuroticism, and negative affect do not demonstrate emotion-modulation of the startle reflex for some categories of affective pictures (Caseras et al., 2006; Corr et al., 1995; Hawk and Kowmas, 2003; Wilson, Kumari, Gray, & Corr, 2000). These findings suggest that certain individuals may not be sensitive to the emotion-modulated startle paradigm.

Although the present study did not include assessment of these personality traits, fifteen of the twenty-four PD patients had recently participated in another study within the laboratory that included self-report measures of state and trait anxiety (State- Trait Anxiety Inventory [STAI]; Spielberger, 1977) as well as trait positive and negative affectivity (Positive and Negative Affect Schedule [PANAS], Watson, Clark, & Tellegen, 1988). Although these data were not available for control participants, the relationship between scores on the negative affect scale of the PANAS and the trait anxiety scale of the STAI and emotion-modulated startle magnitudes were examined to determine whether emotion-modulated startle magnitudes systematically varied as a function of different levels of these traits. For the negative affect scale of the PANAS, scores for the fifteen PD patients who completed the questionnaire ranged from 10 to 28 (maximum score is 50, indicating very high trait negative affectivity). The mean was 14.40 (SD = 5.87), indicating that overall patients were fairly low in negative affect. For the trait anxiety scale of the STAI, scores ranged from 15 to 59 (the maximum possible score is 60, indicating extremely high trait

anxiety), with a mean of 29.47 (SD = 11.04). This mean score is in the average range for trait anxiety. A series of multiple regressions with negative affect score and trait anxiety score simultaneously entered as the independent variable and eyeblink magnitude T-score as the dependent variable produced nonsignificant results for neutral, pleasant, threat, disgust-contamination, and disgust- mutilation pictures (p's > .1). Thus, within the PD group, personality trait differences do not account for a significant portion of the variance in emotion-modulated eyeblink magnitude. The lack of a significant relationship suggests that at the between-groups level, personality differences are unlikely to account for the finding of reduced eyeblink magnitude to mutilation pictures.

Influence of Depression on Eyeblink Magnitude

Next, the relationship between BDI-II scores and eyeblink magnitudes in response to each *a priori* picture category was examined through a series of five separate linear regressions (one for each *a priori* picture category: neutral, pleasant, threat, disgust- contamination, disgust-mutilation). BDI-II scores, diagnostic group, and the BDI-II x diagnostic group interaction term were entered simultaneously as the independent variables, whereas eyeblink magnitude T-scores served as the dependent variable. The BDI-II x diagnostic group interaction term was included in the equation because the two groups differed with respect to mean BDI-II scores. None of the resulting regression models were statistically significant, although the model for disgust-mutilation pictures approached significance (p = .06). Within this model, the regression coefficient for "group" was significant (B = -3.13, SE B = 1.18, β= - 0.40; t[44] = -2.64, p = .01), as would be expected based on the known between-groups difference for eyeblink magnitudes in response to these pictures. Otherwise, none of the regression coefficients for the independent variables entered into the neutral, pleasant, threat, or disgust- contamination models were significant. Thus, the prediction that BDI-II scores and startle eyeblink magnitudes would not

have a significant linear relationship was confirmed. Table 3-5 displays the unstandardized and standardized beta- weights, associated standard error, and *t*-tests for significance associated with each independent variable in each model, as well as the overall R^2 and adjusted R^2 for each model.

Influence of Psychotropic Medications

Because anti-depressants and anxiolytics may dampen startle reactivity in healthy individuals (Davis and Gallagher, 1988; Harmer, Reid, Ray, Goodwin, & Cowin, 2006), the influence of psychotropic medications on startle reactivity was examined. To do so, the seven PD patients on antidepressants and/or anxiolytics were removed from the sample and a 2 (Group) x 5 (A priori picture category) repeated measures ANOVA was conducted with the data from this smaller sample. As with the analysis including the full sample, there was a significant main effect of *A Priori* Picture Category ($F[4,156] = 10.77$, $p < .001$, $\eta^2_p = .22$) as well as a significant Group x *A Priori* Picture Category interaction ($F[4,156] = 3.31$, $p < .03$, $\eta^2_p = .08$). Decomposition of the interaction with separate one-way ANOVAs for each *a priori* picture category revealed that the PD group had significantly smaller eyeblink magnitudes in response to mutilation pictures as compared to controls ($F[1,39] = 98.33$, $p < .01$ means: PD = 47.95 [SD = 3.39], controls = 51.10 [SD = 3.47]). Between-groups differences for neutral, pleasant, threat, and contamination pictures were all non-significant. Thus, diminished reactivity to mutilation pictures by PD patients was maintained when excluding patients on psychotropics. This finding suggests that psychotropic medication is not responsible for the effect.

Spousal Perception of Depression: Relationship to Self-Reported Depression and Startle Eyeblink Magnitude

A secondary aim of the current study was to examine the congruency between self- and spousal- report ratings of depression. It was predicted that spouses of PD patients would

perceive them as being more depressed than they truly are, due to misattributing symptoms of PD (such as masked facies) to depression. Thus, it was predicted that there would be a larger discrepancy between self- and surrogate- BDI-II scores for the PD patients as compared to the controls. Additionally, the relationship between discrepancy in self- versus spousal- depression ratings and emotion-modulated startle eyeblink magnitudes was examined. The purpose of this analysis was to determine whether decreased physiological emotional reactivity in PD was associated with misattribution of mood state by spouses.

Surrogate BDI-II: Comparison with Self-Report BDI-II

A 2 (Group) x 2 (Self-report BDI-II, Surrogate BDI-II) repeated measures ANOVA yielded a main effect of Group ($F[1,37] = 4.66$, $p < .05$, $\eta 2p = .11$), reflecting higher mean BDI-II scores in the PD group on both the self-report and surrogate measure. The main effect of self-report BDI-II vs. Surrogate BDI-II was not significant, nor was the Group x Self-/Surrogate BDI-II interaction (p's > .1). The lack of significant Group x Self-/Surrogate BDI-II interaction does not support the prediction that spouses of PD patients would perceive them as being more depressed than they truly are. To further explore the accuracy of spousal ratings of participants' level of depression, Pearson's bivariate correlations between self-report and surrogate- report BDI-II scores were computed. Interestingly, the two measures were significantly correlated for PD patients, whereas they were not for controls. Although the difference between the two correlation coefficients is not statistically significant, these findings further bolster the finding that spouses of PD patients can perceive their partner's mood quite well, contrary to study predictions. Mean self-report BDI-II and Surrogate BDI-II scores, as well as the correlation coefficients between the two, are shown in Table 3-6.

Relationship between Surrogate BDI-II and Startle Eyeblink Magnitude

A series of five multiple regressions (one per *a priori* picture category) with BDI-II self-report scores, Surrogate BDI-II scores, diagnostic group, and BDI-II x Surrogate BDI-II interaction term entered simultaneously as independent variables and eyeblink magnitude T-score as the dependent variable did not yield any significant models. Once again, other than the significant regression coefficient for "group" in the disgust- mutilation model, none of the independent variables contributed a significant amount of variance. This suggests that neither Surrogate BDI-II scores nor degree of discrepancy between self versus surrogate ratings are associated with emotion-modulated startle magnitude. Table 3-7 shows the unstandardized and standardized beta- weights, associated standard error, and t-tests for significance associated with each independent variable in each model, as well as the overall R^2 and adjusted R^2 for each model.

Influence of Disease Severity and Duration on Startle Eyeblink Magnitude

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 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 eyeblink magnitudes (F[2,21]= 47.02, p = .22; R^2 = 0.13, adjusted R^2 = 0.05.)

Table 3-1. 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 (Fahn & Elton, 1987).

