Prefrontal Cortical Function during Interpersonal Inclusion and Exclusion in Borderline Personality Disorder

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DEDICATIONS

This work is dedicated to my loving family for their unwavering support and guidance.
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Borderline personality disorder (BPD) is a condition characterized by interpersonal difficulties and hypersensitivity to rejection. Inefficient recruitment of the prefrontal cortex in persons with BPD has been demonstrated in functional neuroimaging studies involving affective processes, although little is know regarding the neurocognitive basis of interpersonal function in BPD. The present investigation used functional near infrared spectroscopy to examine levels of evoked cerebral blood oxygenation in nine females with BPD and 10 healthy female participants during conditions of interpersonal inclusion and exclusion. BPD participants demonstrated relative decreases in hemodynamic oxygenation of right prefrontal cortex during the inclusion condition compared with healthy controls. During the exclusion condition, all participants reported very high levels of rejection; however, no differences in rejection ratings or cerebral blood oxygenation were observed between BPD and healthy groups. Higher levels of oxygenation in right prefrontal cortex during the inclusion condition were associated with gregarious-extraverted personality traits, whereas lower levels of oxygenation in this region were associated with aloof-introverted traits and fears of abandonment. These findings suggest a role of prefrontal systems in negotiating the relationship between characterologic interpersonal function and social difficulties in BPD, possibly related to deficits in reciprocal social interaction, interpersonal engagement, and awareness of self and others.
1. BACKGROUND AND LITERATURE REVIEW

Borderline personality disorder (BPD) is a condition characterized by interpersonal difficulties, affective lability, marked impulsivity, unstable identity, chronic feelings of emptiness, fears of abandonment, dissociation, and self-harm (American Psychiatric Association, 2000). The psychopathology of BPD revolves around four core areas of dysfunction: cognition, affect, interpersonal relationships, and impulsivity. The prevalence of BPD in community studies using criteria from the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (American Psychiatric Association, 1994) has been estimated at 0.5% and 0.7% in American (Samuels et al., 2002) and British (Coid, Yang, Tyrer, Roberts, & Ullrich, 2006) samples, respectively. BPD and other related personality disorders are associated with early institutional care and criminality (Coid et al., 2006), and individuals diagnosed with BPD are among the highest users of inpatient mental health services in the United States (Comtois et al., 2003).

Historically, a number of terms have been used to describe BPD psychopathology, including “ambulatory schizophrenia” (Zilboorg, 1941), “pseudoneurotic schizophrenia” (Hoch & Polatin, 1949), “psychotic character” (Frosch, 1964), and “borderline personality organization” (Kernberg, 1967). Stern (1938) was among the first to describe what he termed the ‘borderline group of neuroses’, which represented a group of patients who were neither frankly psychotic nor neurotic. He characterized these patients as difficult to manage therapeutically, describing a number of personality traits which made treatment of the ‘psychoneuroses’ difficult, including narcissism, ‘psychic bleeding’ in response to painful or traumatic experiences, inordinate
hypersensitivity, rigid personality, deep insecurity or anxiety, and difficulties in reality testing, particularly in personal relationships. The writing of Knight (1953) also provided one of the earliest accounts of the borderline state, which he considered more a representation of uncertainty and indecision on the part of the psychiatrist in determining whether the patient was psychotic or neurotic when evidence for both was present. The term “borderline” was originally used by Millon (1969) to describe schizoid, cycloid, and paranoid conditions, which were primarily characterized by interpersonal dysfunction and transient but reversible psychoses. BPD as a diagnostic entity first appeared in the third edition of the DSM (American Psychiatric Association, 1980), evolving from its predecessor, the cyclothymic personality, which appeared in the second edition of the DSM (American Psychiatric Association, 1968). Validity studies of DSM-IV BPD criteria have provided support for a categorical model, indicating that the prototypical feature of BPD is interpersonal difficulties, whereas frantic efforts to avoid abandonment, stress-related paranoia, and chronic feelings of emptiness are among the least typical features (Blais, Hilsenroth, & Fowler, 1999; Fossati et al., 1999; Johansen, Karterud, Pedersen, Gude, & Falkum, 2004; Sanislow et al., 2002).

From the establishment of a reasonably well validated and reliable set of diagnostic criteria emerged several clinical reports of cognitive disturbance in BPD patients. Kroll (1988), for instance, described the hysterical cognitive style of BPD, characterized by tendencies toward global perceptions, loss of attention to details, confusion and disorganized thinking, diminished ability to process information, and spotty amnesias. Compelling reports of memory (Adler, 1993; Korfine & Hooley, 2000; Paris, 1995; Startup et al., 2001) and perceptual distortions (George & Soloff, 1986;
Sternbach, Judd, Sabo, McGlashan, & Gunderson, 1992; Yee, Korner, McSwiggan, Meares, & Stevenson, 2005) have also been reported in BPD patients. Contrasting with traditional psychodynamic conceptualizations of the borderline state or organization, these findings provided some of the first indications of an “organic” or neurobiological component to BPD psychopathology.

1.1. Neurodevelopmental History

The earliest forays of research examining neurologic abnormalities in BPD sought to identify a clinical history of “minimal brain dysfunction” (i.e., intact intellectual abilities with mild to severe learning and behavioral disability). Minimal brain dysfunction was thought to be associated with dysfunction of the central nervous system and manifested as impairments on tests of perception, conceptualization, language, memory, and motor function (Clements, 1966). Robbins (1966) was the first to report an association between a childhood history suggestive of minimal brain dysfunction and a borderline personality adjustment. The behavioral characteristics of the child who would go on to develop a borderline personality were described by Murray (1979) as highly correspondent with those of the child with minimal brain dysfunction, demonstrating developmental delay and marked difficulties with impulsivity, hyperactivity, learning, and attention. He viewed these impairments as etiologic in problems with early interpersonal relationships for minimal brain dysfunction children, which could in turn spur development of an adult borderline personality structure.

Findings from the child development literature provided the impetus for subsequent retrospective investigations of neurodevelopment in BPD patients. Andrulonis and colleagues (1981) found that the prevalence of disorders with organic
components (e.g., residual minimal brain dysfunction, episodic dyscontrol) was 38% in their sample of 91 BPD patients. Soloff and Millward (1983) found that BPD patients, compared with schizophrenic and depressed groups, reported significantly more complications of pregnancy, childhood temper tantrums, and persistent rocking or head banging. In a single-blind case-control study of 24 patients with BPD, van Reekum and colleagues (1996) discovered that 13 patients had a history of developmental or acquired brain insult. Eight patients were positive for other developmental insults that included attention deficit hyperactivity disorder (ADHD), developmental delay, learning disability, and pregnancy complication.

Given these findings, many authors have speculated that there may be a link between childhood neurobehavioral disorders (e.g., ADHD, epilepsy, and episodic dyscontrol syndromes) and subsequent development of adult BPD. Consistent with this hypothesis, some evidence has revealed a positive history of ADHD and learning disorder in BPD (Fischer, Barkley, Smallish, & Fletcher, 2002), with significant overlap of BPD and ADHD symptoms (Dowson et al., 2004). Whereas the co-occurrence of personality disorder and learning disability varies widely across settings (e.g., hospital versus community), the significant amount of overlap indeed warrants further investigation (for a review, see Alexander & Cooray, 2003).

Based on the evidence reviewed, the developmental histories of BPD patients were often remarkable for learning disorder, developmental delay, and acquired cerebral insult. Further exploration of these histories in prospective research designs may aid in elucidating the causal relationships among personality disorder, learning disorder, and other manifestations of aberrant neurodevelopment.
1.2. Neuropsychological Studies

Studies of neurologic soft signs perhaps provided some of the first indications of disrupted higher-order cognitive systems in BPD patients. Gardner, Lucas, and Cowdry (1987) examined female patients with DSM-III BPD and compared them with healthy control subjects on a soft sign neurological examination that was adapted from Quitkin, Rifkin, and Klein (1976). BPD patients displayed a significantly greater number of soft signs than the healthy comparison group with regard to right-left confusion, awkward gait, adventitious overflow, and difficulty hopping on one foot. A cutoff value of two or more soft signs was indicated as correctly classifying 65% and 32% of the BPD and healthy groups, respectively. Additionally, there were reports of mixed laterality in personality disorder groups (Fleminger, Dalton, & Standage, 1977; Standage, 1983), although these findings remain equivocal (Gardner et al., 1987).

Berg (1983) provided a more systematic method to examine neurocognitive dysfunction in BPD. He did so by considering typical performance patterns of BPD patients on a series of psychological tests. Essentially, he emphasized the use of a complex inference process for diagnosing BPD based on examinations of test-taking behaviors (e.g., affective lability, sudden shifts in attitude toward testing and the examiner, abrupt changes in self-esteem) and performances on projective personality tests within the context of relatively preserved intellectual function. The advent of neuropsychology, however, provided the opportunity for more sophisticated study of cognitive processing in BPD with the backing of enlightened theories of the workings of the human brain.
Cornelius and colleagues (1989) were among the first to report the results of neuropsychological testing in a group of patients diagnosed with BPD. They examined 24 patients who met criteria for BPD based on the Diagnostic Interview for Borderlines (Gunderson & Singer, 1975) on measures of intelligence, memory, language, motor, and visuospatial-constructional functions. BPD patients’ scores were consistently within normal limits and comparable to historical controls. Given these findings, the authors posited that the neuropsychological and neurodevelopmental abnormalities observed in past investigations of BPD were likely uncommon etiologies of the disorder. In contrast, O'Leary, Brouwers, Gardner, and Cowdry (1991) found that whereas BPD outpatients and healthy controls had high average overall intellectual function, BPD patients performed more poorly on tests of speeded processing, verbal intellectual abilities, immediate and delayed memory for stories, visual perception, and immediate and delayed memory for a complex design. Deficits in recalling details of a story and complex figure were interpreted as a possible reflection of a hysterical cognitive style, also described in Kroll (1988) and Millon, Davis, and Millon (1997), as patients may be drawn toward global perceptions with less attention paid to detail.

Burgess (1990) examined patients using a brief neurocognitive screen instrument. The results showed that patients performed worse than controls on tests of delayed memory for objects, rhythm reproduction, serial sevens, and perseverative errors. Burgess theorized that deficits in cognitive information processing in BPD might come about as a result of stress, abuse, or deprivation during vulnerable stages of early development. He asserted that these deficits later hinder the ability of these patients to
proceed appropriately through developmental stages and impede the formation of interpersonal relationships throughout adulthood.

A series of subsequent neuropsychological investigations incorporating a broader range of more sophisticated cognitive measures revealed remarkable findings across several cognitive domains. Swirsky-Sacchetti and colleagues (1993) found that BPD patients were inferior to healthy controls on tests of motor skills, immediate and delayed figural memory, copying of a complex design, and inhibition of a prepotent response. Subsequent investigations confirmed and extended these findings to other cognitive domains (Dinn et al., 2004; Judd & Ruff, 1993; Monarch, Saykin, & Flashman, 2004). More specific attention has been paid to executive functions and other frontal lobe-mediated cognitive skills thought to be specifically affected in BPD. Dowson and colleagues (2004) and Bazanis and coworkers (2002) examined planning abilities and found that BPD patients made more attempts to arrive at a correct solution on tasks which required them to think through complex problems and solve the problems making as few attempts as possible. In these studies, patients also tended to show disinhibited and impulsive responses on a gambling task, as well as slowed and maladaptive responses on a token test which required them to make choices among competing actions, both tests linked to orbitofrontal cortex function. These findings have been replicated with BPD patients (Haaland & Landro, 2007) and with Cluster B personality disorder groups (Ruocco, McCloskey, Lee, & Coccaro, 2008). Stevens, Burkhardt, Hautzinger, Schwarz, and Unckel (2004) implemented a visual backward masking task and a delayed matching to sample task with visual, auditory, and cross-modal conditions. They found that despite slowed basic visual perception and impaired working memory in BPD patients, increased
task demands did not tax working memory abilities of patients more than healthy controls. Posner and colleagues (2002) used a specialized reaction-time task designed to measure three attentional networks: alerting, orienting, and executive attention, with BPD patients demonstrating a specific impairment for an attentional network involved in the executive function of conflict resolution. Lenzenweger, Clarkin, Fertuck, and Kernberg (2004) also obtained results which they interpreted as consistent with an effortful control deficit for information-processing in BPD. Overall, these findings from the neuropsychological literature suggested inefficiencies in discrete higher-order cognitive abilities linked to prefrontal and orbitofrontal cortex function.

