HOW CLINICIANS RESPOND TO BORDERLINE PERSONALITY DISORDER:

AN FMRI STUDY

by

QINGYANG LI

(Under the Direction of Jennifer E. McDowell)

ABSTRACT

The current study used functional magnetic resonance imaging (fMRI) to evaluate clinicians’ brain activity associated with their attitudes toward borderline personality disorder (BPD). Nine clinicians were surveyed about their experience with BPD patients and then were scanned while they read vignettes describing clients with BPD and clients without any mental disorder in alternating blocks. For each vignette, a score was provided by the participants to evaluate their efficacy to treat the client described in the vignette. Each vignette was presented in a series of three screens, the first screen providing gender and diagnosis of the client (diagnosis screen), the 2nd and 3rd screen describing three salient symptoms from that diagnosis (symptom screen I and II).

Reading the word borderline (in the diagnosis screen) resulted in increased activity in the left amygdala, left thalamus, bilaterally in putamen, caudate, substantia nigra, insula, in the left superior and middle temporal gyri, left fusiform, left parahippocampal gyrus, left inferior parietal lobule, left angular cortex, and in the bilateral superior frontal gyrus.

Reading BPD symptoms in symptom I screen was associated with increased activity in the left caudate, cerebellum, bilaterally in visual cortex and posterior cingulate gyrus. One area of deactivation was also found in the right postcentral gyrus. In the symptom II screen, reading BPD related content resulted in increased activity in the right fusiform,
parahippocampal gyrus, bilaterally in posterior cingulate gyrus, inferior parietal gyrus, angular gyrus, cerebellum, insula, and inferior frontal gyrus. I also found five of regions of interest activated when reading the symptom II screen where activation correlated linearly with the self-reported efficacy score, the bilateral insula, bilateral angular gyrus and right middle frontal gyrus. Deactivations were also found in right postcentral gyurs, right precentral gyrus, left visual cortex and left superior frontal gyurs. This study thus showed that BPD related stimuli had emotional charge to experienced clinicians.

Index word:  borderline personality disorder, professional-patient relations, emotional perception, self-efficacy rating, fMRI, limbic system
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This thesis is dedicated to Qing Liu.
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CHAPTER 1
INTRODUCTION

Borderline Personality Disorder (BPD)

Borderline personality disorder (BPD hereafter) is characterized as a diagnostic disorder for the first time in the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) published by the American Psychological Association in 1980. In the most current version of DSM, BPD is defined as a "pervasive pattern of instability of personal relationships, self-image, and affects, and marked impulsivity that begins by early adulthood and is present in a variety of contexts" (pp. 706, 4th edition, text revision, DSM-IV-TR; American Psychological Association, 2000). Patients with BPD often suffer from affective dysregulation, interpersonal dysregulation, self-dysregulation, behavioral dysregulation and cognitive dysregulation (Linehan, 1993). BPD is often accompanied by multiple Axis I and Axis II disorders (Sansone et al., 2003; Zimmerman et al., 2005).

BPD patients are high users of health, mental health, and social services and the estimated economic cost is as high as $50,000 per person, per year (Bateman & Fonagy, 2003). BPD is a severer mental disorder with high prevalence in clinical settings. BPD is one of the most commonly diagnosed and researched personality disorders (PDs) (Trull, 2001). It is more common than many other very well-known disorders, such as schizophrenia. According to DSM-IV-TR, around 2% of the general population that is approximately four million people in the U.S. have BPD. More recent studies on personality disorders in the U.S. found that the prevalence of BPD were between 0.5% to 5.9% (Lenzenweger et al., 2007; Grant et al., 2008). In primary care, psychiatric inpatient
and outpatient settings, the prevalence rate of BPD was reported to be at least 4 times higher than that in the general population (Gross et al., 2002;) and the reported prevalence rate were ranging from 6.4% to 50% (Bender et al., 2001; Gunderson, 2009; Korzekwa et al., 2008; Sansone et al., 2003; Sansone et al., 2001; Torgersen, 2005; Trull, 2001; Widiger & Rogers, 1989).

Many patients with BPD have interpersonal style portending difficulty in establishing working alliance with care providers and clinicians (Freeman et al., 2005) and `their effort to get needed services and help often result in frustration, anger, depression and failure' (pp. 504, Ivanoff et al., 2007). BPD is also associated with significant high rate of suicide, suicidal attempts, and other self-harm behaviors (Nehls, 1992; Sansone et al., 2002). BPD patients often create split between staff members when they are in treatment and have high dropout rate from therapy (Cleary et al., 2002; Markham & Trowe, 2003). As a result of direct experience or vicarious learning, clinicians sometimes avoid treating or try to limit the number of patients with BPD in their practice (Ivanoff et al., 2007).

**Clinicians’ Attitude towards BPD**

Given that the most challenging professional stressors identified by therapists are client anger, threats of suicide and suicidal behaviors (Hellman et al., 1986), no wonder BPD has a bad reputation among clinicians. It has been reported that even the word *borderline* has an emotional charge and triggers negative cognitions and emotions toward BPD patients (Fraser & Gallop, 1993; Krawitz & Watson, 2003).

Surveys have been used on psychiatric staff members (Cleary et al., 2002; James & Cowman, 2007) to examine their attitude toward BPD patients and the data showed
most of the respondents perceived BPD patients as more difficult to treat and communicate than other patients. Woollaston and Hixenbaugh (2008) interviewed six members of psychiatric nursing teams with open-ended questions to explore participants’ relationships with BPD patients from their own perspective. Nurses perceived BPD patients in a negative manner and described them as powerful, dangerous, unrelenting “destructive whirlwinds”. In a recent published study, Bodner et al. (2010) have developed an inventory for measurement of emotional attitudes toward BPD patients. They have not only confirmed the negative emotional attitudes among clinicians toward BPD patients and but also showed that the negative emotions could be mainly explained by suicidal tendencies of BPD patients.