[a] Scores obtained in the "on" medication state

Table 3-2. Scores on cognitive and mood measures scores by group

Measure	Parkinson (*N*= 24)	Control (*N*= 24)	Statistical test
Dementia Rating Scale-II raw score (/144)	140.92 (2.83)	141.13 (1.30)	$t(46) = .33$
Dementia Rating Scale-II scaled score	12.04 (2.40)	11.79 (1.56)	$t(46) = .43$
Boston Naming Test raw score (/60)	56.48 (5.43)	57.21 (3.61)	$t(46) = .55$
Boston Naming Test t-score	58.96 (10.50)	59.17 (12.57)	$t(46) = .06$
CVLT-II trials 1-5 total raw score (/80)	45.92 (10.75)	50.38 (6.72)	$t(46) = 1.72$
CVLT-II trials 1-5 total t-score	55.58 (12.10)	60.29 (6.66)	$t(46) = 1.67$
CVLT-II short delay free recall raw score (/16)	10.21 (3.09)	10.71 (2.26)	$t(46) = .64$
CVLT-II short delay free recall z-score	0.65 (1.18)	0.81 (0.93)	$t(46) = .54$
CVLT-II short delay cued recall raw score (/16)	11.63 (2.73)	11.88 (1.96)	$t(46) = .36$
CVLT-II short delay cued recall z-score	0.50 (1.18)	0.62 (0.86)	$t(46) = .42$
CVLT-II long delay free recall raw score (/16)	9.88 (3.31)	11.04 (2.26)	$t(46) = 1.43$
CVLT-II long delay free recall z-score	0.25 (1.15)	0.60 (0.85)	$t(46) = 1.21$
CVLT-II long delay cued recall raw score (/16)	11.38 (2.67)	11.63 (2.18)	$t(46) = .36$
CVLT-II long delay cued recall z-score	0.42 (1.07)	0.54 (0.85)	$t(39) = .45$
WMS-III Logical Memory I raw score (/75)	40.19 (9.01)	41.75 (7.70)	$t(39)^a = .59$
WMS-III Logical Memory I scaled score	11.52 (2.96)	12.35 (2.21)	$t(39)^a = 1.00$
WMS-III Logical Memory II raw score (/50)	25.10 (7.72)	26.80 (6.14)	$t(39)^a = .78$
WMS-III Logical Memory II scaled score	12.57 (3.00)	13.25 (2.65)	$t(39)^a = .77$
Beck Depression Inventory-II	6.17 (4.76)	2.58 (3.45)	$^{**}t(46)= 2.99$

Note: Values are expressed as mean (SD). CVLT-II= California Verbal Learning Test 2nd Edition; WMS-III= Wechsler Memory Scales, 3rd Edition.

[a] Three PD patients and four controls were not administered this test

$^{**}p < .01$

Table 3-3. Valence and arousal ratings of affective pictures by *a priori* picture category and group

	Valence		Arousal	
A Priori Picture Category	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)
Threat	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 3-4. *Post hoc* basic emotion ratings by group

		A priori picture category				
Post hoc emotion	Group	Neutral	Pleasant	Threat	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. Numbers in bold indicate that Parkinson patients rated threat pictures to be significantly higher in disgust compared to controls, $p < .01$. Disgust- contam. = contamination pictures; Disgust-mutil.= mutilation pictures.

Table 3-5. Regression analysis of contributions of group membership and BDI-II scores upon eyeblink magnitudes

A priori picture category	Variable	*B*	SE *B*	*β*	*t*- statistic[a]	Model R^2	Adj. R^2
Neutral	group	0.83	0.74	0.18	1.13	0.03	-0.03
	BDI-II	-0.01	0.09	-0.01	-0.03		
	BDI-II x group	0.02	0.4	0.01	0.04		
Pleasant	group	0.10	0.87	0.02	0.12	0.02	-0.05
	BDI-II	-0.06	0.10	-0.09	-0.53		
	BDI-II x group	0.39	0.47	0.13	0.83		
Threat	group	0.88	0.88	0.16	1.01	0.08	0.02
	BDI-II	0.08	0.10	0.13	0.76		
	BDI-II x group	-0.62	0.47	-0.20	-1.33		
Disgust-contamination	group	0.08	1.20	0.01	0.07	0.04	-0.03
	BDI-II	-0.15	0.14	-0.18	-1.05		
	BDI-II x group	-0.13	0.64	-0.03	-0.21		
Disgust-mutilation	group	-3.13	1.181	-0.40	**-2.64	0.15	0.10
	BDI-II	0.10	0.14	0.12	0.75		
	BDI-II x group	0.40	0.63	0.10	0.62		

[a] For all t-tests, df = 44.
** $p < .01$

Table 3-6. BDI-II self- and surrogate- report scores by group

Group	BDI-II	Surrogate BDI-II	Correlation coefficient	*p* -value
Parkinson	6.00 (5.00)	5.1 (5.34)	$r = 0.41$	0.01
Control	2.67 (3.91)	3.00 (3.24)	$r = 0.55$	0.09

Table 3-7. Regression analysis of contributions of group membership, self-report BDI-II scores, and Surrogate BDI-II scores upon startle eyeblink magnitudes

A priori picture category	Variable	*B*	SE *B*	*β*	*t*- statistic[a]	Model R^2	Adj. R^2
Neutral	group	0.90	0.81	0.20	1.12	0.11	0.01
	BDI-II	0.09	0.10	0.18	0.84		
	Surrogate BDI-II	-0.18	0.12	-0.37	-1.70		
	BDI-II x Surrogate BDI-II	0.17	0.45	0.07	0.37		
Pleasant	group	0.02	0.99	0.00	0.02	0.03	-0.08
	BDI-II	-0.10	0.13	-0.16	-0.75		
	Surrogate BDI-II	0.11	0.55	0.04	0.82		
	BDI-II x Surrogate BDI-II	0.12	0.55	0.04	0.21		
Threat	group	1.00	1.02	0.18	1.00	0.05	-0.06
	BDI-II	0.06	0.13	0.10	0.46		
	Surrogate BDI-II	-0.03	0.14	-0.06	-0.25		
	BDI-II x Surrogate BDI-II	-0.11	0.57	-0.04	-0.19		
Disgust-contamination	group	-0.12	1.34	-0.02	-0.09	0.08	-0.03
	BDI-II	-0.11	0.17	-0.13	-0.62		
	Surrogate BDI-II	0.01	0.18	0.01	0.05		
	BDI-II x Surrogate BDI-II	-0.86	0.75	-0.22	-1.15		
Disgust-mutilation	group	-3.16	1.33	-0.41	* -2.37	0.18	0.08
	BDI-II	0.04	0.17	0.04	0.22		
	Surrogate BDI-II	0.13	0.18	0.16	0.75		
	BDI-II x Surrogate BDI-II	0.30	0.74	0.07	0.40		

[a] For all t-tests, df = 44.