Whereas many studies have reported positive neuropsychological findings with BPD patients, equivocal results have also been reported (Kunert, Druecke, Sass, & Herpertz, 2003; Sprock, Rader, Kendall, & Yoder, 2000). Investigations of the contribution of co-occurring depressive symptoms on neuropsychological findings in BPD patients have revealed no differences in cognitive domains between patients with BPD and current major depressive disorder (Fertuck et al., 2006; Theunissen & Walker, 2003). Other neuropsychological investigations which accounted for mood symptoms in BPD patients using statistical controls or in research design concluded that depressive symptoms generally did not have a significant impact on positive findings (e.g., Dinn et al., 2004; Posner et al., 2002; Stevens et al., 2004).

A consolidated quantitative review of the neuropsychological literature of BPD was carried out to address these apparent inconsistencies. Ruocco (2005a) examined 10 studies comprising a combined sample of 488 participants, including 255 BPD and 263 healthy participants. The neuropsychological domains of attention, cognitive flexibility,
learning and memory, planning, speeded processing, and visuospatial abilities were examined. Despite significant heterogeneity of effect sizes in the domains of attention, learning and memory, planning, and visuospatial abilities, BPD participants performed more poorly than healthy controls in all six of the neuropsychological domains examined. The effect sizes (Cohen’s $d$) ranged from small for cognitive flexibility ($d = -0.29$) to large for planning (-1.43). To explore the heterogeneity of effect sizes in the learning and memory domain and examine the possible lateralization of memory deficits, separate analyses were conducted for verbal and visual memory domains. The results revealed a striking difference between visual ($d = -1.59$) and verbal memory ($d = -0.45$), suggesting a more extensive disruption of visual memory systems in BPD. On the whole, the results implicated a wide range of neurocognitive deficits in BPD, particularly those cognitive functions mediated by frontal and temporal systems, with these deficits possibly lateralized more strongly to the right hemisphere. Unfortunately, the small number of studies precluded any exploration of important potential moderator variables, such as patient gender, diagnostic system utilized for BPD diagnosis, co-occurring Axis I and Axis II disorders, inpatient versus outpatient status, and whether patients were in treatment at the time of testing.

A primarily right-hemisphere neuropsychological deficit is reminiscent of the cognitive profile of the non-verbal learning disability. Individuals with this disorder present with social-emotional deficits which often resemble those associated with Asperger's disorder. That is, these children tend to have difficulties in interpreting and expressing affect and in negotiating interpersonal interactions (Volkmar & Klin, 1998). They tend to be insensitive to nonverbal cues, rigid in social conventions, and have
limited insight into self. Certainly, some of these features may characterize social and emotional aspects of persons with BPD, with deficits of the right hemisphere potentially playing a role in negotiating interpersonal interactions.

While neuropsychological studies have provided a wealth of data concerning cognitive difficulties and potential neuroanatomic systems which may be implicated in BPD patients, the findings on the whole possess limited clinical utility. The differences between BPD patients and healthy control participants are not of sufficient magnitude to specify discrete cognitive markers for the disorder (Ruocco, 2005a). Nonetheless, these data do provide valuable and clinically relevant information. For example, clinicians should be aware of cognitive deficits which may hinder successful engagement and participation in psychotherapy (e.g., difficulties recalling events in past therapy sessions, problems with language abilities which might make communication with the therapist more challenging for these patients). With regard to neurobiological mechanisms of BPD psychopathology, neuropsychological testing is indeed limited in its capabilities. Advances in functional brain imaging technologies have afforded researchers the opportunity to investigate the neural bases of cognitive deficits in BPD and identify neuroanatomic systems which may be involved in the modulation of BPD symptoms.

1.3. Structural Neuroimaging Studies

The implementation of magnetic resonance imaging (MRI) methods in biological psychiatry has allowed researchers to obtain spatially precise images of the structure of the brains of individuals diagnosed with BPD. Investigations employing MRI techniques have discovered smaller volumes of the amygdala and hippocampus in BPD patients compared with controls (Driessen et al., 2000; Schmahl, Vermetten, Elzinga, & Douglas
Bremner, 2003; Tebartz van Elst et al., 2003), as well as smaller amygdala gray matter volumes in female BPD patients relative to healthy controls (Rusch et al., 2003). No significant differences in amygdala volumes were observed between BPD and healthy comparison participants in a study by Brambilla and colleagues (2004); however, BPD participants had smaller right and left hippocampal volumes, particularly in patients with a history of childhood abuse, and significantly larger right and left putamen volumes. Analyses of relative gray matter concentration using high resolution T1-weighted structural MRI scans revealed higher concentrations in amygdala and lower in left rostral/subgenual anterior cingulate cortex (Minzenberg, Fan, New, Tang, & Siever, in press).

Emerging evidence suggests that findings of amygdala abnormalities in BPD patients may be impacted by the presence of depressive symptomatology. Indeed, many BPD studies which detected such abnormalities encountered substantial comorbidity of BPD and major depressive disorder, which typically was accounted for using statistical controls. For instance, 70% of BPD patients had a lifetime history of major depressive disorder in the Rusch and colleagues (2003) investigation, and 40% had a current major depressive episode in the Schmahl, Vermetten and colleagues (2003) study. BPD patients in the Driessen and coworkers (2000) study had six times higher levels of depression than control participants. Whereas Zetzsche and colleagues (2006) found no differences between BPD inpatients and healthy control participants in amygdala volumes, BPD patients with a current major depressive episode had larger amygdala volumes bilaterally than non-depressed BPD patients, and left-sided amygdala volume was correlated with depressive symptoms. Certainly, the contributions of current major
depressive episode and history of major depressive disorder on findings of amygdala volumes in BPD are unclear given confounds in most such studies.

Several other studies have reported smaller frontal lobe volumes in BPD patients (Lyoo, Han, & Cho, 1998; van Elst et al., 2001), with only left orbitofrontal volumes correlating significantly with amygdala volumes in one study (Tebartz van Elst et al., 2003). A computed tomography study comparing BPD patients with healthy controls found no differences between groups in frontal lobe volume and ventricle-brain ratio; however, BPD participants had a smaller third ventricle, a finding most likely attributable to narrower third ventricle found in females (Lucas, Gardner, Cowdry, & Pickar, 1989). BPD patients have also been found to have smaller reduced anterior and posterior cingulate gray matter volume, with those who additionally met criteria for schizotypal personality disorder demonstrating a more diffuse pattern of volumetric abnormalities in several regions of the cingulate (Hazlett et al., 2005).

With regard to parietal cortex involvement, 30 female BPD inpatients with a history of severe childhood abuse had smaller right parietal cortex and hippocampus volumes compared to healthy controls (Irle, Lange, & Sachsse, 2005). Reduced symmetry of the parietal cortex in BPD patients was suggested as reflecting a possible neurodevelopmental deficit of the right hemisphere, a supposition consistent with neuropsychological findings (Ruocco, 2005a).

1.4. Functional Neuroimaging Studies

Resting Cerebral Metabolism

A growing literature has emerged examining the functioning of the brain in BPD patients while at rest (i.e., not engaged in a motor, cognitive, or affective task). Positron
emission tomography (PET) is a functional neuroimaging technique which utilizes radiopharmaceutical agents to examine various parameters associated with brain function. Fluorodeoxyglucose (FDG)-PET is a procedure which provides a quantitative measure of the brain’s resting metabolic rate using glucose reuptake rates. de la Fuente and colleagues (1994) conducted the first FDG-PET investigation of BPD patients with the purpose of examining epileptic signs as indicated by temporal lobe hypometabolism. No evidence of metabolic asymmetry in BPD patients was found; however, a follow-up study revealed reduced FDG uptake in prefrontal cortical areas, anterior cingulate, and the thalamic, caudate, and lenticular nuclei (De La Fuente et al., 1997). A number of other FDG-PET studies observed reductions in FDG uptake in impulsive BPD patients relative to healthy controls bilaterally in medial orbitofrontal cortex, including Brodmann areas 9, 10, and 11 (Soloff, Meltzer, Greer, Constantine, & Kelly, 2000; Soloff et al., 2003) and in temporo-parietal cortices in BPD women with histories of severe childhood abuse and dissociative symptoms (Lange, Kracht, Herholz, Sachsse, & Irle, 2005). A study of five BPD patients found reduced uptake of fenfluramine-activated FDG-PET in medial and orbital prefrontal cortex (PFC) bilaterally, left superior temporal gyrus, and right insular cortex (Soloff et al., 2000), whereas greater relative uptake for BPD patients in temporal and parietal regions before and after fenfluramine activation has been found relative to major depressive disorder patients (Oquendo et al., 2005). Additionally, using FDG metabolism as one measure of treatment outcome, New and colleagues (2004) found increased metabolism in orbitofrontal cortex and medial temporal lobe in impulsively aggressive BPD patients after a 12-week trial of fluoxetine.
Contrary to most previous findings, there are additional data which suggest frontal and prefrontal hypermetabolism of FDG at rest in patients with BPD relative to controls (Goyer et al., 1994), as well as hypometabolism in the hippocampus and cuneus (Juengling et al., 2003). Similarly, Goethals and colleagues (2005) tested patients with BPD or antisocial personality disorder with brain perfusion single photon emission computed tomography and found reduced regional cerebral blood flow in right temporal and frontal regions.

Affective Paradigms

Several lines of evidence implicate aberrant functional MRI (fMRI) blood oxygen level dependent signal for BPD patients compared with healthy controls in frontal (e.g., prefrontal, medial, orbitofrontal) and limbic (e.g., amygdala, parahippocampus) regions in association with viewing emotionally aversive and neutral photos or drawings (Herpertz et al., 2001; Schnell, Dietrich, Schnitker, Daumann, & Herpertz, 2007), recalling unresolved or traumatic life events (Beblo et al., 2006; Driessen et al., 2004), listening to scripts describing personal abandonment events (Schmahl et al., 2003), and viewing emotional faces (Donegan et al., 2003; Minzenberg, Fan, New, Tang, & Siever, 2007a). Interestingly, a repeat fMRI study of BPD patients during a 10-week trial of dialectic behavioral therapy revealed neural changes in limbic and other cortical regions while viewing emotional photographs. A novel application of fMRI studied pain perception in BPD, demonstrating higher pain thresholds in BPD patients, with the perception of pain associated with greater activity in dorsolateral PFC and deactivation in perigenual anterior cingulate gyrus and amygdala (Schmahl et al., 2006). Overall, augmented activation of the amygdala in BPD patients was thought to reflect intense and
slowly subsiding emotions in response to emotionally-relevant stimuli, potentially in interaction with frontal and parietal cortices.

*Impulse Control Paradigms*

Behavioral impulsivity was the focus of two functional neuroimaging studies of BPD, both of which employed a go/no-go task as a laboratory measure of behavioral inhibition. Leyton and colleagues (2001) utilized brain measurements of regional alpha-[11C]MTrp trapping with PET to investigate brain activity during commission errors of the go/no-go task, hypothesizing that dysfunctional neurotransmission of serotonin would underlie impulsive behavior in BPD patients. Results indicated lower serotonin synthesis capacity in the medial frontal gyrus, anterior cingulate gyrus, temporal gyrus, and striatum for BPD patients compared with healthy controls. Complementary findings were obtained in a study which also employed the same task, where BPD patients activated different neural networks to successfully inhibit pre-potent responses compared with healthy controls, namely, a more bilateral and extended pattern of activation across the medial, superior, and inferior frontal gyri and extending to the anterior cingulate (Vollm et al., 2004).

In summary, these findings from the structural and functional neuroimaging literature indicate that BPD is characterized primarily by abnormalities in frontal and limbic regions of the brain. These neural systems appear central in modulating BPD psychopathology, particularly the processes of affect regulation and impulse control. These studies also implicate the involvement of subcortical regions in concert with frontal and other cortical regions. On the whole, brain imaging data seem to converge with neuropsychological findings in localizing functional abnormalities within frontal
and temporal (i.e., limbic) brain regions, with neurocognitive inefficiencies possibly lateralized to the right hemisphere.