It has been reported recently that exposure to dialectical behavior therapy (DBT) is linked to more positive outcomes (Linehan, 1993; Linehan et al., 1991; Linehan et al., 2006). DBT is an evidence-based treatment for BPD developed by Linehan and colleagues (Linehan, 1993; Linehan et al., 1991). Linehan suggested that the common factor underlying all the abnormal behaviors was dysregulation of emotion. Thus, DBT combined standard cognitive-behavioral techniques and mindful awareness largely derived from Buddhist meditative practice for emotion regulation. Comparing to treatment-as-usual, DBT is associated with fewer incidences of suicide attempts, less medically server parasuicides, fewer impatient hospitalization, less self-harm behavior, reduced anger expression, and increased treatment retention (Evershed et al., 2003; Koons et al., 2001; Linehan et al., 1991; Linehan et al., 1999; Turner, 2000; van den Bosch et al., 2002; Verheul et al., 2003). DBT also significantly reduces drug use in BPD patient with drug dependence (Linehan et al., 1999; van den Bosch et al., 2002).
No study has been done to explore the effect of DBT on clinicians’ attitude toward BPD at the moment. There is, however, one study evaluated BPD family members’ attitude change in respond to an education program on DBT (Hoffman, 2005). In this study, relatives of patients with BPD participated in a 12-week education program on DBT and completed self-reported questionnaires pre- (baseline), post-, and 6-month after the program. Significant reductions in grief and burden from pre- to post-baseline assessment were found in the participants. The reduction remained according to the 6 months follow up.

Current Study

Although the studies on care providers’ and clinicians’ negative emotional attitudes toward BPD patient mentioned above agree with each other, they all depended on self-reported subjective measures. To provide an objective measure of clinicians’ perception and attitude of BPD, the current study was planned to use functional magnetic resonance imaging (fMRI) to evaluate clinicians’ brain activity while they were presented with BPD related stimuli. The current study aims to determine whether BPD could evoke unique emotional responses from clinicians compared to other, less stigmatized situation.

Our hypotheses are as follows: First, I expect to see increased activity in limbic regions (circuitry known to underlie fear processing) in care providers when presented with BPD-related stimuli compared with neutral stimuli. Second, I hypothesize that brain activity will be correlated with clinically-relevant outcome variables such as willingness to see these types of patients, experiences with DBT, and ratings of perceived self-efficacy in the treatment of BPD.
CHAPTER 2
METHODS

Participants

Nine participants (age: M= 37.4 years, SD= 5.95; 5 males) were recruited via advertisement in the UGA clinic and through email messages to the Athens Area Psychological Association (AAPA) email listserv. All participants were experienced clinicians who had been licensed and practicing independently for at least two years (years of practice: M=5.2, SD = 3.2) prior to participation.

All participants were right-handed, free of serious physical health problems, and absent of known neurological hard signs. Participants were also screened for contraindications for functional magnetic resonance imaging (fMRI). All participants provided informed consent in accordance with University of Georgia’s Institutional Review Board requirements and they were paid $50 for their participation in the experiment.

Procedure

Pre-scanning Questionnaire

A questionnaire was used to assess participants’ experience with BPD patients before fMRI scanning session. This clinician’s experience questionnaire (see Appendix) included a variety of questions pertaining to the participants’ experience with various patient populations, perceptions of success with these various populations, willingness to accept and treat these populations, familiarity with the diagnostic criteria for various disorders (as defined by the DSM-IV-TR), and training in certain treatment modalities (i.e., DBT). Relevant questions (i.e., with regard to BPD) were surrounded with filler
items of a similar type to insure that the participants were unaware of the general focal points of the study.

**Image Acquisition**

Participants’ brain images were scanned with a General Electric 16-channel fixed-site SignaHDx 3 Tesla magnet (General Electric, Milwaukee, WI) at the Bio-Imaging Research Center (BIRC) at the Coverdell Center for Biomedical and Health Sciences at the University of Georgia. Practice stimuli and task instructions were given to the participants before they entered the scanner. Participants were then put into the scanner and positioned in a supine position. During the scan, participants were provided with earplugs to protect their ears from noise from the scanner. Memory foam pads and head strap (NoMoCo™ Pillow Support System, http://www.nomocopillow.com/) were used to help participants to reduce head motion to minimum. An LCD Projector (NEC View technology, Tokyo, Japan) displayed stimuli onto a rear projection screen standing 174 cm from participants' nasion. A mirror box was placed 16 cm above and in front of the participant's eyes so the participants were able to see the stimuli posted outside of the scanner comfortably.

The scanning started with a parallel imaging calibration (ASSET, FOV = 30cm, slice thickness 6.0mm, 31slices, scan time 6 sec) to provide a coarse measurement of the magnetic field in the presence of the participant. Then, a rapid three-dimensional T1-weighted structural MRI scan of high resolution was collected (BRAVO protocol: ASSET factor =2, echo time [TE] = 4.6 msec, repetition time [TR] = 10.8 msec, flip angle = 13°, number of excitations [NEX] = 0.5, matrix = 352 × 224, field of view [FOV] = 24 cm [resulting in an in-plane resolution of 0.68 × 1.07], slice thickness of 1.2 mm,
frequency direction A/P, 150 slices, scan time 3 min 7 sec, bandwidth = 25 kHz, phase FOV = 1, time to inversion [prep time] = 450 ms). The resulted images of this structural scan were used to define the AC-PC oblique plane (the line connecting the superior edge of the anterior commissure and the inferior edge of the posterior commissure) for the following functional scan.

The blood oxygenation level-dependent (BOLD) contrast was obtained during functional run. Prior to the functional run, participants were reminded of specific task instructions. A series of T2*-weighted functional images then were obtained [oblique prescription, gradient-echo echo-planar imaging pulse sequence (EPI) with data points in k-space sampled line by line: matrix = 64 x 64, FOV = 22 cm (resulting in an in-plane resolution of 3.437 x 3.438), slice thickness of 4 mm, TE = 30 msec, TR = 2000 msec with a single-shot interleave, flip angle = 90°, 33 slices, frequency direction R/L, bandwidth = 250 kHz, phase FOV = 1, NEX = 1, ramp-sampling turned on, ASSET (acceleration factory = 2.0 Ph)] while the participants were performing an evaluation task. Brain coverage for functional scans was defined by placing the most superior scan plane tangent to the highest point of the somatosensory cortex and parallel to the oblique plane. Four null repetitions were added to the beginning of the functional run to allow the magnetization to stabilize at steady state equilibrium (brain images acquired during null repetition were not included in the analysis). The scan time of the functional run was 7 min 38 sec.