* $p < .05$

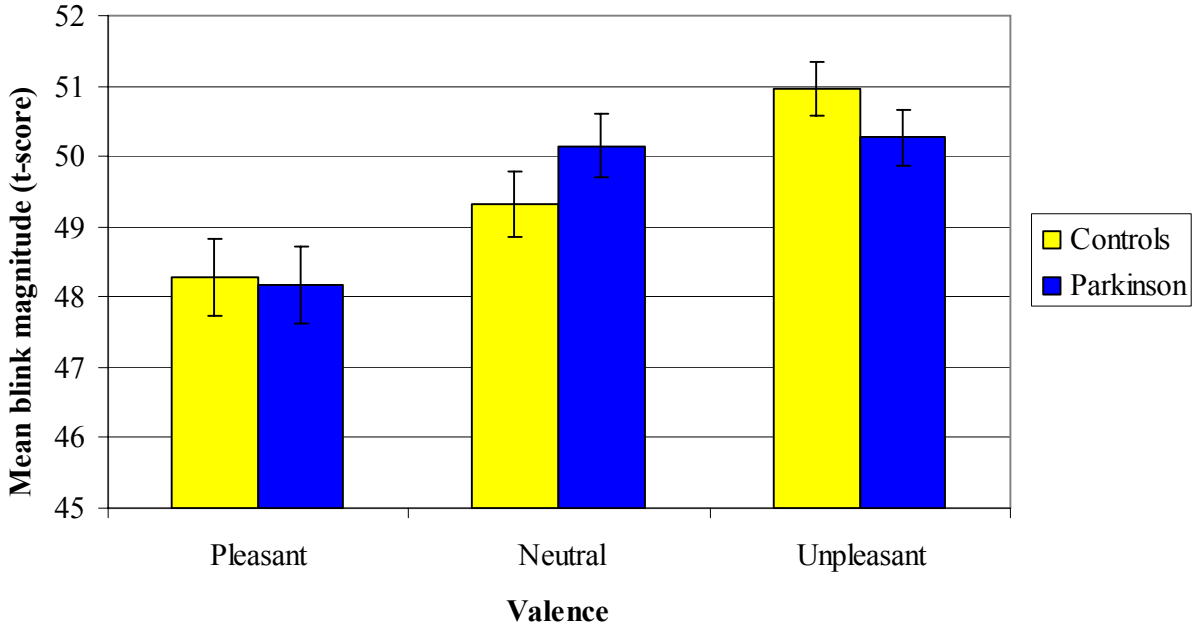

Figure 3-1. Pattern of emotion- modulated startle eyeblink magnitudes by valence and group. A main effect of valence was found, with eyeblink magnitudes to pleasant pictures being significantly smaller than to neutral and unpleasant pictures. Error bars indicate standard errors of means.

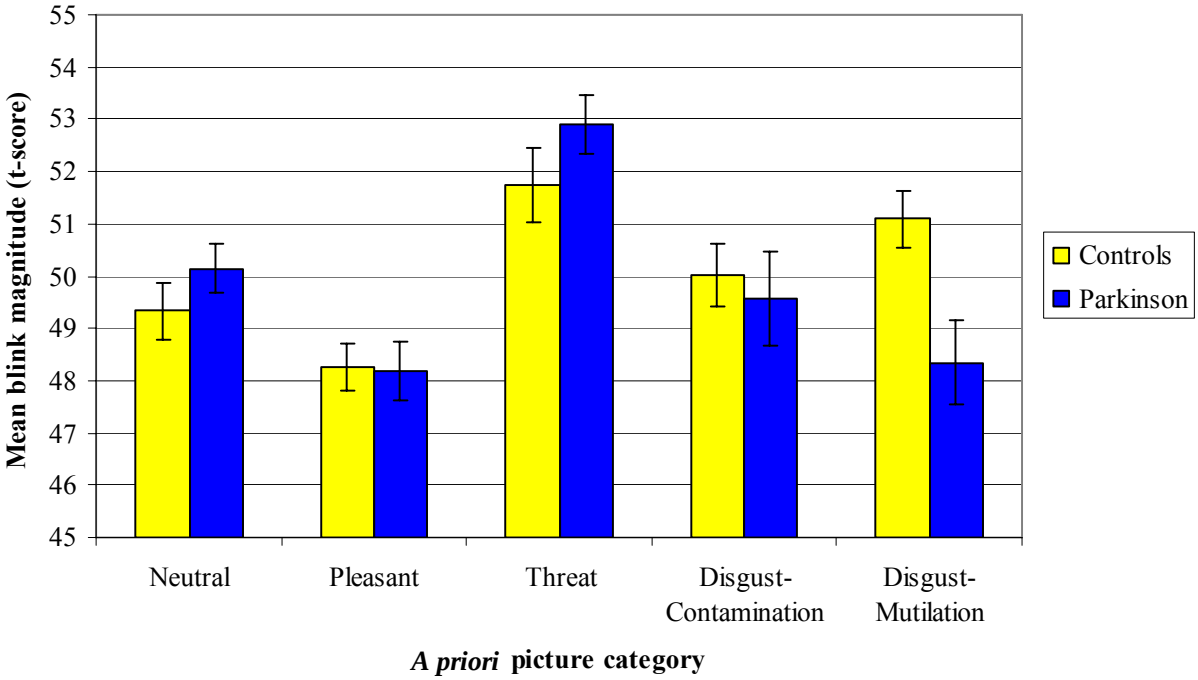

Figure 3-2. Startle eyeblink magnitudes by a priori picture category and group. A main effect of picture category was found, with eyeblink magnitudes to pleasant pictures greater than to threat pictures. The picture category x group interaction was also significant, with eyeblink magnitudes to mutilation pictures smaller for PD patients than controls. Error bars indicate standard errors of means.

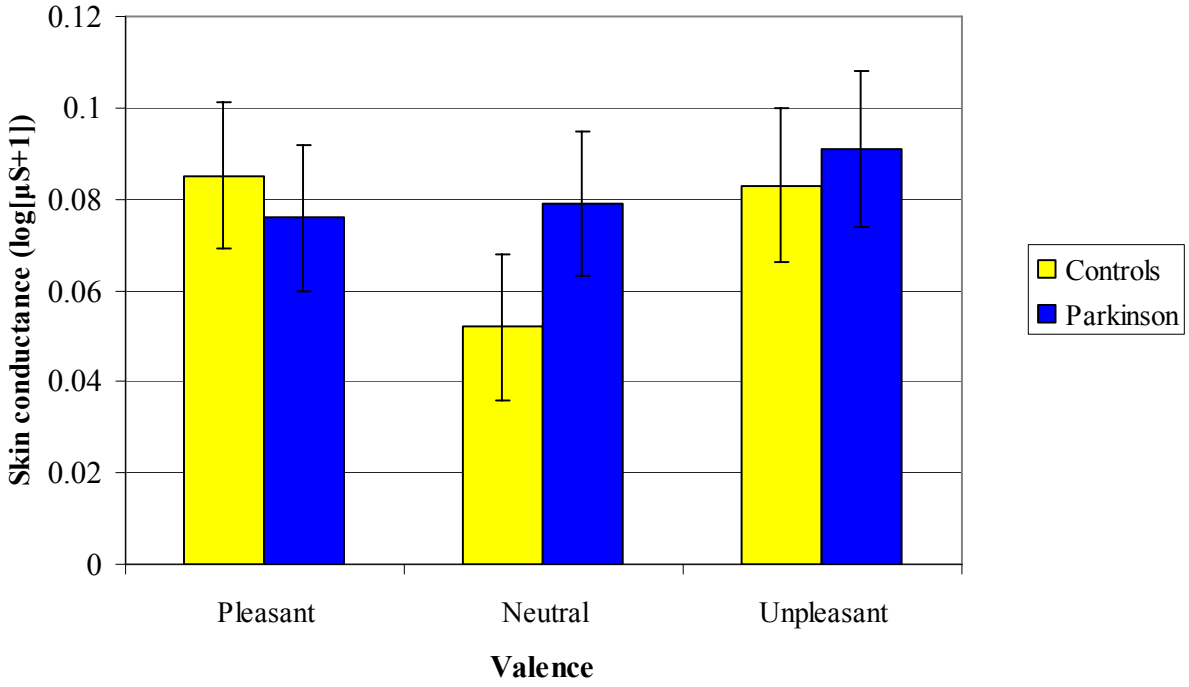

Figure 3-3. Skin conductance response by valence and group. Error bars indicate standard errors of means.