1.5. Functional Near Infrared Spectroscopy

Jöbsis (1977) was the first to describe the noninvasive infrared monitoring of cerebral oxygen and circulatory parameters for research and clinical purposes. Known as fNIRS, this modality has received increased interest in recent years for the study of psychiatric and neurological disorders (see Irani, Platek, Bunce, Ruocco, & Chute, 2007). The technology capitalizes upon the properties of biological materials which allow near infrared light to pass through at specific spectra. Photons are transmitted through tissue and the nature of their transmission is dependent upon reflectance, which is determined by the angle at which light penetrates the tissue, and scattering and absorption, which are dependent on wavelength. Absorption of photons depends on the molecular properties of the biological materials to be penetrated, with wavelengths in the range of 700-900 nanometers (nm) optimally absorbed in animal tissue (Izzetoglu et al., 2005). This wavelength range is often referred to as the “optical window” for biological tissue, within which there is little scattering of photons. The chromophore (or color) of a molecule is determined by the absorption of specific wavelengths of light. Because deoxygenated (deoxy-Hb) and oxygenated (oxy-Hb) hemoglobin are weakly absorbed at approximately 760 nm and 830 nm (Noriyuki et al., 1997), respectively, the chromophores of these molecules fall within the optical window and result in a differential reflection of wavelengths for deoxy-Hb and oxy-Hb. Given that the pattern of photon scattering for deoxy-Hb and oxy-Hb can be reliably predicted and gauged by photodetectors, levels of back-scattering and absorption provide a measure of cortical activation based on a known
relationship between neuronal and vascular activity, also known as neurovascular coupling. Using the modified Beer-Lambert Law (Villringer & Chance, 1997), a formula which relates absorption of light and concentrations of chromophores in the tissue, and performing fNIRS measurements at two different wavelengths and two time points, the relative changes in deoxy-Hb and oxy-Hb can be measured (Izzetoglu et al., 2005). Changes in the relative concentrations of these molecules are taken as indicators of cortical activation.

The technology, however, has several limitations. First, the version of the fNIRS sensor pad which perhaps provides the greatest level of portability solely allows for coverage of specific regions of the frontal lobes, roughly corresponding to Brodmann areas 9, 10, 45, and 46. This sensor pad is typically placed over the forehead because it is susceptible to artifact caused by interference with hair and other physical properties of the participant. Studies using this sensor probe are usually restricted to measurement of PFC to the exclusion of subcortical structures which may have relevance to various phenomena, such as affective processes which typically invoke areas of the limbic system not accessed by fNIRS. Additionally, the technology is limited by its comparatively poor spatial resolution (on the order of centimeters) and depth of penetration, the latter limiting examinations of hemodynamic activity to the neocortex. Other techniques, such as fMRI and PET, may allow for better characterization of subcortical structures and their potential interactions with anterior regions.

Additionally, concerns have been raised with regard to whether fNIRS can provide accurate measurements of oxygenated hemoglobin (Tomita, 2006). The argument revolves around what has been termed the “flow effect”, which essentially
states that changes in concentrations of oxygenated hemoglobin which accompany neuronal activation have an influence upon blood flow. According to this argument, unless the effect of blood flow can be quantified, then accurate measurements of oxygenated hemoglobin concentration cannot be determined. While the issue is an important one, there is strong evidence supporting the concurrent validity of fNIRS using fMRI (Benaron et al., 2000; Sassaroli, deB Frederick, Tong, Renshaw, & Fantini, 2006), the latter of which relies upon parameters which are not confounded by flow effects. In considering the evidence presented in support of this effect, there is good reason to further investigate the phenomenon using in vivo methods rather than artificial models. Despite these limitations, the ecological capabilities of fNIRS make it a highly attractive neuroimaging technology for neurocognitive investigations of psychological phenomena as they come about in real-world circumstances. fNIRS is also unique in that it obtains measurements of both oxygenated and deoxygenated hemoglobin, perhaps providing a better characterization of the hemodynamic response as it relates to various cognitive and affective processes.

Although functional brain imaging using optical techniques is in its infancy, preliminary evidence indicates that fNIRS provides a measure of hemodynamic activity which is reliable across two temporally separated measurements (Plichta et al., 2006; Ruocco et al., 2007) and converges with the biological signals of fMRI (Steinbrink et al., 2006). The advantage of fNIRS, particularly the device described by Izzetoglu and colleagues (2005), relative to other brain imaging modalities, is its portability, cost-efficiency, and ability to continuously monitor brain activity non-invasively. As applied to neurocognitive studies of BPD, fNIRS allows for real-time measurement of cortical
activity in real-word environments, thus allowing for ecologically valid investigation of brain-behavior relationships in BPD.

1.6. Present Investigation

Several domains of function aside from affect regulation and impulse control remain unexamined in neurocognitive investigations of BPD. Perhaps most relevant to the personality disorders is that of interpersonal function, a realm of inquiry which has traditionally fallen within the scope of personality psychology (Wiggins, 2003), yet which may demonstrate enormous potential for distinguishing among various neuropsychiatric syndromes, such as frontal versus temporal variants of frontotemporal dementia (Rankin, Kramer, Mychack, & Miller, 2003). Interpersonal dysfunction is a defining feature of personality disorder (American Psychiatric Association, 2000) and may be the most prototypical symptom of BPD (Blais et al., 1999; Fossati et al., 1999; Johansen et al., 2004). Neurocognitive technologies to date have precluded meaningful study of interpersonal functioning from a neurocognitive perspective, largely because the available technologies have limited the extent to which interpersonal processes can be studied in an ecologically valid fashion. Most interpersonal paradigms which have been developed typically employ fMRI techniques, in a resting magnet, presenting stimuli on a computer screen and requiring participant responses to be delivered non-verbally through peripheral hardware. Clearly, this type of an environment precludes meaningful study of interpersonal processes in BPD, particularly those which may possess an applied value outside of the artificial laboratory setting.

The present investigation examined the neural correlates of interpersonal processes in BPD using an emerging functional neuroimaging technology which has the
potential to overcome the ecological barriers of traditional neuroimaging modalities. The technology, functional near infrared spectroscopy (fNIRS), permits real-time monitoring of cerebral hemodynamic activity in real-world circumstances (Chute, 2002; Zabel & Chute, 2002). Using this technology, the present study examines evoked cerebral blood oxygenation during conditions of interpersonal inclusion and exclusion. Social exclusion has previously been studied with fMRI using healthy individuals involved in a simulated interpersonal interaction (Eisenberger, Lieberman, & Williams, 2003). Essentially, during conditions of social exclusion, increased cerebral activation was observed in the anterior cingulate, part of the limbic cortex shown to be involved in the experience of physical pain (Schnitzler & Ploner, 2000), and right ventral PFC, a region of cortex thought to play a role in the regulation of emotional experiences (Maier, Amat, Baratta, Paul, & Watkins, 2006).

As reviewed above, BPD patients tend to demonstrate structural and functional deficits in limbic and prefrontal brain regions. In light of the striking interpersonal sensitivity and reactivity of BPD patients in response to abandonment, real or imagined, one might expect that BPD patients would demonstrate aberrant activation patterns during conditions of social exclusion compared to healthy individuals, particularly in the frontal lobes (i.e., right ventral PFC). An examination of differences in functioning of the PFC in BPD compared with controls during social exclusion, and the relation of this hemodynamic activity with personality and symptom measures, may provide important information about the ways in which abnormal neural processes may modulate interpersonal problems in BPD.

2. METHODS
2.1. Participants

Recruitment. BPD participants were recruited from two locations: (1) university counseling center, and (2) introductory psychology classes. Approximately 900 individuals were identified for screening purposes using the McLean BPD Screening Inventory (Zanarini et al., 2003). Females who were 18 years and older and who endorsed seven or more items on the inventory were followed up by telephone to complete an additional screen to determine their eligibility to participate in the study.

Inclusion/exclusion criteria. To be eligible to participate, all participants met the following inclusion criteria: 18 years of age or older at the time of recruitment, female, English-speaking, right-handed, and able and willing to provide written informed consent. BPD participants were required to meet DSM-IV criteria for current BPD. Participants were ineligible for participation if they met DSM-IV criteria for schizophrenia or any psychotic disorder, bipolar disorder, current or lifetime history of alcohol or substance use disorder, current eating disorder or lifetime eating disorder that required hospitalization, mental retardation, neurological or severe somatic disorder, or significant head trauma (>5 minutes loss of consciousness). Additionally, healthy participants were excluded if they had a current diagnosis of any Axis I or Axis II disorder. In the week prior to testing, all participants were asked to abstain from cannabis or any other illicit drug use, and severe alcohol consumption. In addition, all subjects were instructed to abstain from coffee and nicotine 24 hours prior to testing.

Screening. A total of 17 individuals with suspected BPD based on a referral from a university counseling center or a positive BPD screen (i.e., 7 or more symptoms endorsed) from introductory psychology classes completed a comprehensive phone
screen. Three individuals did not meet full criteria for DSM-IV BPD, two met criteria for current bipolar disorder, two reported current drug dependence, and one was left-handed. A total of nine individuals with BPD who met inclusion and exclusion criteria were included in the study. Using completed screening inventories from introductory psychology classes, persons who denied all BPD symptoms completed a more comprehensive follow-up phone screen for inclusion in the study as healthy controls. Ten age-, gender-, and education-matched healthy control participants were included in the study.

2.2. Assessment Procedures

Diagostic Assessment

**BPD Module of the Diagnostic Interview for DSM-IV Personality Disorders (DIPD-IV; Zanarini, Frankenburg, Sickel, & Yong, 1996).** The DIPD-IV is a psychometrically sound semi-structured interview to categorically assess DSM-IV personality disorder. For economic purposes, solely the BPD module of the interview was used to obtain a comprehensive assessment of suspected BPD participants. A rating scale ranging from 0 (not at all) to 3 (frequently) was used to dimensionally assess each of the nine DSM-IV criteria for BPD. Given the present study’s focus on interpersonal rejection, a dimensional score for criterion six (i.e., frantic efforts to avoid real or imagined abandonment) was computed. The interview in its entirety has demonstrated good reliability and validity. The DIPD-IV is currently being used in the Collaborative Longitudinal Personality Disorders Study, a large, multisite study on the validity and clinical utility of personality disorder diagnosis (Gunderson et al., 2000).
Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I). The SCID-I is a semi-structured interview for DSM-IV Axis I disorders. It aids researchers in making reliable, valid, and accurate diagnoses of clinical syndromes. The specific modules of the SCID-I to be administered were based on items which were endorsed by the examinee during a screening interview. The comprehensive screen probed several Axis I conditions to include mood, anxiety, somatoform, schizophrenia and other psychotic, substance-related, eating, and impulse-control disorders. Attention-deficit, conduct, and oppositional defiant disorders were also screened.

Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996). The BDI-II is a 21-item self-report instrument developed to measure severity of depression in adults and adolescents. Each item consists of four statements reflecting increasing levels of severity for several depressive symptoms. The total score ranges from 0 to 63, with higher scores reflecting greater depression severity. The BDI-II has demonstrated high internal consistency and good convergent validity with other measures of depression (Beck et al., 1996).

Barratt Impulsivity Scale-11 (BIS-11; Patton, Stanford, & Barratt, 1995). The BIS-11 is a 30-item inventory which assesses five latent factors of impulsivity: lack of persistence, social optimism, lack of motor inhibition, aggression-autonomy, and action-oriented impulsive actions. The BIS-11 shows strong convergence with other measures of impulsiveness and several measures of hostility and anger (Barratt, Stanford, Dowdy, Liebman, & Kent, 1999).