Finally, a three-dimensional T1-weighted structural MRI scan of high-resolution for definition of anatomical structures within each brain was acquired (fast spoiled gradient echo [FSPGR] protocol; TE = Min-Full, TR = 7.8 msec, flip angle = 20°, NEX =
1, matrix = 256 × 256, FOV = 24 cm [resulting in an in-plane resolution of 0.9375 × 0.9375], slice thickness of 1.2 mm, frequency direction A/P, 150 slices, scan time 6 min 20 sec, bandwidth = 31.25 kHz, phase FOV = 0.7, prep time 450 msec).

**Stimulus**

**Evaluation Task**

During functional scanning, each participant performed a silent reading and evaluation task. In each trial, the participant was asked to silently read a vignette describing one client who was referred to the participant for treatment. After the reading of the vignette, the participant was asked to rate the effectiveness on how s/he can treat the client. As shown in Figure 2.1, the stimuli (vignettes and the rating question) were presented on a visual display projected onto the screen in front of the scanner. Each vignette was presented as text through a series of three screens, the first screen providing gender and diagnosis of the patient (Diagnosis screen; capital letters was used to emphasize the diagnosis), the 2\textsuperscript{nd} and 3\textsuperscript{rd} screen describing three salient symptoms from that diagnosis (Symptom screen I and II). Separating one vignette into three screens allowed us to control the reading time more precisely. It also provided us the possibility to see the dynamic brain activation patterns in three time frames so that the distinction can be made from activation by reading the word *borderline personality disorder* and the activation of reading the symptoms of the disorder. The two screens of symptoms (Symptom I &II) were different from each other not only in order of presentation but also in closeness to the response. Although the participant was ask to just read the stimulus during the symptom screens, the preparation of the response might happen paralleled with the reading of the symptom II screen since a response was required right after it
(Hinojosa et al., 2010). The use of two symptom screens could possibly separate the semantic processing from the response preparation.

There was another screen following the vignette and posing the question “how effectively could you treat this patient”. Participants were asked to provide the effectiveness rating with a 1-5 rating scale (1 = Not Effectively; 5 = Very Effectively) by pressing one of the five buttons on an MRI compatible five-button response keypad (LUMItouch™ fMRI Optical Response Keypad, Photon Control Inc., Burnaby, BC, Canada) positioned in the participant’s right hand. Each screen lasted 7.5 seconds. Stimulus delivery and response recording were controlled by Presentation software (Neurobehavioral Systems, Albany, California).

Two types of vignettes were used: a) vignettes describing patients with borderline personality disorder (BPD condition) and b) vignettes describing people without psychological disorder (Neutral control condition, see figure 2.1 and examples below). The functional run consisted of 15 alternating blocks/trials of neutral control (NC) condition (n = 8 trials) and BPD condition (n = 7 trials). Block design was used for the functional run because it can optimize contrast to noise ratio and maximize detection power. The vignettes were matched for level of detail and number of words.

Examples of Vignettes

*Borderline Personality Disorder (BPD):*

Sample 1: a) Rachel is a female diagnosed with BORDERLINE PERSONALITY DISORDER. b) Rachel endorses engaging in impulsive behavior, including risky sex which often co-occurs with alcohol and illicit drug use. c) She also reports recurrent suicidal gestures and self-mutilating behavior, characterized by cutting of her thighs and
stomach. In addition, Rachel reports symptoms of dissociation when confronted with interpersonal stress.

Sample 2: a) Jamie is a male diagnosed with BORDERLINE PERSONALITY DISORDER. b) Jamie reports marked reactivity of mood, characterized by intense episodes of irritability and dysphoria. During these times, he reports that he frequently engages in self-harming behavior and has had several failed suicide attempts. c) He also reports intense, uncontrollable anger which often results in physical fights.

*Neutral Control (NC)*:

Sample 3: a) Kerri is a female who HAS NO PSYCHOLOGICAL DISORDER. b) Kerri reports feelings of worthlessness and sadness following a sports-related injury in her final year as a college athlete. c) She indicates that she is less motivated to complete her schoolwork and is feeling isolated from her teammates since she is not able to compete.

Sample 4: a) Mason is male who HAS NO PSYCHOLOGICAL DISORDERS. b) Mason reports that he is feeling increased pressure to find a long-term partner because many of his close friends have recently gotten married. c) He also reports experiencing increased perspiration and rapid breathing when approaching women and describes thoughts about being inadequate and unattractive.

**Practice Task**

To get the participants prepared for the testing environment, the stimuli, and the response keypad, participants were asked to perform a short practice run while lying in the scanner right before the functional run. The vignettes in the practice run were presented the same way as those in the functional run except that they were irrelevant to
any psychological disorder (e.g. instructions to the reading/evaluation task or general information about the University of Georgia and the BioImaging Research Center). The questions following the vignettes were “How effective were these instructions?” or “how effectively could you read this information?” Participants provided responses via the keypad. Participant’s responses of practice run was inspected right after the run to make sure the participant could read all the stimuli and know which key to press for a specific rating. No brain imaging data was collected during the practice.