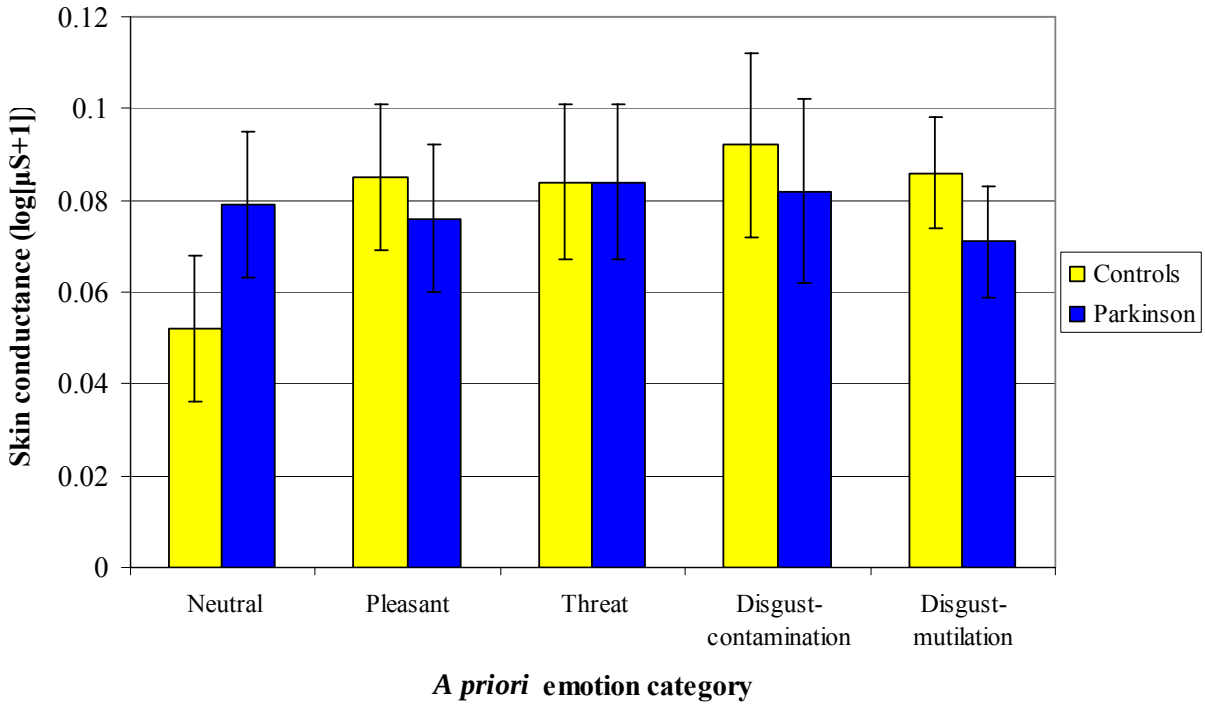

Figure 3-4. Skin conductance response by a priori picture category and group. Error bars indicate standard errors of means.

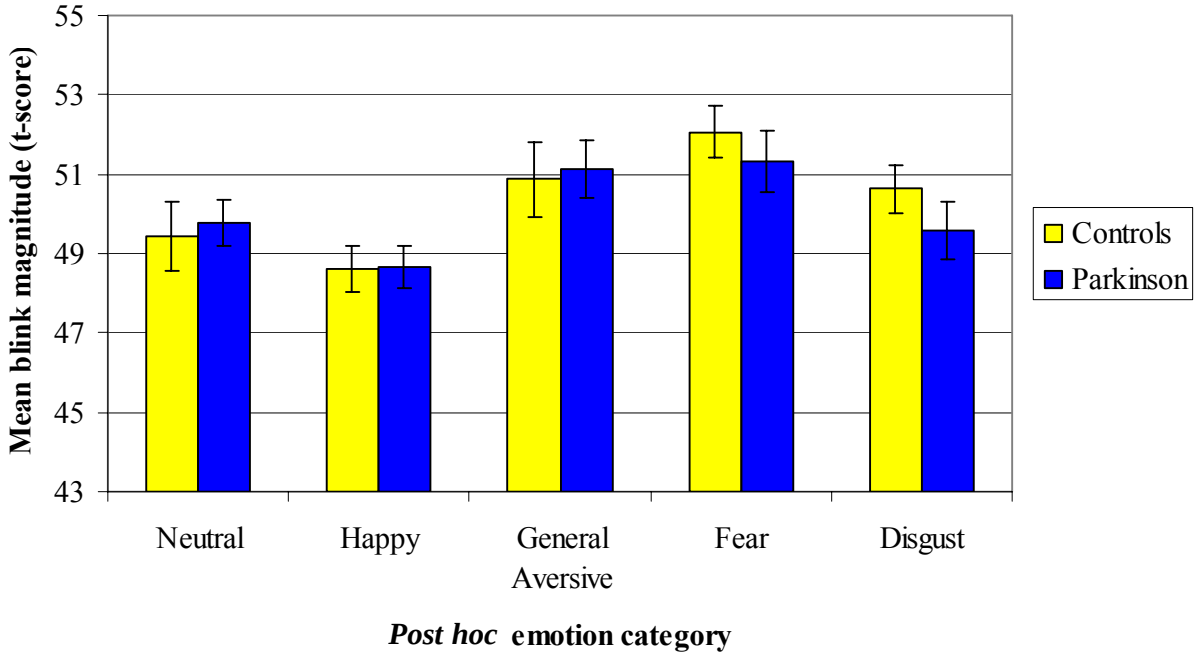

Figure 3-5. Startle eyeblink magnitudes by *post hoc* emotion category and group. A main effect of *post hoc* emotion category was found, with "fear" and "general aversive" pictures associated with larger eyeblink magnitudes than "happy" pictures. Error bars indicate standard errors of means.

CHAPTER 4
DISCUSSION

Summary of Findings

The primary aim of the present study was to test the hypothesis that Parkinson patients would demonstrate reduced emotional reactivity specific to threatening pictures. Emotion-modulated startle eyeblink magnitude was used as an index of emotional reactivity. This hypothesis was based on evidence that the amygdala appears to play a specific role in the processing of threatening stimuli, coupled with prior findings of amygdala atrophy in Parkinson's disease. This hypothesis was not supported. Instead, PD patients demonstrated significantly smaller eyeblink magnitudes to another class of unpleasant pictures, those involving mutilations. Eyeblink magnitudes to pictures of contaminations (e.g., body products, spoiled food) did not differ from controls, suggesting that results were not due to generalized diminished physiological reactivity to disgust-eliciting stimuli. Thus, PD patients showed diminished reactivity, relative to controls, in the context of pictures showing the effects of bodily harm (i.e., mutilations) but not during pictures of threat (i.e., pointed guns, animals ready to attack) or contamination.

A secondary aim of the study was to examine self- and surrogate-report ratings of depression and their association with emotion-modulated startle eyeblink magnitude. First, it was important to determine if any between-groups difference in emotion-modulated startle eyeblink magnitudes could be accounted for by differential levels of depression. Based on findings from prior research (Allen et al., 1999; Bowers, Miller, Mikos et al., 2006), a linear relationship between eyeblink magnitudes and self-reported level of depression was not expected. The data confirmed this prediction, indicating that PD patients' reduced eyeblink magnitudes to mutilation pictures could not be attributed to their higher levels of depression.