Global Assessment of Functioning Scale (GAF). The GAF a 100-point global clinical rating scale and scores are judged on the basis of the participant’s reported and
observed clinical status, interview behavior, and functioning during a specified time
period relevant to the person’s clinical status. The scale comprises Axis V of the DSM-

**Personality Assessment**

*Minnesota Multiphasic Personality Inventory-2 (MMPI-2; Butcher, Dahlstrom,
Graham, Tellegen, & Kaemmer, 1989).* The MMPI-2 is a 567-item true-false self report
inventory. Several studies have shown that the original MMPI personality disorder scales
(Morey, Waugh, & Blashfield, 1985), developed using a rational and empirical approach
are internally consistent, effective in discriminating clinically diagnosed personality
disorders from control participants, and consistent with the hypothetical structure of the
DSM-III (Schuler, Snibbe, & Buckwalter, 1994). Only the items that make up the
personality disorder scales were administered in order to reduce administration time.
Normative data which were used to determine clinically significant scale elevations are
provided in Colligan, Morey, and Offord (1994).

*The Interpersonal Adjective Scales: Big Five Version (IASR-B5; Trapnell &
Wiggins, 1990).* The IASR-B5 is a measure of interpersonal function based on the latent
dimensions of agency and communion (see Figure 1). It provides an assessment of eight
interpersonal domains (arrogant-calculating, cold-quarrelsome, aloof-introverted, lazy-
submissive, unassuming-ingenuous, warm-agreeable, gregarious extraverted, and
ambitious-dominant) based on blends of the two interpersonal dimensions of agency and
communion. In addition, it provides a measure of three of the “big five” personality
factors (neuroticism, conscientiousness, and openness to experience). The IASR-B5 has
demonstrated strong internal consistency and shows good convergence with other personality inventories (Trapnell & Wiggins, 1990).

2.3. Neuroimaging Procedures

*Instrumentation.* The fNIRS system utilized in the present study was originally designed by Dr. Britton Chance at the University of Pennsylvania and advanced at the Drexel University School of Biomedical Engineering, Science, and Health Systems. The system is comprised of three modules: first, a headpiece which holds the fNIRS emitters and sensors, constituting the interface between the control system and the participant’s scalp; second, a control box for hardware control and data acquisition; and third, a computer which runs data acquisition and analysis software. The flexible sensor holds four light-emitting diode sources and 10 photodetectors arranged in a geometry which yields a total of 16 channels or voxels [see Figure 2(a)]. These channels provide coverage over the anterior portions of the frontal lobe which correspond to Brodmann areas 9, 10, 45, and 46 [see Figures 2 (b) and (c)].

Each detector records two time series of absorption measurements, one for each of the two light wavelengths used, which in the present study were 730 and 850 nm. As mentioned previously, changes in the light intensity measured at the surface of the scalp reflect changes in the oxy-Hb and deoxy-Hb concentrations in the sampled cortical brain tissue. From the recorded data, light absorption changes relative to the initial baseline period preceding each task are obtained and then converted to relative concentration changes of oxy-Hb and deoxy-Hb using the modified Beer-Lambert Law (Villringer & Chance, 1997). To elaborate, the variations in concentration of oxy-Hb and deoxy-Hb
(ΔC_{oxy} and ΔC_{deoxy}) at each point \( t \) in time during the activation task for a given channel can be obtained by solving the following set of equations:

\[
\begin{align*}
\log_{10} \frac{I_{730\text{nm} @ \text{rest}}}{I(t)_{730\text{nm} @ \text{task}}} &= \left[ \varepsilon_{\text{oxyHb} @ 730\text{nm}} \cdot \Delta C(t)_{\text{oxyHb}} + \varepsilon_{\text{deoxyHb} @ 730\text{nm}} \cdot \Delta C(t)_{\text{deoxyHb}} \right] \cdot k \\
\log_{10} \frac{I_{850\text{nm} @ \text{rest}}}{I(t)_{850\text{nm} @ \text{task}}} &= \left[ \varepsilon_{\text{oxyHb} @ 850\text{nm}} \cdot \Delta C(t)_{\text{oxyHb}} + \varepsilon_{\text{deoxyHb} @ 850\text{nm}} \cdot \Delta C(t)_{\text{deoxyHb}} \right] \cdot k
\end{align*}
\]

where \( I \) represents the light intensity as recorded by the photodetector, \( \varepsilon \) is the specific absorption coefficient, \( \Delta C \) is the concentration change relative to the rest period, and \( k \) is a constant coefficient depending on the sensor pad geometry and on the optical properties of the sampled tissue (Delpy et al., 1988). For the present study, data were sampled at a rate of once every 500 milliseconds.

**Procedure.** After completing informed consent procedures, the participant’s head was cleansed using rubbing alcohol and cotton pads. Each participant was comfortably seated in a dimly lit room. The sensor pad was positioned over the forehead of each participant, roughly covering Brodmann areas 9, 10, 45, and 46 [see Figure 2 (c)]. The sensor pad was subsequently covered with a dark cloth to further shield ambient light from intruding on the sensor pad.

**Social exclusion paradigm.** Adapted from Eisenberger and colleagues (2003), the participant was seated at a table with two confederates (one male and one female) who were trained in the procedures of the experiment. The participant and confederates were instructed that they would be playing a game with the other two persons at the table. The participants were told that the purpose of the study was to examine brain activity of an interpersonal interaction. The game to be played was called the “secret card game” where the players were presented with one standard deck of 52 playing cards placed face
down on the center of the table. The participant was selected to begin the game. Each player was required to take the card at the top of the deck and place it face-down in front of one of the other two players. The rule was that only the player who had just received a card could take the next card and place it face-down in front of another player; no person could give herself or himself a card. The participants were told that the winner of the game was the player who received the card with the ace of hearts. Given that there was only one of these cards, and that the cards were face down and selected at random, the player that received the most number of cards had the greatest likelihood of being declared the winner of the game. The participants were told that the winner of each game was recorded by the experimenter but that the winners would not be disclosed until all rounds of the game had been completed.

Prior to beginning the first scan, the participant was asked to provide a rating on a scale ranging from 1 (not at all present) to 10 (very severe) of their present levels of depression and anxiety. Participants were first asked to stare directly at the deck of cards placed at the center of the table such that baseline fNIRS parameters could be established. During the first scan (“inclusion condition”), the participant was fully included in the game with the other two players, and the game continued until the full deck of cards had been exhausted. In the second scan (“exclusion condition”), the participant received seven cards from the other players and was then completed excluded when the confederates stopped placing cards in front of the participant for the remainder of the scan (45 cards). Following each scan, the participant completed provided a rating of their current depression and anxiety, as well as a rating of their feelings of inclusiveness and
rejection during the previous trial. At the completion of the task, the deception was revealed and a debriefing protocol was implemented.

2.4. Hypotheses

The following hypotheses are presented with respect to the three primary assessments obtained in the present study: (1) self-report personality inventories; (2) mood and inclusiveness/rejection ratings completed during the interpersonal rejection task; and (3) fNIRS measurements recorded during the interpersonal rejection task.

Symptom and personality measures. It is well-confirmed that BPD patients tend to report higher levels of negative affect and impulsivity relative to healthy comparison groups, with both symptom dimensions thought to be associated with the unique neurobiology of the disorder (Skodol et al., 2002). Based on these findings, BPD participants were hypothesized to score higher on the BDI-II and BIS-11 compared with healthy participants. With regard to the IASR-B5, data from a rigorous ecological momentary assessment study revealed a marked tendency for BPD patients to behave in a submissive manner in daily interpersonal interactions (Russell, Moskowitz, Zuroff, Sookman, & Paris, 2007). Based on these findings, BPD participants were hypothesized to report higher levels of interpersonal submissiveness on the IASR-B5 compared with healthy persons.

Brief rating scales. BPD participants were hypothesized to report greater levels of depression and anxiety during the time immediately prior to initiating the interpersonal rejection task. After the inclusion condition, BPD and healthy participants were expected to report comparable levels of depression, anxiety, and inclusiveness/rejection. Following the exclusion condition, however, all participants were expected to rate higher
levels of rejection but no significant change in depression or anxiety. Given heightened sensitivity to rejection in BPD, it was hypothesized that individuals with BPD would report higher levels of rejection compared with healthy participants following the interpersonal exclusion condition.

FNIRS. During the inclusion condition, BPD participants were hypothesized to demonstrate comparable levels of cerebral blood oxygenation across all probe channels (Brodmann areas 9, 10, 45, and 46, and channels 1-16) relative to healthy participants during the inclusion condition. However, during the exclusion condition, BPD participants were hypothesized to demonstrate lower levels of cerebral blood oxygenation in the regions of interest in right PFC during exclusion (channels 10, 12, 14, 16). The right PFC is the region of cortex in closest measurable proximity to right ventral PFC, which was previously found to demonstrate greater activity during social exclusion relative to inclusion in healthy individuals. The rationale is that BPD participants have demonstrable deficits in their effortful control of subcortical (i.e., limbic) structures associated with governance of interpersonal interactions and affectivity. Activity in the right ventral PFC was associated with activity in the anterior cingulate cortex (ACC) in such a way that the latter mediated the relationship between right ventral PFC activity and self-reported distress. That is, right ventral PFC appears to regulate the distress associated with social exclusion by disrupting activity in the limbic cortex (i.e., ACC). Based on these findings, it was hypothesized that right PFC activity would be correlated with self-report measures of affect (depression, anxiety) and inclusiveness/rejection. Additional analyses were conducted to explore possible links between interpersonal function (IASR-B5 scales, abandonment fears) and evoked cerebral blood oxygenation in
channels which demonstrated different levels of functional hemodynamic activity in BPD compared with healthy participants.

3. DATA ANALYSIS AND RESULTS

3.1. Data Analytic Strategy

The following data analytic strategy is based upon the hypotheses presented above and were carried out by SPSS 16.0 Software Package.

Symptom and personality measures. A two-tailed independent samples $t$-test was used to compare BPD and healthy participant scores on the BDI-II and BIS-11. Exploratory analyses for the IASR-B5 and MMPI-2 personality disorder scales were conducted using independent samples $t$-tests set to a $p < .01$ level of statistical significance.

Brief rating scales. A one-way multivariate analysis of variance was conducted to compare BPD and healthy participants' pre-task ratings of depression and anxiety. A mixed 2 (participant group) x 3 (condition) between-within repeated measures analysis of variance was used to compare ratings of anxiety, depression, inclusiveness, and rejection prior to and after each of the inclusion and exclusion conditions of the interpersonal rejection task.

FNIRS. Oxy-Hb data were averaged across the whole run for each of the inclusion and exclusion conditions, yielding mean levels of oxy-Hb per channel for each participant. A mixed 2 (participant group) x 2 (condition) between-within repeated measures analysis of covariance (depression, number of Axis I disorders) was carried out to compare levels of oxygenated hemoglobin for right hemisphere regions of interest (channels 10, 12, 14, 16). Post-hoc univariate tests (between-subjects or repeated
measures) with appropriate covariates were carried out to contrast simple effects given that there were only two levels of the independent variables. Effect sizes (partial eta squared, or \( \eta^2_{\text{partial}} \)) were reported for fNIRS analyses. Partial eta squared values may be roughly interpreted using the following effect size conventions: small (0.01), medium (0.06), and large (0.14) (Cohen, 1988). Finally, Pearson correlation analyses were carried out between any implicated voxels and brief rating scales and IASR-B5 scales.

Additional exploratory analyses were conducted across the remaining 12 channels. A more stringent level of Type I error \( p < .01 \) was adopted to maintain adequate statistical power while reducing the likelihood of identifying spurious findings.