Analysis

Questionnaire and in-Scanner Ratings

The following eight BPD related items were extracted and scored from the clinician’s experience questionnaire: 1) training in DBT: How much training (e.g., graduate coursework/training, seminars, intensive supervision, etc.), if any, do you have with DBT? 2) Experience with DBT: Rate your experience (e.g., use in grad school, internship, private practice, etc.) with DBT. 3) BPD patients treated [all]: Approximately how many clients have you treated with BPD diagnoses in your career? 4) BPD patients treated [2-year]: Approximately how many clients have you treated with BPD diagnoses in the past two years? 5) Comfort: Rate your level of comfort when treating patients with BPD. 6) Success: Indicate how successful (e.g., increased functioning decreased distress) you have been when treating patients/clients with BPD. 7) Enjoyableness: Indicate how much you enjoy treating patients/clients with BPD. 8) Acceptance: Indicate how likely you would be to accept a referral for a patient/client with BPD. Items 1) ~ 2) and 4) ~ 8) were self-rating questions which could be answered by a 7-point reply scale (1-to-7, 1 = not at all or no, 7=very much or extensive). The scores of these items were then entered
in a Pearson correlation analysis together with the participants’ ratings during the fMRI session.

Participants’ ratings of effectiveness between BPD and NC trials while they were in scanner were subjected to a paired-samples t-test. The differences score (NC - BPD) from the in-scanner ratings was also computed for correlation analysis with values from questionnaire items and brain activities from ROI analysis (see below) to see if participants’ behavioral performance in the scanner could be predicted by self-reported experience and brain activity. The t-test, score computation, and correlation analyses were performed using software Statistical Package for the Social Sciences (SPSS 19.0; IBM SPSS Inc., Chicago, IL).

**FMRI Data**

Image preprocessing and statistical analysis of fMRI data was conducted using Analysis of Functional NeuroImages: AFNI version 2010_10_19_1028, Jan 27 2011 (Cox, 1996). Functional images (2D slices) were converted into three-dimensional volumes in AFNI .BRIK format. The first eight second of images acquired during four null repetitions while the magnet field was gaining stabilization were eliminated. For each participant, all functional data were first subjected to an AFNI program 3dDespike which checked and removed extreme outliers from the data. The functional dataset acquired using oblique prescription was transformed to a cardinal orientation and then aligned to the anatomical structural dataset. To correct for minor head movement over time, all volumes were then registered to an empirically determined optimal base volume. The base volume was derived from an automated recursive analysis of the root-mean-square adjustment for motion correction at each time point. Six motion parameters (three
translations and three rotations) were also calculated at this motion correction step. Data were smoothed spatially with a 4 mm full width, half-maximum (FWHM) Gaussian filter. BOLD signal was scaled to percentage signal deviation from the mean signal of each voxel.

The AFNI 3dDeconvolve program was used to implement multiple linear regression models. To compare differences in the brain activities between BPD and NC conditions on a screen by screen basis, reference vectors were created to model each screen of both the BPD and NC conditions. Three multiple regression models were created with three pair of task related reference vectors (e.g. diagnosis of BPD and NC, symptom I of BPD and NC, and symptom II of BPD and NC). Reference vectors for each screen/condition combination were convolved with a gamma variate model of the hemodynamic response function to account for the hemodynamic delay to peak BOLD responses. All regression models also included baseline parameters to remove nuisance variance in each voxel’s time series related to mean and linear drifts and the motion correction parameters. Resultant statistical parametric maps were then transformed to the standard Talairach space (Talairach & Tournoux, 1988) for further comparison across participants.

Second-level t tests were conducted on a voxel-by-voxel basis according to a random-effects model. Screen by screen neural results from within-group one-sample t tests were reported for the contrast of BPD versus NC to show the significant task-related BOLD signal differences between the two conditions. To correct for the multiple comparisons problem and protect against false positive obtained in fMRI data analysis, the AFNI AlphaSim program, a threshold/cluster method derived from Monte Carlo
simulation bootstrapping procedure (accounting for the 4mm FWHM Gaussian filter and with a connectivity radius of 5.7 mm), was applied to \( t \) maps. The simulations preserved family-wise alpha of .05 with a joint-probability threshold consisting of a voxel-wise threshold of \( p < .025 \) and a minimum three-dimensional cluster-volume threshold \( \geq 1088 \text{ mm}^3 \) (17 voxels \( \times 4^3 \text{ mm}^3 \)) that resulted in the whole-brain analysis. The resultant averaged, clustered \( t \) maps were used to identify regional BOLD signal changes associated with reading of BPD compare to NC vignettes within the participant group. The main effects of interest were BPD > NC and NC > BPD during the reading of the vignettes during each of the 3 screens.

**ROI analysis and correlation analysis**

Based on the statistic maps from each of the three screens, three sets of ROIs were determined to capture the BOLD difference in regions which were positive activated in reading of BPD versus NC vignettes. For each ROI, a sphere (radius 8mm) was positioned at the center of mass of each region that showed a significant effect. Mean percent signal difference for each screen was extracted from each ROI for each individual. The relationship between brain activity of reading the vignettes and behavioral performance of rating them was tested by entering the mean signal change in the voxels of mean activities in these regions into correlation analysis (Pearson’s \( r \)).
Participants performed 30-second trials of NC alternating with 30-second trials of BPD while their brains were scanned for functional images.
CHAPTER 3

RESULTS

Pre-scanning Questionnaire and in-scanner Ratings

Scores/values of the eight BPD related items from the pre-scanning questionnaire were subjected to a Pearson correlation analysis. Correlation coefficients were listed in Table 3.1. Significant and strong correlations were identified in 3 groups of variables. In the first group were the two variables related experience of DBT (more training were associated with more use of DBT in treating BPD), and in the second group were the two variables measuring the number of BPD patients that the participant had treated in his/her whole career or in the recent two years (more BPD patient treated in the recent two years was associated more BPD patient treated in the whole career). In the third group were the variables measuring participant’s level of comfort, enjoyableness while treating BPD patients and his/her willingness to accept BPD patient referrals. These three variables were all subjective measures of the participant’s experience towards BPD patients. The more comfortable and enjoyable the participant was when treating patients with BPD, the more likely s/he would accept a referral for patients with BPD. There was no other significant correlation found between the variables from the questionnaire data. It worth noting that the self-reported success rating on treating patient with BPD were not associated with any items on the questionnaire.