Next, we examined the prediction that discrepancy between self- and surrogate-report depression ratings would be larger for PD patients and their spouses compared to controls and their spouses. This prediction was based on the idea that spouses of PD patients would perceive them as being more depressed than they truly are, due to misattributing symptoms of PD (e.g., masked facies) to depression. This prediction was not supported. Instead, spouses of both controls and PD patients were fairly accurate at assessing their loved one's mood. Additionally, no linear relationship between discrepancy in self- versus surrogate-report depression ratings and emotion-modulated startle eyeblink magnitudes was found. Each of these key findings are discussed in turn below.

Aim 1

Emotion-Modulated Startle Eyeblink Magnitude: Comparison of Present and Prior Study Findings

In the present study, Parkinson patients displayed diminished eyeblink magnitudes to disgusting pictures involving mutilations, while eyeblink magnitudes to threatening pictures were comparable to those of the control group. This finding is in contrast to the pilot study, in which startle hyporeactivity in PD patients appeared to be due to decreased magnitudes to threat pictures (human and animal attacks) as compared to other types of unpleasant pictures (Miller, 2004). One possible explanation for the inconsistency between the current study and the pilot study may be that in the pilot study, the number of threat pictures and "other unpleasant' pictures was so small (seven threat pictures; five "other unpleasant" pictures) that the results were not generalizable to pictures outside those specifically used in the study. For example, an extremely large eyeblink in response to just one of the pictures in a category could inflate an individual participant's mean for that category. Another possible explanation for the discrepancy between the two studies may be that order of stimulus presentation was not carefully controlled in the

pilot study. Only one stimulus order was used, and because the study was *post hoc* in nature, the "threat" and "other unpleasant" pictures were not equally distributed with respect to number of stimuli per category in the first half of the stimulus set versus the second half. Thus, any pictures associated with a strong emotional response that were located at the beginning of the set could disproportionately affect the overall mean due to habituation of the startle response over time. Because the present study overcame both of these methodological limitations of the pilot study, it is more likely to be a valid reflection of true between-groups differences.

Reduced Startle Eyeblink Magnitude to Mutilation Pictures in Parkinson's Disease: Proposed Mechanisms

There are several factors that should be considered in interpreting the finding of decreased startle reactivity to mutilation pictures in PD. First, there is the possibility that the basic startle eyeblink itself may be compromised or altered in PD patients due to dysfunction of the brainstem reflex circuitry involved. The existing evidence suggests this is highly unlikely. In both the previous study (Bowers, Miller, Mikos, et al., 2006; Miller, 2004) and in the current study, latency and magnitude of the basic, unprimed startle eyeblink was similar for PD patients and controls. Additionally, other laboratories have investigated startle eyeblink in PD and reported magnitudes comparable to those of controls (Kofler et al., 2001; Vidaihet et al., 1992 [although both found increased latency to peak eyeblink, which was not observed in the present study]).

A second possibility is that compared to controls, PD patients may have tended to close their eyes in response to the mutilation pictures due to the unpleasant content. This concern was addressed via installation of a video camera in the psychophysiology testing chamber. Overall, both controls and PD patients rarely closed their eyes in response to a picture. When a participant closed his/ her eyes (and thus was not viewing the picture when the startle probe was presented),

this trial was discarded from analysis. Thus, the finding of decreased startle eyeblink magnitudes in PD is not accounted for by deliberate closing of the eyes.

Influence of individual personality differences on emotion-modulated startle eyeblink magnitude

Another possibility is that reduced startle eyeblink magnitudes to mutilation pictures in the PD group is not due to disease status *per se*, but due to systematic group differences in personality variables not measured within the current study. The issue of whether individual personality traits influence emotion-modulated startle has been a topic of recent debate in the literature. It arises from the fact that while startle potentiation to fear/threat pictures has been consistently observed, potentiation to disgust pictures is not always found. For example, Balaban & Taussig (1994) reported that even though disgust pictures were rated as equally arousing and more unpleasant than fear-evoking pictures, the fear pictures produced startle potentiation but the disgust pictures did not. In a study using film clips, Kaviani, Gray, Checkley, Kumari, & Wilson (1999) reported that startle magnitudes were potentiated for clips evoking fear, yet were *inhibited* for a film clip of a graphic toe surgery. In contrast, Bradley et al. (2001) and Yartz and Hawk (2002) found no differences in startle magnitudes to pictures of attack, contamination, or mutilations (all three potentiated startle). Examination of control data from the current study only adds to the complexity of interpreting existing findings. Threatening pictures strongly potentiated startle compared to pleasant pictures, mutilation pictures somewhat potentiated startle (although this was not significant after Bonferroni correction), but contamination pictures did not. Thus, the variability in reactions to disgusting pictures across studies begs the question of whether individual differences in personality traits lead to startle potentiation for some participants, but not others.

Studies that have examined the relationship between individual differences in emotion-modulated startle reactivity and personality traits have produced conflicting results. Several studies have approached the issue by dividing subjects into two groups based on self-reported personality traits. One group is characterized by high levels of neuroticism, negative affectivity, and propensity to experience anxiety in the face of punishment or nonreward; the other group is characterized by low levels of these traits. Using this approach, several studies have reported an absent or diminished effect of emotion-modulated startle in response to affective pictures or film clips for the group that has low neuroticism, negative affectivity, and anxiety (Caseras et al., 2006; Corr et al., 1995; Hawk & Kowmas, 2003; Wilson et al., 2000; although for an exception, see Kumari et al., 1996). Thus, it is possible that systematic differences in personality traits between the PD and controls groups could account for the between-groups difference found in eyeblink magnitudes to mutilation pictures. Although the present study did not include administration of measures designed to assess the personality traits described above, fifteen of the PD patients had completed measures of trait anxiety (STAI) and negative affectivity (PANAS) as part of another study. There appeared to be no relationship between scores on either of these personality traits and emotion-modulated startle eyeblink magnitudes. Clearly, this analysis was limited by the fact that these measures were not available for all PD patients or for the control group; additionally, the small number of participants did not allow for subdivision of participants into "extremely high" versus "extremely low" negative affect and anxiety groups. Nonetheless, this limited analysis suggests that startle reactivity did not systematically vary as a function of these personality variables. As such, it is unlikely that any overall group differences in trait anxiety or negative affectivity are responsible for the finding of reduced reactivity to mutilation pictures in the PD group.

Reduced emotional reactivity in PD: Specific to "horror"?

An examination of brain regions putatively involved in the processing of disgust-inducing pictures may aid in interpretation of startle eyeblink data. The fact that the PD group displayed diminished emotional modulation of the startle response to mutilation pictures but not contamination pictures, yet rated both as equally disgusting, suggests that Parkinson patients do *not* display hyporeactivity to disgust-eliciting stimuli in general. This conclusion is further bolstered by the results of the idiographic analysis, in which patients and controls did not differ in startle reactivity to stimuli they rated as disgusting. Instead, the data suggest that there is a distinct difference between emotional processing of mutilation and contamination pictures, even though both types of pictures are typically thought of as eliciting disgust.