### 3.2. Demographic and Clinical Features

Table 1 lists the demographic characteristics for BPD and healthy participants. The groups did not differ by age, \( t (17) = -1.42, p = .17 \), years of education, \( t (17) = -.49, p = .63 \), or ethnicity, \( \chi^2 (2) = 1.35, p = .51 \). All participants completed a comprehensive screen for DSM-IV Axis I disorders. BPD participants additionally met criteria for the following Axis I disorders: major depressive disorder, recurrent \( (n = 3) \); major depressive disorder, single episode, in full remission \( (n = 4) \); social phobia \( (n = 2) \); dysthymic disorder \( (n = 1) \); and post-traumatic stress disorder \( (n = 1) \). Number of Axis I disorders was entered as a covariate in analyses of fNIRS data given the substantial comorbidity of Axis I disorders with BPD. Three BPD participants were currently receiving treatment: psychotherapy alone \( (n = 1) \), pharmacologic treatment alone \( (n = 1) \), and combined psychotherapy and pharmacologic treatment \( (n = 1) \). Participants receiving pharmacologic treatment were taking stimulant \( (n = 1) \) and antipsychotic \( (n = 1) \) medications.
3.3. Symptom and Personality Measures

Table 2 displays the scores of BPD and healthy participants on symptom rating scales and personality measures. BPD participants reported greater levels of depressive symptomatology over the previous two weeks and more impulsiveness. With regard to interpersonal function, BPD participants reported significantly higher scores on the Aloof-Introverted scale of the IASR-B5 based on the more stringent level of Type I error ($p < .01$). Conversely, BPD participants scored lower on the Extraverted-Gregarious scale. Persons with BPD tended to report more personality disorder traits compared with healthy controls, with the exception of histrionic and narcissistic scales for which there was no significant difference between these groups. Differences between the groups on dependent and schizoid scales did not reach statistical significance based on the more stringent level of Type I error ($p < .01$). Based on normative data presented in Colligan and colleagues (1994), BPD participants reported notable paranoid and antisocial personality styles, their scores falling equivalent to or above the 90th percentile compared to women of similar age.

3.4. Social Exclusion Paradigm

*Brief rating scales.* The results of self-report ratings of mood immediately prior to the interpersonal rejection task, and participants’ ratings of inclusiveness and rejection during the task, are presented in Table 3. There was a main effect of group for depression, $F (1, 19) = 14.88, p = .001$, with the BPD group reporting higher levels of depression immediately prior to initiating the interpersonal rejection task. Depression was entered as a covariate in subsequent analyses using fNIRS data.
Results of mixed between-within analysis of variance revealed no main effect of group on anxiety ratings, and no group x condition interaction (all p’s > .05). There was, however, a main effect of group on depression ratings, $F(1, 16) = 9.31, p < .01$, but no group x condition interaction, $F(1, 16) = .15, p = .71$, with BPD participants reporting greater levels of depression after inclusion, $t(16) = -3.97, p = .001$, and exclusion conditions $t(17) = -2.45, p = .03$. A main effect of condition was found for inclusiveness ratings, $F(1, 17) = 172.86, p < .001$, and rejection ratings, $F(1, 16) = 95.43, p < .001$. As expected, participants reported higher levels of inclusiveness during the inclusion condition compared with the exclusion condition, $t(18) = 13.44, p < .001$, and higher ratings of rejection during the rejection condition relative to the inclusion condition, $t(18) = -9.45, p < .001$. No group x condition interaction for inclusiveness or rejection ratings was found (all p’s > .05).

**FNIRS.** A mixed between-within repeated measures analysis of covariance was carried out to examine mean levels of oxy-Hb in each of the 16 channels spanning Brodmann areas 9, 10, 45, and 46. The covariates entered into the model included number of Axis I disorders and ratings of depression immediately prior to initiating the interpersonal rejection task. Estimated marginal means and standard errors of oxy-Hb for each fNIRS channel for BPD and healthy participants are presented in Table 4.

**Region-of-interest analyses.** Analyses are first presented for those channels covering the right PFC (channels 10, 12, 14, 16; see Figure 2) which previously have been implicated as involved in the effortful control of limbic regions in a social exclusion task. For channel 10, there was no main effect of group, $F(1, 15) = 1.63, p = .22, \eta^2_{partial} = .10$, or condition, $F(1, 15) = .93, p = .35, \eta^2_{partial} = .06$. However, there was a group x
condition interaction, $F(1, 15) = 4.64, p = .048, \eta^2_{\text{partial}} = .24$. Figure 3(a) displays the interaction effect for channel 10. Post-hoc analyses revealed lower levels of oxy-Hb during the inclusion condition for BPD participants relative to controls, $F(1, 15) = 4.74, p = .02, \eta^2_{\text{partial}} = .31$. The activation map showing greater levels of oxy-Hb for healthy controls compared to BPD participants in right PFC can be seen in Figure 4. The time course of oxy-Hb for channel 10 during the inclusion condition is displayed in Figure 5.

In examining the relation between interpersonal function and cerebral oxygenation in this region, indices of the IASR-B5 were correlated with mean levels of oxy-Hb in channel 10. During the inclusion condition, oxy-Hb in this channel was correlated with Gregarious-Extraverted ($r = +.56, p = .01$) and Aloof-Introverted scales ($r = -.54, p = .02$) (see Figure 6). Mean oxy-Hb in channel 10 was also correlated with a dimensional rating of rejection/abandonment fears from the BPD module of the DIPD ($r = -.48, p = .038$), as well as paranoid ($r = -.57, p = .01$) and antisocial ($r = -.57, p = .01$) personality traits.

Table 5 displays Pearson correlations among personality disorder traits, interpersonal scales, and mean oxy-Hb in channel 10. There was no significant correlation between evoked oxy-Hb in channel 10 and any rating of inclusiveness, rejection, depression, or anxiety after inclusion or exclusion conditions.

A similar pattern of results to that of channel 10 was obtained for channel 16, which roughly corresponds to Brodmann area 45, or right lateral PFC (see Figure 2). During the exclusion condition, a group x condition interaction was found for this channel, $F(1, 15) = 5.07, p = .04, \eta^2_{\text{partial}} = .25$. No main effect of group, $F(1, 15) = 1.36, p = .26, \eta^2_{\text{partial}} = .08$, or condition, $F(1, 15) = 1.07, p = .32, \eta^2_{\text{partial}} = .07$ was observed. BPD participants demonstrated slightly lower levels of oxy-Hb in channel 16
during the exclusion condition but the difference did not reach statistical significance in univariate analyses, $F(1, 15) = 3.14, p = .097, \eta^2_{\text{partial}} = .17$. The IASR-B5 scales were correlated with mean level of oxy-Hb in channel 16. During the exclusion condition, a robust correlation was observed between mean oxy-Hb in channel 16 and the Unassured-Submissive scale of the IASR-B5 ($r = -.60, p < .01$). No significant correlation was observed between evoked oxy-Hb in channel 16 and any rating of inclusiveness, rejection, depression, or anxiety after inclusion or exclusion conditions.

**Whole-probe analyses.** With regard to left hemisphere channels, a main effect of condition was found for channel 8 (left PFC), $F(1, 15) = 6.92, p = .019, \eta^2_{\text{partial}} = .32$, demonstrating a decrease in oxy-Hb during the exclusion condition (see Figure 7). There was no main effect of group, $F(1, 15) = 2.04, p = .17, \eta^2_{\text{partial}} = .12$, or group x condition interaction, $F(1, 15) = .26, p = .62, \eta^2_{\text{partial}} = .02$. No additional left hemisphere channels demonstrated any main or interaction effects (all $p$’s > .05).

Analyses were subsequently conducted for channels spanning the right lateral PFC region. For channel 13 (see Figure 2), there was a main effect of group, $F(1, 15) = 4.70, p = .047, \eta^2_{\text{partial}} = .24$, with BPD participants demonstrating higher levels of oxy-Hb. No main effect of condition, $F(1, 15) = 1.40, p = .26, \eta^2_{\text{partial}} = .09$, or group x condition interaction, $F(1, 15) = 2.16, p = .16, \eta^2_{\text{partial}} = .13$, was found. A group x condition interaction was observed for channel 15, $F(1, 15) = 6.88, p = .019, \eta^2_{\text{partial}} = .31$, with no main effect of group, $F(1, 15) = .32, p = .58, \eta^2_{\text{partial}} = .02$, or condition, $F(1, 15) = .54, p = .47, \eta^2_{\text{partial}} = .04$. Post-hoc analyses for this channel revealed higher levels of oxy-Hb for BPD participants during the inclusion condition, $F(1, 18) = 9.51, p < .01, \eta^2_{\text{partial}} = .41$ [see Figure 3(b)], but not during the exclusion condition, $F(1, 18) =$
.81, \( p = .38 \), \( \eta^2_{\text{partial}} = .06 \). Whereas these findings from whole-probe analyses did not meet the aforementioned criterion for statistical significance \((p < .01)\), it is important to note that several of these effect sizes fell within the moderate to large range.

Channels with significant findings in whole-probe analyses (channels 8, 13, and 15) were not correlated with post-inclusion or post-exclusion ratings of inclusiveness, rejection, anxiety, or depression. There were also no significant correlations between mean oxy-Hb for channels 8, 13, and 15, and IASR-B5 scales. Of note, the total number of correlations conducted between levels of oxy-Hb in significant channels and self-report measures was approximately 40 in total. One would expect at \( p < .05 \) level of Type I error that two correlations may have been spurious.

*FNIRS analyses without covariates.* Analyses were conducted which did not covary for depression and Axis I disorders in order to determine the impact of these covariates on FNIRS data during the social exclusion paradigm. A main effect of condition emerged for channel 6, \( F (1, 17) = 9.28, \ p < .01, \ \eta^2_{\text{partial}} = .35 \), demonstrating with oxy-Hb declining from the inclusion to the exclusion condition, but no group x interaction, \( F (1, 17) = 1.88, \ p = .19, \ \eta^2_{\text{partial}} = .10 \). In addition to the interaction effect observed in analyses using covariates, a main effect of condition was found for channel 10, \( F (1, 17) = 8.75, \ p = < .01, \ \eta^2_{\text{partial}} = .34 \), with a decrease in oxy-Hb during the exclusion condition. For channels 8 and 10 which demonstrated significant results when covarying for depression and Axis I disorders, the effects were magnified but the pattern of results was unchanged.

*Analyses excluding social phobia participant.* Two BPD participants additionally met criteria for social phobia, a condition with clear relevance to interpersonal function.
Analyses for channel 10 were conducted with these participants excluded. The group x condition interaction remained statistically significant without covariates; however, when covarying for depression and Axis I disorders, the effect was marginally significant, $F(1, 12) = 4.49, p = .056, \eta^2_{\text{partial}} = .27$.

4. DISCUSSION

The present investigation examined evoked cerebral blood oxygenation using fNIRS to study the neural correlates of social exclusion in BPD. The demographic characteristics and clinical features of participants included in the present study are consistent with previous neuroimaging studies of BPD (e.g., Beblo et al., 2006; Driessen et al., 2004). There are, however, several important distinguishing features of the present study which include a younger age range, female cohort, less severe clinical status of BPD participants (i.e., most were recruited from the community, very few had past hospitalizations), and only a small number of BPD participants were receiving psychotherapeutic treatment or taking psychoactive medication. In this context, BPD participants, as expected, reported higher levels of impulsiveness and depression, also consistent with previous studies (Koch et al., 2007; Ruchsow et al., 2008).

BPD participants reported higher levels of personality disorder symptomatology than healthy controls. The mean scores of BPD participants indicated additional tendencies toward paranoid and antisocial personality styles, their scores falling equivalent to or above the 90th percentile compared to women of similar age (Colligan et al., 1994). These findings are similar to the pattern of Axis II comorbidity found in other studies of BPD (Critchfield, Clarkin, Levy, & Kernberg, in press; Zanarini et al., 1998). BPD participants’ interpersonal styles also departed significantly from healthy controls.
BPD participants were characterized by marked aloofness and introversion, falling within a more submissive domain of interpersonal function (see Figure 1). Healthy controls, on the other hand, reported significantly greater levels of gregariousness and extraversion, tending toward a more dominant interpersonal stance. These findings are consistent with ecological momentary assessments of BPD patients who show greater interpersonal submissiveness in their daily social interactions than healthy persons (Russell et al., 2007). Despite tendencies toward interpersonal submissiveness for persons with BPD, there are also indications that BPD traits demonstrate less consistent or distinct interpersonal tendencies than other personality disorders traits (Locke, 2000).

Ratings made immediately prior to initiating the interpersonal rejection paradigm indicated that BPD participants were significantly more depressed than healthy controls. This was an expected finding given that these participants reported higher levels of depressive symptomatology on the BDI-II over the previous two weeks. Following the inclusion condition of the interpersonal rejection task, BPD participants reported comparable levels of depression and anxiety relative to healthy controls. They also felt highly included in the task, at a level commensurate with that of healthy participants. Following the exclusion condition, all participants rated very high levels of rejection (and low feelings of inclusiveness). Contrary to expectations, BPD participants did not report higher levels of rejection than healthy controls. The most likely explanation for this finding is that the manipulation of exclusion was particularly strong and resulted in all participants reporting very strong feelings of rejection, with participants’ reports essentially reaching ceiling levels. Thus, any heightened sensitivity to rejection on the part of BPD participants may have been obscured by the strong effects of the
manipulation across all participants. It is possible that these feelings of rejection subsided more slowly for BPD participants; however, measurements of rejection feelings at times beyond completion of the exclusion condition were not incorporated into the present study.