The effectiveness ratings in BPD and NC conditions obtained during the functional scan were also entered in the correlation analysis. Firstly, the effectiveness rating for the two conditions were significantly correlated ($r (7) = .72, p < .05$). Participants’ effectiveness in treating patient with BPD was associated with their
effectiveness in treating client with no mental disorders. Secondly, the self-reported success measure from the questionnaire was significantly correlated with the effectiveness rating in BPD \( r (7) = .79, p < .05 \) and NC \( r (7) = .76, p < .05 \) conditions. Higher success rating in BPD was associated with higher effectiveness rating in BPD and NC. At last, there was a strong correlation between participants’ training in DBT and their ratings in effectiveness in treating patients with BPD \( r (7) = .81, p < .05 \). More training in DBT was associated with higher effectiveness rating in treating BPD.

A paired-samples t-test was conducted to compare effectiveness rating scores in BPD and NC conditions. There was a significant difference in the scores on BPD \( (M=2.63, SD=1.18) \) and NC \( (M=4.47, SD=.45) \) conditions; \( t (7) = 5.77, p = 0.01 \). The difference score (NC - BPD) was calculated for further analysis (see below).

**FMRI Data**

One sample t-tests revealed significant differences in activity between BPD and NC trials in all the three screens (dx, sx1, sx2). Results from the whole-brain analyses of the functional run are shown in Figure 3.1.

\[ \text{BPD} > \text{NC} \] Reading the phrase “BORDERLINE PERSONALITY DISORDER” compared to “NO PSYCHOLOGICAL DISORDER” in the diagnosis screen significantly increased activity in the left superior and middle temporal cortex (BA 22), the fusiform gyrus (FUS, BA 37), inferior parietal lobule (IPL) and angular gyrus (AG) in the left parietal cortex, the left thalamus, the left pulvinar, the left amygdala, and adjacent left parahippocampal gyrus (PHG). Additional clusters of activation were found in the middle and superior prefrontal cortex, insula, putamen, caudate, and substantia nigra, bilaterally (See Figure 3.1a and Table 3.2).
The regions that showed greater activity when reading the symptoms of BPD patients compared to neutral control clients were reported for the two symptom presenting screens (Symptom I and II, see Method section). Significant differences in brain activity were found during the presentation of the Symptom I screen in left caudate, left cerebellum, and bilateral cingulate gyrus. There also was a large cluster covering bilateral occipito-parietal regions (cuneus, lingual gyrus, and precuneus) showing increased activity (see Figure 3.1b and Table 3.3). The clusters that showed enhanced activity in BPD compared to NC trials during the presentation of symptom II screen were increased in number, decreased in size, and more pronounced in frontal regions comparing to those during the presentation of symptom I. The clusters overlapped with right FUS and PHG, bilateral posterior cingulate gyrus, insula, PFC (inferior and middle frontal gyrus), AG, as well as the cerebellum (Figure 3.1c and Table 3.4).

NC < BPD (deactivation). Brain activity was also found enhanced during reading of neutral control versus BPD symptoms in several small and regionally distinct brain areas. During the presentation of symptom I, only a small region in right postcentral gyrus showed this increase. This increase of activity in reading of NC symptom (compare to BPD condition) in postcentral gyrus remained during the presentation of symptom II (with a small shift of the center of mass). Significant increases in activity of reading NC vs. BPD symptoms were also found in the left superior frontal gyrus, the left occipital cortex, and the right precentral gyrus.

ROI analysis and correlation analysis

To learn whether there was a relationship between brain activity and the effectiveness ratings as determined by the difference scores in participants’ ratings on
BPD compared to NC vignettes (NC – BPD). Three sets of ROIs were created for three screens of stimuli based on the activated clusters in the statistical parametric maps. See Figure 1 for the maps and Table 3.2, Table 3.3, and Table 3.4 for coordinates of the centers of mass of the clusters. Within the activation map associated with the reading of BPD compared to NC symptoms in the Symptom II screen (the third screen in one trial), there were 5 regions/clusters where the effect BPM > NC showed significant correlation with the effectiveness ratings, $r_s > 0.71$, $p < .05$ (see Figure 3.2). The regions were right insula/inferior frontal gyrus (IFG), left middle frontal gyrus (MFG)/insula, right MFG/IFG, right inferior parietal lobule (IPL)/ angular gyrus (AG), and left precuneus/AG. In all five ROIs, the difference in percent BOLD signal change was directly proportional to the differences in rating scores (see graphs in Figure 3.2). There was no significant correlation between brain activity and behavioral ratings found in ROIs identified during the reading of diagnosis information or symptom I (e.g. the first two screens of the vignettes). No significant correlation between items in pre-scanning questionnaire and brain activities was found, either.
Table 3.1 Correlations between BPD related items from the pre-scanning questionnaire.

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
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<tbody>
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</tr>
</tbody>
</table>

Note: Significant correlations are shown in bold fonts. *, p < 0.05; **, p < 0.01, (2-tailed). df = 6.
Figure 3.1 Activations for the contrast BPD - NC

Axial slices (top left z = -34 through bottom right z = 58, spacing = 4mm) displaying significant BOLD signal changes between BPD and NC in three screens: a) Diagnosis screen; b) Symptom screen I; and c) Symptom screen II. Areas associated with more BPD related than more NC related activation are shown in warm colors and areas associated with NC related activations are shown in cool colors. The background anatomical image was an averaged structural image of all 9 participants. Brain images were shown using radiological convention. BOLD, blood oxygenation level-dependent; BPD, borderline personality; NC, neutral control.
Table 3.2 Talairach Coordinates of the Centers of Mass for ROIs for the diagnosis screen.
Comparisons of overall brain activity obtained during reading of BPD diagnosis versus neutral condition.