Evidence from lesion case reports and fMRI studies suggests that the insula is selectively involved in processing facial expressions of disgust (Adolphs, Tranel, & Damasio, 2002; Calder, Keane, Manes, Antoun, Young, 2000; Murphy, Nimmo-Smith, and Lawrence, 2003) as well as complex visual scenes evoking disgust (Phillips et al., 2000; Shapira et al., 2003; Wright et al., 2004). Not all investigators have replicated these findings; however, with some studies reporting equal activation of the insula in response to both disgust- and fear- eliciting pictorial stimuli (Schienle et al., 2002; Stark et al., 2003). These authors have interpreted their results as an indication of a common affective circuitry shared between different emotions. Recently, Wright et al. (2004) noted that some studies used contamination pictures (such as bodily waste products and spoiled food) along with mutilated bodies to elicit disgust, whereas other studies used only contamination pictures. In a subsequent fMRI study, they examined the neural substrates associated with viewing contamination pictures versus mutilation pictures (a comparison with neutral and fear pictures was also included). These authors found that both contamination and mutilation pictures significantly activated the insula, whereas fear pictures (human attacks) did

not; moreover, strength of activation was correlated with subjective ratings of disgust. They interpreted their findings as evidence that the insula is selectively involved in processing disgust. They also found that mutilation pictures caused greater activation of the occipito-temporal cortex as compared to contamination pictures, which appeared to be due to the greater arousal associated with the mutilation pictures, as well as unique activation of the right superior parietal cortex. This unique area of activation for mutilation pictures indicates that the neural substrates involved in processing mutilation and contamination pictures are slightly different. Wright et al. (2004) posed the question of whether this indicates that mutilation pictures evoke a distinct emotion, such as "horror." Further investigation of whether the "horror" reaction is a specific discrete emotional response and replications of the neural circuitry involved in this emotional response are needed before determining if PD patients have a selective deficit in physiological reactivity to horror.

Subjective ratings of valence, arousal, and basic discrete emotions

Another explanation for the emotion-modulated startle eyeblink finding is that Parkinson patients found mutilation pictures to be 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 (Bowers, Miller, Mikos, et al., 2006). 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, threat, 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. Together, these findings

suggest that the lack of startle potentiation to mutilation pictures is not due to a) decreased subjective unpleasantness or arousal from the standpoint of a dimensional model of emotion; or b) decreased subjective disgust from a discrete categorical approach to emotion. It is, however, possible that participants responded to demand characteristics while making their ratings; that is, they rated pictures based on perceived social norms as opposed to based on how they truly felt. For example, a participant may have rated a picture of a man attacking a woman as very high in arousal because that is the socially expected rating even though he may have not felt highly negatively aroused when viewing the picture. The concern about demand characteristics in the present study is particularly relevant in light of findings from two different laboratories indicating that PD patients rate highly arousing negative pictures as less arousing than controls (Bowers, Miller, Mikos, et al, 2006; Wieser et al., 2006). One fact that may have increased participant's bias to respond in line with social norms is the fact that most participants were aware that the current study is the experimenter's dissertation. Thus, some participants may have been particularly motivated to "perform well" to help a student in school.

Arousal as measured by skin conductance response

To address the concern of potential between-groups differences in arousal level that may not be detected by examining self-report ratings alone, skin conductance response (SCR) was examined. Unlike self-report ratings, SCR is an objective measure, and is known to be a strong index of sympathetic nervous system arousal (Bradley, 2000). In the present study, controls showed a trend towards increased SCR for unpleasant and pleasant pictures compared to neutral pictures. In contrast, PD patients showed similar SCR for all categories of pictures; that is, they did not display emotional modulation of SCR. While results indicated that controls and PD patients did not significantly differ with respect to SCR to mutilation pictures, this analysis was hindered by extremely low power. Thus, overall, arousal as measured objectively by SCR did not

correspond to self-report ratings of arousal in PD patients due to a lack of emotional modulation of SCR. Additionally, prior SCR results from a different sample of PD patients also showed a lack of emotional modulation (Bowers, unpublished data), as well as an overall pattern of hyporeactivity. While this finding does not explain why startle eyeblink magnitude was reduced in response to mutilation pictures specifically (indeed, it only complicates data interpretation), it clearly suggests that physiological reactivity is aberrant in PD, as indexed by two different measures of physiological response to emotional stimuli.

Reduced physiological arousal: A translational deficit?

Recently, Bowers, Miller, Mikos, et al. (2006) suggested that PD patients' lack of apparent physiological arousal in response to pictures that evoke high levels of arousal in controls may be due to faulty communication between the amygdala and prefrontal cortical areas, putatively due to low levels of dopamine in PD. More specifically, these authors hypothesized that PD patients are able to analyze the emotional significance of a stimulus, but the amygdala is unable to "translate" the results of this emotional appraisal into a physiological response. This hypothesis is based on a series of animal studies that elucidate the key role played by dopamine in modulating amygdala activity via cortically- controlled inhibition and disinhibition. The basolateral nucleus of the amygdala is normally under inhibitory control from the prefrontal cortex (PFC) due to GABAergic interneurons (Rosenkranz and Grace, 1999, 2002)[1]. This inhibition is thought to be essential to emotional homeostasis, as selective blocking of the inhibition produces an acute anxiety-like state in rats (Sanders and Shekhar, 1995). In response to sensory-driven stress (e.g., viewing an aversive picture), dopamine is released in the

[1] In the introduction, reference was made to decreased amygdala volume and structural changes to the integrity of the amygdala in Parkinson's disease (Harding, Stimson, Henderson, & Halliday, 2002; Braak & Braak, 2000). The basolateral complex of the amygdala is *not* one of the specific nuclei in which these changes have been reported, thus it is assumed this nucleus is generally intact.

basolateral amygdala (Inglis and Moghaddam, 1999). This results in suppression of the PFC's inhibition of the amygdala (net effect: excitation) via feedforward interneurons (Marowsky, Yanagawa, Obata, and Vogt, 2005). Thus, dopamine acts to modulate PFC-controlled inhibition and disinhibition of the amygdala in response to stress-inducing stimuli.

According to Bowers, Miller, Mikos, et al. (2006), one can speculate that in Parkinson's disease, dopaminergic depletion would reduce the extent to which amygdalar 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, Price, Pitkanen, & Carmichael, 1992) the net effect would potentially be reduced physiologic reactivity, as indexed by measures such as emotion-modulated startle eyeblink or skin conductance response. While this theory explains a general reduction in physiological reactivity to aversive pictures in PD, it does not explain why decreased startle eyeblink magnitudes were found specific to mutilation pictures. One possible explanation, although mere speculation at this point, is that the mutilation pictures are actually more arousing than the threat and contamination pictures, even though participants rated them as equally arousing and SCR in controls was equivalent for all three negative picture categories. In fact, in a recent large-scale study, Bradley, Codispoti, Cuthbert, et al. (2001) found that mutilation and animal attack pictures were associated with significantly higher SCR and arousal ratings than other negative picture contents (such as pictures of vehicular accidents or contamination). Following this line of reasoning, a significant difference in eyeblink magnitude between controls and PD may have been found for the mutilation pictures specifically because they were the only category of aversive pictures sufficiently arousing to detect the muted responsivity in PD. Thus, reduced physiological reactivity in PD may vary as a function of

arousal level in response to a negative stimulus, with those stimuli eliciting higher arousal being sensitive enough to detect between-groups differences. The potential significance of decreased physiological reactivity to arousing aversive stimuli will be addressed later on in this section. First, the findings with regards to Aim 2 are discussed.

Aim 2

Influence of Depression on Emotion-Modulated Startle Eyeblink Magnitude

A secondary aim of the present study was to examine the influence of depression upon startle eyeblink magnitudes. This aim tested the possibility that between-groups differences in startle eyeblink magnitudes may simply be due to differences in level of depression. As predicted, results indicated that depression was not associated with startle reactivity. This finding is consistent with prior reports that mild depression does not affect emotion-modulated startle, although severe depression has been associated with a lack of modulation in response to emotional stimuli (Allen et al., 1999). Furthermore, a reanalysis of the data removing all participants on psychotropic medications produced the same findings as with the full sample. These results indicate that the decreased eyeblink magnitude to mutilation pictures in the PD group was not due to depression or the influence of psychotropic medications.