4.1. Interpersonal Function and Right PFC in BPD

Measurements of evoked cerebral oxygenation were obtained during inclusion and exclusion conditions of the interpersonal rejection paradigm. Regions of interest were isolated in right PFC based on previous findings using a similar task with healthy individuals (Eisenberger et al., 2003). The regions of interest were specific to channels 10, 12, 14, and 16, which were selected because of their proximities to right ventral PFC, a region found to be involved in the regulation of limbic structures associated with the experience of social exclusion. Individuals with BPD have previously been found to demonstrate inefficient recruitment of prefrontal regions thought to be invoked in the effortful regulation of affect (Beblo et al., 2006; Herpertz et al., 2001; Schmahl et al., 2003). The hypothesis was that BPD participants would demonstrate less activation in these regions of the right medial and lateral PFC relative to healthy controls during the exclusion condition, consistent with the notion that individuals with BPD have greater difficulties engaging frontal processes involved in regulation of affectively laden interpersonal circumstances.

After controlling for depression and Axis I disorders, BPD participants demonstrated diminished levels of evoked cerebral oxygenation in the right PFC compared with healthy controls; however, contrary to hypotheses, the difference was isolated to the inclusion, rather than the exclusion, condition. This was an unexpected
finding given that relative deactivation of this region compared to controls occurred
during an interpersonal interaction which appeared comparatively benign in nature.
Interestingly, this robust finding remained significant while statistically controlling for
depression and Axis I pathology, suggesting that these findings may be specific to BPD.
BPD participants did not report greater levels of depression or anxiety following the
inclusion or exclusion conditions, nor did they differ from controls in ratings of rejection
or inclusiveness. Thus, it was unlikely that the relative deactivation of right PFC during
the inclusion condition could be accounted for by perceived rejection, depression,
anxiety, or comorbid Axis I disorder.

Perhaps surprisingly, robust relationships were found between self-report ratings
of characterologic interpersonal function and levels of oxygenated hemoglobin in right
PFC during the inclusion condition. There was also a significant association between
oxygenation in this region and a dimensional rating of fears of abandonment. As
previously mentioned, BPD participants reported higher levels of aloofness and
introversion than age- and gender-matched healthy controls. Quite the opposite, healthy
participants described themselves as more gregarious and extraverted relative to
individuals with BPD. Interestingly, lower levels of oxygenation in right PFC were
strongly associated with greater aloofness and introversion. Conversely, higher levels of
oxygenation in this region were strongly related to elevated levels of gregariousness and
extraversion. This pattern of findings may indicate that individuals with BPD, even
during a seemingly benign interpersonal interaction, may demonstrate diminished
recruitment of right PFC by way of a characterologic interpersonal stance which lends
them toward detachment and aloofness. On the other hand, healthy participants may
more efficiently engage right PFC in an inclusive interpersonal situation by virtue of their tendencies toward extraversion and interpersonal engagement. Overall, these findings seem to provide evidence which relates right PFC function to the interpersonal dimension of agentic extraversion and submissive introversion. The results also seem to implicate that the relative deactivation of right PFC during conditions of social inclusion may be related to this basic interpersonal dimension rather than the diagnosis of BPD per se.

These findings are consistent with a right-hemisphere dysfunction revealed by neuropsychological studies of BPD (Ruocco, 2005a). This relative inefficiency of right PFC may reflect a characterologic feature of BPD in the context of benign social interactions and which may be associated with a particular interpersonal or personality style. These results are also surprisingly consistent with the literature regarding the neurocognitive basis of empathy and insight about the self. As previously mentioned, the pattern of neuropsychological deficits in BPD may be considered similar to that observed in persons with non-verbal learning disability and Asperger’s disorder. These individuals have characteristic interpersonal styles which predispose them toward disturbances in reciprocal social interaction, possibly related to inefficiencies in their attribution of mental states to others (Rinehart, Bradshaw, Brereton, & Tonge, 2002). There is a growing literature which relates this deficit in empathy or conceptualization of self to the right PFC (Platek, Keenan, Gallup, & Mohamed, 2004; Platek et al., 2006), which is certainly consistent with the present study. Thus, individuals with BPD may have similar right hemisphere mediated difficulties with reciprocal social interaction which, possibly in combination with affective and impulsive features, may be related to interpersonal difficulties associated with BPD psychopathology.
Whereas the etiology of this right hemisphere deficit is unclear, there is evidence which suggests an experience-mediated disruption of prefrontal circuits in BPD. This disruption is thought to cause a cascade of neurocognitive deficits, most notably those cognitive functions which rely upon the functional integrity of PFC (Meares, Stevenson, & Gordon, 1999). A dysfunction of frontal circuits is also likely to have consequences for affective regulation, reflective functions involving the self, and interpersonal relations. Thus, the neurocognitive deficit in BPD may be associated with experiential events (e.g., traumatic histories) which may have deleterious effects on cognitive, affective, and interpersonal function. The effects of traumatic experience on the brain may be mediated by the impact of stress hormones on structures within the limbic system, such as the hippocampus (Jelicic & Merckelbach, 2004; Sala et al., 2004).

Another explanation for the observed pattern of findings is that BPD participants were simply disengaged from the task during the inclusion condition. This is certainly a plausible hypothesis given that the group was clearly characterized by a marked interpersonal style which might lend them toward interpersonal detachment in this situation. Given their significant paranoid personality styles, the findings of relative deactivation of right PFC may reflect participants’ suspiciousness during the inclusion condition, possibly questioning the purpose of the study and the motives of the confederates.

One might also imagine that the “secret card game” which was implemented as part of the social exclusion task required some level of cognitive processing which may have differed between the two groups. Healthy participants may have recruited more PFC activation in an attempt to strategize and win the game, whereas BPD participants
may not have taken the task seriously and simply cognitively disengaged from the task. It would be difficult to determine whether this was the case without ratings of participants’ behaviors during the inclusion condition. Given the relative simplicity of the game, it could be argued that the cognitive demands required to complete the task were relatively small compared with the more social-cognitive aspects of the paradigm. Nevertheless, it seems that the relative ambiguity of the inclusion condition demonstrated a greater differential effect on neurocognitive function between participant groups compared with the more salient exclusion condition. This may suggest that individuals with BPD may differ from healthy controls in the ways that they perceive relatively ambiguous social situations, possibly affording them the opportunity to implement maladaptive schemas under these circumstances. It is possible that differences in neurocognitive function reflect their misperceptions of interpersonal situations and the social-cognitive processing invoked by these situations.

Given the pattern of associations among BPD participants’ interpersonal style and PFC function, the findings of the present study may suggest a model of BPD abandonment-related symptoms which may be mediated by the brain and rooted in interpersonal disposition (see Figure 8). The model proposes that persons with BPD are predisposed toward an aloof, introverted, and submissive interpersonal style, whether etiologically tied to genetic substrate or experiential learning. The aloof-introverted interpersonal stance may be associated with a relative deactivation compared with healthy persons of right PFC in the context of even mundane interpersonal interactions. This relatively inefficient engagement of the prefrontal region may be causally linked to maladaptive interpersonal interactions within the person’s life, possibly by means of poor
reciprocal social interactions. It is possible that deactivation of this socially-relevant region of PFC may mediate a sense of interpersonal detachment and foster the eventual dissolution of relationships. Healthy persons, on the other hand, seem to preferentially engage this area of the brain during interpersonal interactions, and thus may be more likely to cultivate mutually satisfying interpersonal relationships and experiences. Although this aspect of the model was not specifically tested in the present study, the robust link between activity in right PFC and BPD-related fears of abandonment makes a strong argument for a brain-mediated disruption of interpersonal interactions which has consequences for anticipatory fears of rejection and abandonment in seemingly benign interpersonal interactions. This model may also be supported by evidence of marked tendencies toward interpersonal submissiveness in an ecologically valid assessment of daily social interactions for patients with BPD (Russell et al., 2007). The proposed model may be tested as part of a similar ecological momentary assessment program which allows for remote measurement of interpersonal function and brain activity during a person’s daily interactions, with fNIRS serving as the most suitable imaging technique given its ecological advantages.

These data also provide evidence for the involvement of right PFC in the personality dimension of submissive-introversion, and on the other end of the spectrum, agentic-extraversion. These interpersonal styles represent opposite ends of one dimension on the interpersonal circumplex as conceptualized by Wiggins (1995) (see Figure 1). This is among the first studies to examine the neurocognitive correlates of the IASR-B5, considered among the most well-validated measures of interpersonal function. These data are consistent with research which implicates right-lateralized findings
involving the frontal cortex in association with the personality trait of extraversion (Gurrera et al., 2007; O'Gorman et al., 2006; Wright et al., 2006). The paradigm employed in the present study may lend greater credence to the notion of right-hemisphere involvement in extraversion and interpersonal engagement. Indeed, this paradigm possesses greater ecological validity by means of investigating the neural correlates of these interpersonal dimensions within the context of an actual social interaction.

4.2. Social Exclusion and PFC

Under conditions of social exclusion, participants showed decreased activity as compared with social inclusiveness. These findings suggest a role of left PFC during conditions in which persons are included or excluded from a social interaction. Specifically, there is a sharp decrease of oxygenation in left PFC associated with the experience of social exclusion which is independent of personality disorder diagnosis. Interestingly, mean levels of evoked cerebral oxygenation in this area were strongly inversely associated with the interpersonal trait of unassured submissiveness. That is, lower levels of oxy-Hb in left PFC were strongly linked to higher levels of interpersonal submissiveness and insecurity. Thus, under conditions of interpersonal exclusion, left PFC may be relatively deactivated in association with a tendency toward a submissive interpersonal stance.

There is strong evidence for the role of anterior PFC in social-interpersonal phenomena. This region has been implicated in fMRI studies of affective social evaluation (Harris, McClure, van den Bos, Cohen, & Fiske, 2007), social disconnection and distress (Eisenberger, Gable, & Lieberman, 2007), social cooperation (Babiloni et al.,
2007), and judgments of ironic social situations (Wakusawa et al., 2007). The PFC is also considered to be a component of the self-referential (i.e., “Theory of Mind”) neural circuit (Ciaramidaro et al., 2007). Furthermore, abnormalities in cerebral hemodynamic activity in PFC are implicated in a range of neuropsychiatric disorders with well-documented social-cognitive deficits such as schizophrenia and autism (Abdi & Sharma, 2004). Whereas there were clear differences between BPD and healthy participants in right PFC, no differences in blood oxygenation were identified within any channel during social exclusion. Nevertheless, the present findings provide evidence for the involvement of left PFC in social interaction, demonstrating a relative deactivation of this region during conditions of social exclusion.

4.3. Implications for Conceptualization of BPD

Several alternative models to DSM-IV have been put forth to conceptualize the psychopathology of BPD. The interpersonal tradition has long considered personality disorders to be represented by characterologic interpersonal stances which are maintained in either a highly rigid or variable manner across interpersonal interactions (Wiggins, 2003). As previously mentioned, BPD may be characterized by fluctuating interpersonal stances with tendencies toward submissiveness in daily interpersonal interactions (Russell et al., 2007). Results from the present study additionally suggest that individuals with BPD may be more introverted and aloof than healthy individuals, which also lends them toward a more submissive interpersonal stance. This interpersonal conceptualization may have important consequences for the development of BPD-related psychopathology (i.e., fears of abandonment), such that an aloof interpersonal stance may
lead one to be less engaging in interpersonal relationships and have difficulty initiating and maintaining such relationships.