<table>
<thead>
<tr>
<th>Hemisphere</th>
<th>Brain Regions</th>
<th>Brodmann area (BA)</th>
<th>Cluster size</th>
<th>Talairach coordinates</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>x</td>
</tr>
<tr>
<td><strong>BPD &gt; NC</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temporal cortex</td>
<td>Superior Temporal Gyrus/Middle Temporal Gyrus</td>
<td>22</td>
<td>18</td>
<td>51</td>
</tr>
<tr>
<td>L</td>
<td>Fusiform/Parahippocampal Gyrus</td>
<td>37</td>
<td>34</td>
<td>29</td>
</tr>
<tr>
<td>Subcortical</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>Putamen/Caudate/Insula</td>
<td>130</td>
<td>-21</td>
<td>-6</td>
</tr>
<tr>
<td>L</td>
<td>Putamen/Caudate/Insula/Amygdala</td>
<td>92</td>
<td>21</td>
<td>-2</td>
</tr>
<tr>
<td>L</td>
<td>Thalamus/Pulvinar</td>
<td>23</td>
<td>12</td>
<td>27</td>
</tr>
<tr>
<td>L/R</td>
<td>Substantia Nigra</td>
<td>19</td>
<td>3</td>
<td>18</td>
</tr>
<tr>
<td>Parietal cortex</td>
<td>Inferior Parietal Lobule/Angular Gyrus</td>
<td>7/39</td>
<td>17</td>
<td>34</td>
</tr>
<tr>
<td>Frontal Cortex</td>
<td>PFC (Middle /Superior Frontal Gyrus)</td>
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<td>-24</td>
</tr>
<tr>
<td>L</td>
<td>PFC (Middle /Superior Frontal Gyrus)</td>
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<td>30</td>
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<td><strong>NC &gt; BPD</strong></td>
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<tr>
<td>None</td>
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</tbody>
</table>

* Cluster size is represented by the number of voxels.
Table 3.3 Talairach Coordinates of the Centers of Mass for ROIs for the Symptom I screen.
Comparisons of overall brain activity obtained during reading of BPD symptoms versus neutral condition.

<table>
<thead>
<tr>
<th>Hemisphere</th>
<th>Brain Regions</th>
<th>Brodmann area (BA)</th>
<th>Cluster size</th>
<th>Talairach coordinates</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>x</td>
</tr>
<tr>
<td><em>BPD &gt; NC</em></td>
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<td></td>
</tr>
<tr>
<td>L/R</td>
<td>Occipito-Parietal cortex</td>
<td>7/18</td>
<td>721</td>
<td>-6</td>
</tr>
<tr>
<td>L/R</td>
<td>Cuneus/Precuneus/Lingual Gyrus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L/R</td>
<td>Limbic System</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>Cingulate Gyrus</td>
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<td>43</td>
<td>0</td>
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<tr>
<td></td>
<td>Subcortical</td>
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<td></td>
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</tr>
<tr>
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<td>Caudate</td>
<td>23</td>
<td>19</td>
<td>34</td>
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<tr>
<td>L</td>
<td>Cerebellum</td>
<td>32</td>
<td>25</td>
<td>52</td>
</tr>
<tr>
<td><em>NC &gt; BPD</em></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>R</td>
<td>Postcentral Gyrus</td>
<td>3</td>
<td>20</td>
<td>-33</td>
</tr>
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</table>

* Cluster size is represented by the number of voxels.
Table 3.4 Talairach coordinates of the Centers of Mass for ROIs for the Symptom II screen.

<table>
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<tr>
<th>Hemisphere</th>
<th>Brain Regions</th>
<th>Brodmann Area (BA)</th>
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<th>Talairach coordinates</th>
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<td></td>
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<td>x   y   z</td>
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<td></td>
<td>Temporal cortex</td>
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<td></td>
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</tr>
<tr>
<td>R</td>
<td>Fusiform/Parahippocampal Gyrus</td>
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<td>48</td>
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<tr>
<td></td>
<td>Limbic system</td>
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<tr>
<td>L/R</td>
<td>Posterior Cingulate Gyrus</td>
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<td>39</td>
<td>-1   34  21</td>
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<tr>
<td></td>
<td>Parietal cortex</td>
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<td></td>
<td></td>
</tr>
<tr>
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<td>20</td>
<td>-33  56  41</td>
</tr>
<tr>
<td>L</td>
<td>Precuneus/Angular Gyrus</td>
<td>7</td>
<td>23</td>
<td>28  51  34</td>
</tr>
<tr>
<td></td>
<td>Frontal Cortex</td>
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<td></td>
<td></td>
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<tr>
<td>L</td>
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<td>75</td>
<td>35   -30  9</td>
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<tr>
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<tr>
<td>R</td>
<td>Insula/Inferior Frontal Gyrus</td>
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<td>22</td>
<td>-33  -22  1</td>
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<tr>
<td></td>
<td>Cerebellum</td>
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<td></td>
</tr>
<tr>
<td>L</td>
<td></td>
<td>25</td>
<td>16</td>
<td>64  -27</td>
</tr>
<tr>
<td>R</td>
<td></td>
<td>21</td>
<td>-8</td>
<td>73  -32</td>
</tr>
<tr>
<td><strong>NC &gt; BPD</strong></td>
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<tr>
<td></td>
<td>Occipital cortex</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>L</td>
<td>Lingual Gyrus/Cuneus</td>
<td>17</td>
<td>19</td>
<td>12   90   3</td>
</tr>
<tr>
<td></td>
<td>Parietal cortex</td>
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<td></td>
</tr>
<tr>
<td>R</td>
<td>Postcentral Gyrus</td>
<td>3</td>
<td>26</td>
<td>-29  32  51</td>
</tr>
<tr>
<td></td>
<td>Frontal cortex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L</td>
<td>Superior Frontal Gyrus</td>
<td>10</td>
<td>18</td>
<td>13  -61  24</td>
</tr>
<tr>
<td>R</td>
<td>Precentral Gyrus</td>
<td>43</td>
<td>22</td>
<td>-58  10   10</td>
</tr>
</tbody>
</table>

* Cluster size is represented by the number of voxels.
Figure 3.2 ROIs predicting the behavioral performance.