Accurately Assessing Depression: Comparison of Self- and Surrogate Report Measures

An additional goal was to determine if symptoms of Parkinson's disease (e.g., masked facies, rigidity) lead spouses of PD patients to perceive of them as being more depressed than they truly are. This prediction was not supported; that is, spouses of patients did not misattribute disease symptoms to depression. In fact, spousal ratings and self-ratings of depression were highly correlated, suggesting that in general spouses of PD patients are well-attuned to how their loved ones are feeling. These spousal-report results are in contrast to prior studies using health care professionals and laypersons as raters, which found that negative traits were often

misattributed to PD patients. For example, PD patients were rated as more anxious, unhappy, and hostile than controls (Pentland et al.,1987, 1988; Pitcairn et al., 1990). This present study is the first to examine *family* member perceptions of mood states in Parkinson's patients, and findings suggest that spouses do not tend to make the misattributions that people who do not know the patient very well may make. These findings further suggest that spouses may adequately serve as surrogate reporters of a patient's mood in clinical settings when the patient is unable or unwilling to report his or her own mood.

Alternatively, the significant correlation between self- and spousal- report of depression symptoms in PD could be interpreted as an indication that cognitively intact PD patients do not exhibit self-awareness deficits (often referred to as *agnosagnosia*, or denial of the illness) in the domain of assessing their own mood. This is relevant when examined in the context of literature suggesting that PD patients may show self-awareness deficits with regard to other aspects of their functioning. For example, Leritz, Loftis, Crucian, Friedman, & Bowers (2004) found that PD patients rated themselves as more independent in their ability to carry out activities of daily living compared to their caregiver's ratings. In this study, as with the present study, the caregiver was often a spouse. Similarly, Seltzer, Vasterling, Mathias, & Brennan (2001) found that PD patients rated themselves as less impaired than their caregivers did in terms of their motoric functioning, self-care, and social skills. Leritz et al. (2004) proposed that damage to frontal-subcortical connections in PD (Alexander et al., 1986) may account for these awareness deficits. In contrast, a recent examination of self- and caregiver- ratings of affect found that PD patients were generally aware of their reduced facial expressivity (Mikos et al., 2007). One explanation for this discrepancy between studies may be that self-awareness deficits may be specific to certain domains of the functioning, with awareness of emotional functioning and mood being

spared. A more likely explanation is that global self-awareness deficits may be related to severity of cognitive impairment. Future studies are needed to address whether self- and spousal mood ratings correlate for PD patients that are cognitively impaired.

Relationship between Surrogate-Report Depression and Emotion-modulated Startle Eyeblink Magnitude

Relating these finding back to the primary startle paradigm data, neither spousal-completed Surrogate BDI-II scores or self- vs. spousal- discrepancy were significantly associated with emotion-modulated startle eyeblink magnitude. This is not surprising, given that self- and spousal- BDI-II scores were correlated and self-report BDI-II scores were found to be unrelated to eyeblink magnitude.

Study Limitations

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 Parkinson's disease. The sample had an average of 16 years of education, with many individuals having obtained master's degrees, Ph.D.s, and medical degrees. Although it is unlikely that educational status influences the emotion-modulated startle eyeblink, as it is thought to be a fairly automatic reaction (Bradley, 2000), it is possible that education could potentially influence subjective emotion ratings in terms of participants "overthinking" their responses or trying to anticipate the desired response from the examiner.

The sample also had an imbalance of men and women (14 men and 10 women per group). Although preliminary analyses including "sex" as a dependent 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, Bradley, Codispoti, Sabatinelli, et al. (2001) reported that in general, women tend to respond with greater

defense activation to aversive pictures whereas men show greater reactivity to erotic pictures. This raises the possibility that sex may interact with startle potentiation to the fear, disgust-contamination, or disgust- mutilation pictures. Additionally, studies of women with PD are surprisingly lacking in the existent literature. Most studies include only men, or a significantly greater proportion of men that women. Thus, there is a need for studies that examine the unique effects that Parkinson's disease may have upon women.

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 eyeblink magnitude exists (as was found by Bowers, Miller, Mikos, et al., 2006), but was not detected by the restricted range in the current study. 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.

A major limitation of the spousal Surrogate-BDI-II rating portion of the study was that it was not sufficiently powered to detect any interaction with group membership. The observed power for the Surrogate BDI-II x Group interaction was .14, which is clearly inadequate. Thus, the finding that spouses of controls and PD patients can serve as adequate surrogate reporters of mood should be interpreted with caution. Larger scale studies are needed to confirm that spouses are adequate surrogate reporters, and to examine the potential practical clinical utility of a surrogate mood measure for use with PD patients.

This study included a unique idiographic approach to startle eyeblink data analysis, in which each participant's emotion-modulated startle eyeblink magnitude T-scores were created based on his or her *post hoc* ratings of the amount of happiness, disgust, fear, and sadness felt for each picture. This rating system had several important limitations. First, ratings of all six "primary" discrete emotions (happy, sad, disgusted, fearful, angry, and surprise; Ekman & Friesen, 1976) were not included. This was due to concerns that requiring patients to make such a large number of ratings for each picture would be exhausting or confusing. Thus, anger and surprise were eliminated from the rating process, as these emotions were not directly relevant to study aims. "Sad" was retained so that participants would not be biased to rate all aversive pictures as simply disgusting or fearful. Clearly, ratings of all six primary discrete emotions could more fully capture the subjective experiences of participants. Secondly, the *post hoc* rating scale used for indicating degree of emotion experienced was anchored on one end with a descriptor that was relative, as opposed to absolute. Specifically, the highest rating on the scale had the descriptor "I strongly felt this emotion." In a critique of psychophysical measurement, Bartoshuk, Fast, & Snyder (2005) pointed out that a vague intensity descriptor such as "strongly" can vary in interpretation from person to person, creating invalid comparisons. A more appropriate descriptor for the high end of the rating scale would have been "This emotion was the strongest imaginable," particularly since the low end of the scale was anchored with an absolute descriptor ("I did not feel any of this emotion"). Thirdly, although the pictures chosen to evoke specific emotions were generally effective in doing so, the negatively-valenced pictures often evoked more than one emotion. This finding is hardly unusual; indeed, other investigators (Bradley, Codispoti, Sabatinelli, et al., 2001; Yartz & Hawk, 2002) have also observed that pictorial stimuli tend to produce "blends" of emotions. However, this created difficulty in

categorizing individual stimuli for the idiographic analysis of eyeblink magnitudes. Because the *a priori* fear and disgust- mutilation pictures often were rated as high in disgust and fear, it was necessary to create a "general aversive" emotion category when analyzing startle eyeblink magnitude data from an idiographic approach. The lack of a significant group x *post hoc* emotion category interaction in the idiographic analysis was likely due to the fact that mutilation pictures were subsumed by either the "disgust" or "general aversive" category, effectively masking group differences specific to the mutilation pictures. Additionally, some participants interpreted the meaning of "disgust" in a way not intended. For example, PD patients rated fear pictures (pictures of animal and human attacks) significantly higher in disgust than controls. It appears that in this case they were not referring to disgust as a visceral reaction to grotesque stimuli, but as a moral judgement within the context of a social situation (i.e., "I am disgusted by your behavior"). Although the purpose behind the idiographic approach was to account for individual differences in emotional reactions, the possibility that participants might interpret the emotion labels differently that the experimenter intended was not anticipated. Clearly, individual differences in conceptualization of what makes a stimulus "disgusting" can affect overall results. These issues complicate the interpretation of the present data, but also raise important questions about methodological and conceptual concerns within emotion research in general.