The present investigation may provide support for a combined dimensional and categorical model of BPD. Certainly, these data indicate that interpersonal function may serve as a useful means by which to conceptualize personality disorder from a dimensional perspective. While preliminary, the results seem to suggest that dimensional measures of interpersonal function may be more relevant to the neurocognitive bases of personality disorder than the specific personality disorder diagnosis itself. This may have important implications for future conceptualizations of Axis II. As the neurocognitive basis of interpersonal function emerges, it may be that basic dimensions of interpersonal function are associated with unique neurocognitive underpinnings. If this is the case, then perhaps greater support may be given to a dimensional interpersonal diagnosis of personality disorder rather than the current categorical system in which interpersonal problems may take several forms even within a single personality disorder.

Overall, the pattern of findings suggests that there is a robust relationship between neurocognitive function and the characterologic interpersonal stances of individuals with BPD. As the neurocognitive bases of affective, cognitive, impulsive, and interpersonal aspects of personality disorder become known, the conceptualization of BPD and other personality disorders may require some modification. Given these findings, BPD may be conceptualized as a neuropsychiatric disorder, of which the core symptomatology may be traced to distinct neural systems which mediate the relationship between characterologic traits and manifest symptomatology. This notion of BPD as a neuropsychiatric disorder is truly a departure from traditional conceptualizations of personality disorder and has
important implications for the classification of BPD as an Axis I or Axis II disorder (for a review, see Ruocco, 2005b).

4.4. Limitations

Several limitations restrict the external validity and types of conclusions which can be drawn from the present study. Demographically, the younger age of participants limits the generalizability of these findings to other BPD studies which tended to recruit participants in middle-adulthood. The use of female BPD participants only, while minimizing within-subjects variation, restricts the applicability of these findings to males. Some advantages of using BPD participants recruited primarily from the community were the inclusion of individuals who mostly were not in treatment, did not suffer from a large number of Axis I disorders, and were functioning well in their day-to-day lives. Whereas this allowed for greater precision in attributing findings to the BPD diagnosis rather than other factors related to severity of illness, the participants included in the present study do not necessarily represent the typical BPD patient being seen in acute treatment settings.

The methodology implemented in the present study had the advantage of using both between- and within-subjects variables, allowing for characterization of patterns of hemodynamic activity associated with an ecologically valid interpersonal paradigm. Although the effect sizes for significant findings were of a very strong magnitude ($\eta^2_{\text{partial}} > .30$), other effects of small to moderate strength may not have been detected due to limited statistical power. The data analytic strategy was selected so as to minimize Type I error while maintaining sufficient statistical power to detect sufficiently strong effects. The study also sought to statistically control confounding factors which often co-occur
with BPD (e.g., Axis I disorders, depression); however, there may have been other variables which were not measured in the study design and which may have exerted an influence on the present findings.

In considering study design, the manipulation of rejection was successful. The manipulation appeared so powerful that feelings of rejection reached a ceiling level for BPD participants and healthy controls. Thus, the manipulation may have obscured anticipated differences in perceptions of the severity of interpersonal rejection between participant groups (i.e., BPD participants would report greater levels of rejection). It is possible that feelings of rejection subsided more slowly for individuals with BPD; however, measurements of rejection were not taken beyond completion of the paradigm. A less powerful manipulation of rejection (e.g., including participants more so in the task rather than completely excluding them) may have been more sensitive to potentially skewed perceptions of interpersonal rejection on the part of BPD participants.

The proposed model of the relationships among characterologic interpersonal function (aloofness and introversion), brain activity, and BPD-related abandonment fears could not be fully tested in the present study (see Figure 8). The results, however, support strong associations of right PFC activity with submissive introversion and fears of abandonment. To explore the possible causal relationships among these factors, as previously mentioned, an ecological momentary assessment study which examines the relationships among interpersonal function, brain activity, and daily interpersonal interactions may provide greater validity to the proposed model. Nevertheless, the present study has the advantage of greater ecological validity for examining the meditational role of PFC as it relates to interpersonal function and psychopathology.
Longitudinal studies may also allow for characterization of how brain function interacts with interpersonal function in mediating the development of BPD psychopathology over time.

The substantial comorbidity of other personality disorders and traits with BPD has a strong influence on the conclusions which can be drawn from the present findings. Indeed, strong paranoid and antisocial personality styles tended to characterize the patients presently studied. Given the very robust correlations between these personality disorders traits and the interpersonal scales of the IASR-B5 (i.e., Aloof-Introverted, Gregarious-Extraverted), the proposition is that these factors represent a single personality dimension which is better represented by these interpersonal dimensions rather than discrete personality disorder traits. Thus, the impact of these personality disorder traits on the present findings is considered to have been accounted for by dimensional ratings of interpersonal function which are strongly associated with these traits both empirically and theoretically.

With regard to technological limitations, the fNIRS sensor implemented in the present study solely provided coverage of specific regions of the frontal lobes, roughly corresponding to Brodmann areas 9, 10, 45, and 46. Indeed, there are other brain regions with relevance to the processes invoked during the interpersonal rejection task, most notably, the amygdala. Unfortunately, measurement of this region was not carried out due to the physical limitations of the fNIRS sensor, including coverage solely over the prefrontal regions and inability to examine subcortical structures. Indeed, one primary limitation of the sensor pad is its susceptibility to artifact caused by interference with hair
and other physical properties of the participant, permitting investigation only of cortical regions near the bare forehead (i.e., PFC).

Additionally, the technology is limited by its comparatively poor spatial resolution (on the order of centimeters) and depth of penetration, the latter limiting examinations of hemodynamic activity to the neocortex. There may have been additional subcortical structures with significance to the interpersonal rejection task which were unexamined because of this technological limitation. Other techniques, such as fMRI and PET, may allow for better characterization of subcortical structures which may be involved in processes of interpersonal inclusion and exclusion in BPD. The use of alternative iterations of the technology may also allow for more whole-brain cortical coverage; however, inadequate measurement of subcortical structures remains a significant limitation of the technology. Nevertheless, the ecological capabilities of fNIRS make it a highly attractive neuroimaging technology for neurocognitive investigations of interpersonal processes. The potential for implementation of fNIRS in clinical settings given its relatively low cost, portability, and ability to continuously monitor cortical hemodynamic activity (Irani et al., 2007) also bodes well for its adoption in therapeutic settings for persons with personality disorders.

The present study would benefit from a stronger characterization of the hemodynamic response as it applies to the social exclusion paradigm. Distinguishing between total blood flow and oxy-Hb may assist in determining whether a relative decrease in oxygenation within a specific brain region for BPD participants is associated with a lack of a hemodynamic response. Another important and related limitation of the present study is that characterization of the structural integrity of the frontal lobes was not
carried out. The relative deactivation of right PFC during interpersonal exclusion for persons with BPD may be related to structural abnormalities as well as functional deficits (Hillary & Biswal, 2007).

5. CONCLUSIONS AND FUTURE DIRECTIONS

The present study provides evidence of potentially important interactions among interpersonal function, personality, and psychopathology. The personality disorders are certainly complex neurobehavioral conditions with a multitude of factors which may influence the development of severe character pathology. It is at the intersection of biological and psychosocial influences where traditional neurocognitive investigations have been limited. Ecological functional neuroimaging technologies afford the opportunity to examine the interplay among biological and psychosocial factors, suggesting possible neurocognitive mechanisms which may underlie the development of specific personality disorder symptoms. The present findings are among the first to demonstrate abnormal functioning of right PFC during an actual social interaction for persons with BPD, linking relative deactivation of this region with core interpersonal and psychopathological features of BPD. These findings are consistent with previous neurocognitive investigations implicating predominantly right hemisphere deficits in BPD, and they highlight the potential relevance of deficits in social-cognitive processes involving the self to BPD psychopathology.

Future investigations should further explore the relationship between interpersonal function in BPD, as well as other personality disorders, and PFC function during social interactions. Measures of self-other attributions of mental state may provide further information regarding the mechanism of right hemisphere deactivation
and interpersonal dysfunction in BPD. The advantage of using fNIRS as a measure of cortical function is the ability to gauge hemodynamic activity during genuine rather than contrived or simulated social interactions. Studies may benefit from identifying the neural circuits involved in specific interpersonal dysfunctions which may be associated with particular personality disorders. Characterization of these cortical systems may allow for targeted interventions to alter these specific brain regions or circuits which seem to function aberrantly in interpersonal interactions.

Interventions may include biological treatments as well as psychosocial therapies. Once such biological intervention is repetitive transcranial magnetic stimulation, a noninvasive technique which has demonstrated some utility in alleviating mood symptoms, possibly by disrupting dysfunctional interactions among implicated neural circuits (Mitchell & Loo, 2006). With regard to psychosocial interventions, the implementation of neurocognitive technologies in clinical settings may provide clinicians with an additional tool for treatment. fNIRS may be a particularly attractive technology for translation to clinical settings given the technology’s portability and cost efficiency (Chute, 2002; Irani et al., 2007; Zabel & Chute, 2002). In considering the utilization of fNIRS and other cognitive technologies in psychotherapy, one might imagine that specific psychotherapeutic approaches or techniques may exert an influence upon functioning of specific brain regions or systems. Using a biofeedback-type approach, clinicians could potentially use patterns of brain activity evoked by specific therapeutic techniques as reliable predictors of the effectiveness of a given technique for modifying the behaviors or cognitions of an individual patient. As applied to BPD, fNIRS may serve as a form of biofeedback regarding the engagement of certain cortical systems
during dysfunctional social exchanges, perhaps allowing the patient to learn how changes in subtle interpersonal behaviors or utilization of specific cognitive techniques may recruit brain regions necessary for successful interpersonal engagement. With regard to mindfulness-based psychotherapeutic approaches, allowing the patient to “see” the brain while anxious or depressed or interpersonally disengaged may assist the patient in gaining perspective on these internal events, perhaps aiding them in simply observing the neurophysiological manifestations of these internal events rather than engaging in an internal “struggle” with them. Indeed, the possibilities for integrating ecological neurocognitive technologies such as fNIRS in clinical settings are boundless.

Modifications of the current paradigm seem warranted should the paradigm be considered in future studies. First, it would be useful to video record the social exclusion paradigm in order to make ratings of behaviors which occur during the course of the task. This may be useful to test various explanations for why BPD participants might demonstrate inefficient recruitment of PFC regions during the inclusion condition (i.e., disengagement, suspiciousness, not taking the task seriously). Second, the level of ambiguity of the interpersonal situation seemed to be an important factor in elucidating the neurocognitive differences between BPD and healthy participants. The more salient manipulation of exclusion revealed in the present study appeared to reach ceiling levels with regard to perceived feelings of rejection. Thus, the paradigm may benefit from increasing the ambiguity of the social exclusion condition by perhaps withholding more cards from the participant compared with the inclusion condition but not to the extent that the manipulation was so obvious. Creating conditions which vary according to the extent
to which the participant is included in the task may yield interesting findings, presumably by way of BPD participants’ misreading of ambiguous social interactions.

Finally, the present findings demonstrate the utility of integrating personality theory-based interpersonal conceptualizations of personality disorder with studies of neurocognitive function. Cross-disciplinary collaborations seem crucial to disentangle the complex etiologies of personality disorder which likely involve an interaction among biological and psychosocial factors in a developmental context. Prospective studies which trace the development of cognitive, affective, and interpersonal processes in an ecologically valid fashion may yield a more comprehensive account of the etiologies involved in the development of personality disorder. Future investigations necessitate a multitrait-multimethod approach (Campbell & Fiske, 1959) to the conceptualization of personality disorder, with due emphasis placed on both neurobiological and psychosocial variables in the development and maintenance of these complex neurobehavioral conditions.
Table 1. Demographic characteristics of BPD and healthy participants.

<table>
<thead>
<tr>
<th></th>
<th>BPD ($n = 9$)</th>
<th>HC ($n = 10$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>22.44 (7.62)</td>
<td>19.00 (1.05)</td>
</tr>
<tr>
<td>Education (years)</td>
<td>13.22 (1.86)</td>
<td>12.90 (.876)</td>
</tr>
<tr>
<td>Ethnicity ($n$)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White (not of Hispanic Origin)</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Black (not of Hispanic Origin)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Asian or Pacific Islander</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

*Note:* Means and standard deviations provided for age and education. BPD = borderline personality disorder, HC = healthy controls.
Table 2. BPD and healthy participant scores on personality measures.