Axial views displaying significant BOLD signal change associated BPD > NC contrast and scatter graphs showing relationships between changes in BOLD signal and self-rating score. Brain activity in five regions demonstrated significantly strong correlations with the behavioral performance as represented by the difference rating scores of perceived self-efficacy in treating BPD and NC patients (NC - BPD). The regions were right insula/IFG and left MFG/insula (upper panel) and right MFG/IFG, right IPL/AG, and left precunues/AG (lower panel). The statistical threshold was set at p<0.05 at the cluster level, corrected for multiple comparisons, with an underlying voxel-level threshold of p<0.025, as displayed refers to the location of the axial slice. The graphs plot the BOLD signal change (BPD versus NC) against the difference rating score at each ROI. *, p > .05; **, p > .001. BPD, borderline personality disorder; NC, neutral control; IFG, Inferior frontal gyrus; MFG, middle frontal gyrus; FUS, fusiform gyrus; PHG, parahippocampal gyrus; IPL, inferior parietal gyrus; AG, angular gyrus.
CHAPTER 4
DISCUSSION

The current study provided both subjective (e.g. self-reported ratings) measures and brain activity to investigate clinicians’ emotion and attitude toward BPD. The fMRI study delineated brain structures in clinicians active during silent reading of BPD related vignettes in contrast to neural vignettes. Besides the identification of the general BPD related brain structures, I was also interested in two questions: first, do activations occur in emotion-related brain network (e.g. amygdala) during reading of BPD related stimuli. If so, do the activations last throughout a whole vignette or only show in response to specific stimuli (e.g. diagnosis or symptoms)? Second, can I find evidence for a relationship between brain activities and clinicians’ ratings of perceived self-efficacy in the treatment of BPD? To answer these questions, nine clinicians were surveyed on their experience with BPD and scanned using fMRI while they were reading and rating BPD related stimuli.

Questionnaire and in-scanner Ratings

As reported in the questionnaire, the clinicians’ willingness to accept a client with BPD as referral was predicted by the positive feelings and experience (comfort and enjoyableness) they had when treating BPD patients. This result was in line with the fact that clinicians and care providers often avoided to see BPD patients or limited the number of BPD patients in their practice (Ivanoff et al., 2007) since positive feelings were seldom associated with BPD (Bodner et al., 2010; Cleary et al., 2002; James & Cowman, 2007; Woollaston & Hixenbaugh, 2008). It was a little surprising that self-reported successfulness in treating BPD was not associated with any variables from the
questionnaire or the in-scanner ratings. This does not agree with either the reported relationship between DBT training and positive outcome in the literature (e.g. Linehan et al., 1999; Evershed et al., 2003) or the positive correlation between the DBT training and the in-scanner ratings of participants’ effectiveness to treat BPD found in this study. On the other hand, the fact that self-reported measures (e.g. survey and interviews) on efficacy on treating BPD patients were not stable across time suggested that BPD was hard to treat (even years of experience could not help).

The ratings provided by the participants to the BPD and NC vignettes in the scanner were consistent. Specifically, participants all reported themselves to be less effective when treating BPD patients compared to clients without diagnosed mental disorders. The difference score in ratings (represented by NC – BPD) between the two conditions was in addition positively correlated with the self-reported successfulness in treating BPD in the pre-scanning questionnaire. This finding indicated that training in DBT was associated with more positive clinical outcomes (Evershed et al., 2003; Koons et al., 2001; Linehan et al., 1991; Linehan et al., 1999; Turner, 2000; van den Bosch et al., 2002; Verheul et al., 2003).

**FMRI Session**

Overall, modulation of brain activity by the vignettes was identified in multiple regions within cerebral cortex, subcortical structures, as well as cerebellum. Reading of different part of the vignettes (e.g. diagnosis information and symptoms) seemed to be associated with different activation patterns in the brain. Specifically, reading “borderline personality disorder” (diagnosis screen) activated more subcortical regions in contrast to reading the two symptom screens. Activations in temporal, parietal, and frontal regions
were observed in both the diagnosis and symptom II screens but not in the symptom I screen. The cortical activations during the presentation of the diagnosis and symptom II, however, were different from each other in the locus of the activated regions. Diagnosis screen activated superior part of the frontal cortex bilaterally along with the left temporal and parietal cortex while the symptom II screen activated more inferior part of the frontal cortex, right temporal cortex and bilateral parietal cortex. Only reading BPD stimuli in the symptom I screen activated a large cluster in the visual cortex. The activations in the left posterior cingulate gyrus and left cerebellum in symptom I were replicated in symptom II, with an expansion to the right hemisphere. Interestingly, the superior frontal cortex activated in diagnosis screen and the visual cortex activated in symptom I were deactivated when the symptom II screens were on. These findings were discussed below.