Conceptual and Methodological Issues in Emotion Research

Taken together, the data from the *post hoc* ratings portion of the study suggests that laboratory experiments attempting to parse apart emotional reactions based on a discrete categorical approach to emotions may be overly simplistic. Unfortunately, many studies in the emotion literature ask participants to "pick a label" amongst the choices of happy, sad, disgusted, fearful, angry, or surprised in response to presentation of a facial expression, prosodic utterance, or to describe how they are feeling. This approach is understandable and often necessary to

make sense of the data; however, in reality discrete emotions do not occur in relative isolation of all other emotions. Similarly, it may not be easy for participants to decompose their emotional reactions into their basic discrete components. For example, asking participants how happy, sad, disgusted, fearful, angry, or surprised they feel may not fully capture the complex emotional reactions associated with certain interpersonal situations, such as seeing a gun held to a person's head or a disfigured body. As stated by Lang, (1995) "emotional judgments, physiology, and behavior can present a confusing rock pile that resists a simple classification by specific emotional states." Future studies may benefit from a taking a dimensional approach to emotional experiences, as suggested by Lang (1995), in which emotional response to an aversive stimulus is classified by an action tendency to withdraw, and emotional response to an appetitive stimulus is classified by a tendency to approach. Alternatively, future studies may benefit from having participants rate emotions from both discrete emotion and dimensional approaches, as was done in the current study, then examining results from both perspectives. Finally, it may be fruitful to ask participants to describe in their own words their emotional reactions, rather than forcing them to choose from a pre-determined set of responses. Although this poses problems in quantitative data analysis, it more fully captures the complexity of human emotional experience.

This same problem also exists with respect to classifying emotion-eliciting stimuli when designing an experiment. As previously mentioned, Wright et al. (2004) pointed out that some authors have used only contamination pictures to induce a disgust response, whereas others used both contamination and mutilation pictures. While this raises the issue of how to best classify mutilation pictures (should they be with the other "disgust" pictures, or in their own category?), further exploration of this issue is unlikely to advance scientific knowledge of emotional reactions. A more productive direction to take might be an examination of the *emotional*

significance behind mutilation pictures. At a more primitive level, a mutilated body represents destruction of the victim's bodily integrity, and thus could be perceived by the viewer as a threat to his or her own bodily integrity. From this perspective, it is clear that mutilations evoke a strong aversive emotional reaction, regardless of whether the semantic label of 'disgust' or 'horror' is given to the reaction.

Significance of the Study

The present research has two important findings that add to the literature on emotion in Parkinson's disease. First, PD patients showed diminished reactivity, as measured by emotion-modulated startle eyeblink, to pictures of mutilations. While it might be tempting to propose that this finding represents a "mutilation-specific" emotional processing deficit in PD, such an interpretation is overly simplistic and does not take into consideration other relevant factors. For example, one possibility is that the diminished reactivity in PD is not emotion- or content-specific, but represents a deficit in physiological responsivity to highly arousing negative stimuli in general. Mutilation pictures are highly arousing stimuli because they represent a threat to bodily integrity; as such, it may be that the mutilation pictures were the only category of pictures sufficiently arousing to detect a between-groups difference in physiological reactivity. In the present study, we attempted to further investigate the issue of reduced physiological arousal in PD by examining skin conductance response (SCR) data; however, this was problematic because PD patients did not appear to exhibit emotional modulation of SCR for any of the picture categories. The interpretation of skin conductance data is further complicated by the fact that autonomic nervous system dysfunction is often found in patients with PD as a result of cell loss and Lewy bodies within the sympathetic ganglion (for a review, see Chauduri, 2001). Thus, the abnormalities in SCR observed in the present study may be due to general autonomic dysregulation. One possible way to bypass this problem in future studies is to examine other

variables associated with arousal level. For example, an important area for future research is examination of cortisol levels in responses to stress in PD. Because measurement of cortisol levels provides a neuroendocrine marker of reactions to stressful stimuli, this method could approach the problem of decreased reactivity to arousing, aversive stimuli from a new angle. Although the literature on cortisol levels in PD is sparse, one study found that PD patients showed overall elevations in plasma cortisol levels, yet a "flattening" of cortisol variations typically observed throughout the day (Hartmann, Veldhuis, Deuschle, Standhardt, & Heuser, 1997). Interesting, this pattern of flattened amplitude variations in cortisol has been found in depressed patients (Deuschle et al., 1997; Halbreich, Asnis, Shindldecker, Zumoff, & Nathan, 1985; Linkowski et al., 1985). Clearly, future research is needed to explore cortisol levels in PD and their potential association with depression in this patient population.

The second important finding from the present study is that a strong convergence emerged between spousal and PD patient ratings of the patient's mood. Although the evidence is limited by inadequate statistical power, the issue of surrogate mood reporting is particularly important in the later stages of Parkinson's, when patients may be unable to report upon their own mood due to dementia or speech deficits. Logsdon & Teri (1995) have already reported that spouses served as valid surrogate reporters of mood for patients with Alzheimer's disease. A similar validation of the Surrogate BDI-II for use with caregivers of PD patients may lead to useful clinical applications. Such a measure could be used with spouses of patients unable to report upon their mood, or unwilling to discuss mood due to embarrassment or concerns about social stigma. Recognizing that spouses can serve as important sources of information concerning a patient's mood may lead to improved detection of depression in Parkinson's disease.

Although studies of emotion have many methodological challenges to overcome, this study represents an attempt at further characterizing changes in emotional reactivity that may occur with Parkinson's disease. Hopefully, future studies will continue to explore these changes not simply in isolation, but from the framework of an integrated model that considers how emotion, cognition, and motor symptoms interact to affect the well-being of the whole person.

APPENDIX A
NORMATIVE VALENCE AND AROUSAL RATINGS FOR PICTURE STIMULI

Table A-1. 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)
		Average	*4.97 (1.16)*	*2.68 (1.83)*
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)
	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)
		Average	*7.41 (1.52)*	*6.22 (2.18)*

Table A-1. Continued

Picture Category	IAPS #	Picture Description	Valence[a]	Arousal[a]
Threat				
	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)
		Average	*2.83 (1.67)*	*6.56 (2.07)*
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)
		Average	*2.36 (1.56)*	*6.20 (2.23)*

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.
[a] From Lang et al., 2001b

APPENDIX B
SKIN CONDUCTANCE RESONSE DATA ACQUISITION AND REDUCTION PROCEDURES

Data Acquisition

The skin on the palm of the hand was prepared by washing the hands with a mild soap, then wiping the skin with rubbing alcohol. Next, surface Ag-AgCl electrodes were filled with an isotonic eylectrolyte gel and positioned on the thenar and hypothenar eminence of left and right palm. During the psychophysiology experiment, SCR was sampled at 20 Hz using two Coulbourn Isolated Skin Conductance couplers in DC mode.

Data Reduction

Each picture trial was scored for the largest change in SCR between 0.9 and 6.0 seconds after picture onset. Raw values for the left and right palms were averaged into a composite score for each trial. A value of "1" was added to these composite scores to eliminate negative values. This new value was then subjected to a log transformation to reduce skewness (Bradley, Codispoti, Cuthbert, et al., 2001). Because SCR habituates rapidly, only responses to the first half of the entire stimulus set (i.e., responses to the first 32 pictures) were included in the data analyses reported. Because SCR habituates rapidly, only responses to the first half of the entire stimulus set (i.e., responses to the first 32 pictures) were included in the data analyses reported.

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BIOGRAPHICAL SKETCH

Kimberly Miller was born in San Jose, California. She received her B.A. in psychology from the University of California at Berkeley. She has been a graduate student in Clinical & Health Psychology student at the University of Florida for the past five years, where she is specializing in neuropsychology. This dissertation is an extension of the ideas originating from her master's thesis, completed in 2004 under the mentorship of Dawn Bowers. Outside of psychology, Kim enjoys reading, running, and spending time at the beach.