<table>
<thead>
<tr>
<th>Measure</th>
<th>BPD (n = 9)</th>
<th>HC (n = 10)</th>
<th>t (two-tailed)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BDI-2 (total)</td>
<td>16.22 (5.36)</td>
<td>1.30 (1.06)</td>
<td>8.65</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>BIS-11 (total)</td>
<td>66.00 (7.91)</td>
<td>53.50 (6.65)</td>
<td>3.74</td>
<td>.002</td>
</tr>
<tr>
<td>DIPD Rejection Fear (total)</td>
<td>2.22 (0.55)</td>
<td>0.10 (0.21)</td>
<td>11.40</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>IASR-B5 (z-score)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assured-Dominant</td>
<td>-0.06 (0.81)</td>
<td>0.17 (1.17)</td>
<td>-0.50</td>
<td>.62</td>
</tr>
<tr>
<td>Arrogant-Calculating</td>
<td>0.33 (0.76)</td>
<td>-0.45 (1.01)</td>
<td>1.89</td>
<td>.08</td>
</tr>
<tr>
<td>Cold-hearted</td>
<td>0.52 (0.88)</td>
<td>-0.55 (0.86)</td>
<td>2.68</td>
<td>.02</td>
</tr>
<tr>
<td>Aloof-Introverted</td>
<td>0.52 (0.95)</td>
<td>-0.059 (0.69)</td>
<td>2.94</td>
<td>.009</td>
</tr>
<tr>
<td>Unassured-Submissive</td>
<td>0.09 (0.77)</td>
<td>-0.23 (1.12)</td>
<td>.72</td>
<td>.48</td>
</tr>
<tr>
<td>Unassuming-Ingenuous</td>
<td>-0.46 (0.74)</td>
<td>0.50 (1.02)</td>
<td>-2.3</td>
<td>.03</td>
</tr>
<tr>
<td>Warm-Agreeable</td>
<td>-0.44 (0.96)</td>
<td>0.41 (0.95)</td>
<td>-1.92</td>
<td>.08</td>
</tr>
<tr>
<td>Gregarious-Extraverted</td>
<td>-0.45 (0.95)</td>
<td>0.59 (0.58)</td>
<td>-2.95</td>
<td>.009</td>
</tr>
<tr>
<td>MMPI-2 (raw scores)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paranoid</td>
<td>10.89 (2.57)</td>
<td>2.90 (2.64)</td>
<td>6.66</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Schizoid</td>
<td>7.89 (3.89)</td>
<td>4.40 (2.95)</td>
<td>2.22</td>
<td>.04</td>
</tr>
<tr>
<td>Schizotypal</td>
<td>14.67 (5.55)</td>
<td>3.80 (3.91)</td>
<td>4.98</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Antisocial</td>
<td>10.00 (2.06)</td>
<td>3.60 (2.76)</td>
<td>5.68</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Borderline</td>
<td>13.22 (3.63)</td>
<td>5.50 (2.22)</td>
<td>5.66</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Histrionic</td>
<td>11.33 (3.08)</td>
<td>14.00 (2.62)</td>
<td>-2.04</td>
<td>.06</td>
</tr>
<tr>
<td>Narcissistic</td>
<td>14.89 (2.76)</td>
<td>16.90 (2.92)</td>
<td>-1.54</td>
<td>.14</td>
</tr>
<tr>
<td>Avoidant</td>
<td>19.89 (6.13)</td>
<td>6.50 (5.06)</td>
<td>5.21</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Dependent</td>
<td>9.00 (3.71)</td>
<td>3.20 (3.26)</td>
<td>3.63</td>
<td>.002</td>
</tr>
<tr>
<td>Compulsive</td>
<td>7.33 (1.58)</td>
<td>3.10 (1.66)</td>
<td>5.67</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

*Note:* Means and standard deviations provided for all scales. BPD = borderline personality disorder, HC = healthy controls; BDI-2 = Beck Depression Inventory-2; BIS-11 = Barratt Impulsiveness Scale-11; DIPD = Diagnostic Interview for DSM-IV Personality Disorders; IASR-B5 = Interpersonal Adjective Scales: Big Five Version; MMPI-2 = Minnesota Multiphasic Personality Inventory-2 Personality Disorder Scales (Morey et al., 1985).
Table 3. BPD and healthy participant scores on brief rating scales during interpersonal rejection task.

<table>
<thead>
<tr>
<th></th>
<th>BPD (n = 9)</th>
<th>HC (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pre-task Rating:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>3.44 (1.59)</td>
<td>1.40 (.52)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>3.89 (1.83)</td>
<td>2.60 (1.96)</td>
</tr>
<tr>
<td><strong>Post-Inclusion Condition:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>2.67 (1.00)</td>
<td>1.22 (.44)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>3.33 (1.50)</td>
<td>2.67 (2.50)</td>
</tr>
<tr>
<td>Inclusiveness</td>
<td>8.56 (1.13)</td>
<td>8.80 (1.40)</td>
</tr>
<tr>
<td>Rejection</td>
<td>2.22 (.83)</td>
<td>1.20 (.63)</td>
</tr>
<tr>
<td><strong>Post-Exclusion Condition:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>3.33 (2.00)</td>
<td>1.67 (1.00)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>3.78 (1.99)</td>
<td>2.78 (2.68)</td>
</tr>
<tr>
<td>Inclusiveness</td>
<td>2.89 (1.36)</td>
<td>2.60 (1.27)</td>
</tr>
<tr>
<td>Rejection</td>
<td>6.44 (2.65)</td>
<td>7.10 (1.79)</td>
</tr>
</tbody>
</table>

*Note: All ratings were made using a scale ranging from 1 (not at all) to 10 (extremely severe). Means and standard deviations provided for all scales. BPD = borderline personality disorder; HC = healthy control.*
Table 4. Estimated marginal means and standard errors of oxy-Hb per channel for BPD \((n = 9)\) and healthy participants \((n = 10)\) for inclusion and exclusion conditions.

<table>
<thead>
<tr>
<th>Channel</th>
<th>Inclusion Condition</th>
<th>Exclusion Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BPD</td>
<td>HC</td>
</tr>
<tr>
<td>1</td>
<td>.631 (.296)</td>
<td>-.150 (.274)</td>
</tr>
<tr>
<td>2</td>
<td>.821 (.429)</td>
<td>-.183 (.398)</td>
</tr>
<tr>
<td>3</td>
<td>.890 (.359)</td>
<td>-.309 (.333)</td>
</tr>
<tr>
<td>4</td>
<td>.644 (.581)</td>
<td>.534 (.539)</td>
</tr>
<tr>
<td>5</td>
<td>.655 (.339)</td>
<td>-.315 (.314)</td>
</tr>
<tr>
<td>6</td>
<td>.415 (.281)</td>
<td>.488 (.261)</td>
</tr>
<tr>
<td>7</td>
<td>.777 (.407)</td>
<td>-.324 (.377)</td>
</tr>
<tr>
<td>8</td>
<td>1.444 (.423)</td>
<td>.662 (.392)</td>
</tr>
<tr>
<td>9</td>
<td>.624 (.545)</td>
<td>-.491 (.506)</td>
</tr>
<tr>
<td>10</td>
<td>-.141 (.377)</td>
<td>1.449 (.349)</td>
</tr>
<tr>
<td>11</td>
<td>.454 (.296)</td>
<td>-.031 (.274)</td>
</tr>
<tr>
<td>12</td>
<td>-.064 (.265)</td>
<td>.717 (.246)</td>
</tr>
<tr>
<td>13</td>
<td>.900 (.299)</td>
<td>-.255 (.277)</td>
</tr>
<tr>
<td>14</td>
<td>-.189 (.369)</td>
<td>.685 (.342)</td>
</tr>
<tr>
<td>15</td>
<td>.724 (.392)</td>
<td>-.746 (.363)</td>
</tr>
<tr>
<td>16</td>
<td>.380 (.303)</td>
<td>.157 (.281)</td>
</tr>
</tbody>
</table>

*Note:* Means and standard deviations provided above.  BPD = borderline personality disorder; HC = healthy control.
Table 5. Correlation matrix of interpersonal scales, personality disorder traits, and mean oxy-Hb in channel 10 during the inclusion condition.

<table>
<thead>
<tr>
<th></th>
<th>PAR</th>
<th>ANT</th>
<th>FG</th>
<th>NO</th>
<th>Oxy-Hb</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAR</td>
<td>-</td>
<td>.72*</td>
<td>.63*</td>
<td>-.60*</td>
<td>-.57*</td>
</tr>
<tr>
<td>ANT</td>
<td></td>
<td>-</td>
<td>.74*</td>
<td>-.77*</td>
<td>-.57*</td>
</tr>
<tr>
<td>FG</td>
<td></td>
<td></td>
<td>-</td>
<td>-.96*</td>
<td>-.54*</td>
</tr>
<tr>
<td>NO</td>
<td></td>
<td></td>
<td></td>
<td>-</td>
<td>-.56</td>
</tr>
<tr>
<td>Oxy-Hb</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-</td>
</tr>
</tbody>
</table>

Note: FG = Aloof-Introverted; NO = Gregarious-Extraverted; Oxy-Hb = mean level of oxygenated hemoglobin in channel 10

* Correlations significant at $p \leq .01$
Figure 1. Circumplex model of interpersonal behavior. From Trapnell and Wiggins (1990).
Figure 2. Diagram of fNIRS sensor pad (a), corresponding channels on standard brain (b), and areas of coverage corresponding to Brodmann areas 9, 10, 45, and 46 (c).
Figure 3. Mean levels of oxy-Hb during inclusion and exclusion conditions for regions of interest in channels 10 (a) and 15 (b).
Figure 4. Activation map displaying greater oxy-Hb in right prefrontal cortex for healthy controls compared with borderline personality disorder participants during interpersonal inclusion condition.

*Note:* Activation map (healthy control > borderline personality disorder) overlaid on standardized brain image. Represents univariate \( F \) statistic (covarying for depression and Axis I disorders) comparing healthy control and borderline patients during inclusion condition \((p = .02)\).
Figure 5. Time course of oxy-Hb during the inclusion condition for channel 10 for borderline personality disorder and healthy control participants.
Figure 6. Scatterplot displaying mean levels of oxy-Hb in channel 10 and scales from the Interpersonal Adjective Scale-Revised ($n = 19$).
Figure 7. Mean level of oxy-Hb in channel 8 for inclusion and exclusion conditions.

Note: Error bars represent 95% confidence interval.
Figure 8. Theorized model relating interpersonal disposition to abandonment fears as mediated by right prefrontal cortex function.
LIST OF REFERENCES


APPENDIX A: DSM-IV DIAGNOSTIC CRITERIA FOR BORDERLINE PERSONALITY DISORDER

A pervasive pattern of instability of interpersonal relationships, self-image, and affects, and marked impulsivity beginning by early adulthood and present in a variety of contexts, as indicated by five (or more) of the following:

1. Frantic efforts to avoid real or imagined abandonment. Note: Do not include suicidal or self-mutilating behavior covered in Criterion 5.
2. A pattern of unstable and intense interpersonal relationships characterized by alternating between extremes of idealization and devaluation.
3. Identity disturbance: markedly and persistently unstable self-image or sense of self.
4. Impulsivity in at least two areas that are potentially self-damaging (e.g., spending, sex, substance abuse, reckless driving, binge eating). Note: Do not include suicidal or self-mutilating behavior covered in Criterion 5.
5. Recurrent suicidal behavior, gestures, or threats, or self-mutilating behavior
6. Affective instability due to a marked reactivity of mood (e.g., intense episodic dysphoria, irritability, or anxiety usually lasting a few hours and only rarely more than a few days).
7. Chronic feelings of emptiness
8. Inappropriate, intense anger or difficulty controlling anger (e.g., frequent displays of temper, constant anger, recurrent physical fights)
9. Transient, stress-related paranoid ideation or severe dissociative symptoms

From American Psychiatric Association (2000).
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2006          Philadelphia Neuropsychology Society Student Research Award
2006          American Neuropsychiatric Association Young Investigator Award
2005–2008     Postgraduate Doctoral Fellowship, Natural Sciences and Engineering Research Council
2004–2005     Postgraduate Masters Fellowship, Natural Sciences and Engineering Research Council
2003–2005     Dean’s Fellowship, Drexel University

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