Subcortical Regions and Insula

The findings regarding the activations in subcortical regions and insula indicated insignificant differences in emotional valence between the BPD and NC stimuli in the experienced clinicians (Bodner et al., 2010). In addition, the BPD-related activations in the subcortical regions (including in the left amygdala, thalamus, pulvinar and bilateral putamen, substantia nigra) associated with the presentation of the diagnosis screen indicated that the label “borderline personality disorder” could trigger strong negative emotions regarding BPD patients (Fraser & Gallop, 1993; Krawitz & Watson, 2003). The caudate’s activation in the presentation of symptom I screen and insula’s activation in symptom II screen indicated that the content about BPD symptoms also had evident emotional valence to clinicians.
Both amygdala and thalamus are parts of the limbic system which was posited as the emotional center of the brain (Cannon 1927; LeDoux, 1987; Papez, 1937). Amygdala plays a key role in processing of emotionally significant stimuli (LeDoux, 2000) which could be negative (e.g. Ohman & Mineka, 2001; Adolphs, 2002; Vuilleumier, 2002) or positive (Williams et al., 2005, Herbert et al., 2009). Herbert et al. (2009) reported that reading both pleasant and unpleasant in contrast to neutral word could activate amygdala in the left hemisphere. Based on a series of investigation on emotional word reading, Landis (2006) proposed that left amygdala (via extrastriate connections) acted as a detector of emotional word content at a very early stage of processing and subsequently modulated the cortical response to emotional words. Thalamus has also been reported as part of the brain circuits of emotion (limbic system) by many authors (e.g. Cannon 1927; LeDoux, 1987; Papez, 1937). Activation in thalamus was observed in processing of emotional (Oyoshi et al., 1996; Price et al., 1996; Price, 1999; Vertes, 2006) or salient stimuli (Seeley et al., 2007). Pulvinar’s involvement in the processing of emotional faces and natural scenes stimuli had been reported in numerous human fMRI and PET studies. It recently was confirmed by a coordinates-based meta-analysis of more than a hundred articles that pulvinar and the medial dorsal nucleus of the thalamus were associated with processing of emotional scenes (Sabatinelli et al., 2011). The fact that neurons in monkey pulvinar responding differentially to emotional expressions of human faces also suggested that pulvinar might also be involved in early stages of emotional facial processing (Maior et al., 2010). The activation in amygdala and thalamus confirmed that clinicians’ negative attitude toward BPD patients (Bodner et al., 2010; Fraser & Gallop, 1993; Krawitz & Watson, 2003).
Putamen, substantia nigra, and caudate are all nuclei in basal ganglia. Putamen is one of the mostly active regions in studies involving both positive (Stoleru et al., 1999; Morris et al., 1996) and negative emotions (George et al., 1995; Lane et al., 1997; see Maddock, 1999 for review). Putamen has a role related to the perception of disgust (Phillips et al., 1998; Sprengelmeyer et al. 1998; Thielscher & Pessoa, 2007) and fear (Surguadze et al., 2003). Substantia nigra has multiple roles including reward seeking and motor control. It has been reported that this region regulated aversive responses in rats (Maisonnette et al., 1996). Specifically, lesion of the substantia nigra increases the aversive consequences and amplifies defensive behavioral in the expression of fear and disgust. The caudate nucleus is also commonly activated during emotional processing (e.g. Bartels & Zeki, 2000; Calder et al., 200; George et al., 1995; Phillips et al., 1998).

Insula is part of the cerebral cortex and folds closely to the subcortical regions. The joint activation of putamen and insula indicated that BPD related emotional responses in clinicians might be aversive (Calder et al., 2000; Zeki & Romaya, 2008). Activations in putamen and insula were reported to be uniquely related to strong emotional feelings of hate (Zeki & Romaya, 2008). Moreover, Calder et al. (2000) reported a case of a patient who lost the ability to recognize stimuli of disgust after the damage of putamen and insula. Insula itself is involved in response to disgust and aversive stimuli (Buchel et al., 1998; Phillips et al., 1998).

The activation of subcortical limbic regions, basal ganglia, and insula in response to BPD stimuli indicated that BPD related stimuli, even the name of the disorder, had emotional charge to clinicians (Bodner et al., 2010; Cleary et al., 2002; Ivanoff et al., 2007; James & Cowman, 2007; Woollaston & Hixenbaugh, 2008).
Cerebellum

Significant activation observed in cerebellum when the participants were reading the symptoms of BPD compared to NC condition further proved that reading of BPD symptoms could elicit emotional neural responses in clinicians’ brain. Although it is commonly accepted that the role of cerebellum is in fine-tuned motion control and coordination of motor behavior (e.g. Fine et al., 2002), more and more of empirical studies have identified its important role in cognitive functioning and emotional processing. Herbert et al. (2009) observed only increased activity in the cerebellum, but no other brain region, when unpleasant adjectives were compared to pleasant adjectives. Several other imaging studies have also found cerebellar activation in response to emotional stimuli (e.g., George et al., 1993; Paradiso et al., 2003). Damage to cerebellum is associated with “the cerebellar cognitive-affective syndrome” which is characterized by impairment of executive functions, difficulties with spatial cognition, blunting of affect or disinhibited, inappropriate behavior, and language deficits (Andreasen et al., 1999; Parvizi et al., 2001; Schmahmann, 2004; Schmahmann & Sherman, 1998; Wiser et al., 1998). Cerebellum may also be responsible for modulating emotion processing in other cortical and subcortical brain regions. A PET study revealed that patients with cerebellar lesions, compared to healthy participants, showed significantly lower activity in the limbic system (amygdala, thalamus, and retrosplenial cingulate gyrus) and left dorsolateral prefrontal cortex when presented with frightening stimuli (Turner et al., 2007). The activation observed in the current study further confirmed that the clinicians perceived BPD related stimuli as contents with negative emotional change (Bodner et al., 2010; Ivanoff et al., 2007; James & Cowman, 2007; Woollaston & Hixenbaugh, 2008).
Cortical Regions

In the current study, the activated cortical regions, unlike the activated subcortical regions and cerebellum which all have a role in emotion processing, can be categorized into three groups based on their functions: those are responsible for emotion processing, those are involved in sensory processing, and those are required for decision making and response preparation. Although the regions in the latter two groups are not specialized for emotion processing, they have all been reported to be affected by the emotional valence of visual stimuli. It worth noting that the BPD and NC trial were matched for visual properties of the stimuli and the nature of the task so that the differences in activities observed in these regions cannot be explained by interference from higher-order cognitive processes imposed by additional attention or task performance during silent reading of the stimuli.

Emotion processing region: An enhancement of activity in posterior cingulate cortex (BA 23), an integral part of limbic-system, was observed during reading of BPD symptoms. This result seemed in line with the findings of Maddock et al. (2003). The authors reported bilateral activation in posterior cingulate cortex during the presentation of both unpleasant and pleasant compared to neutral words. Besides the role in emotion processing, posterior cingulate gyrus was also known as a key region which involved in retrieval of autobiographical memories (Fink, 1996; Gilboa, 2004; Lou et al., 2004; Maddock, 1999; Maddock et al., 2003; Piefke et al., 2003). Since the BPD and NC stimuli presented in the current study were both highly related to the participants’ profession, the enhanced activity in posterior cingulate gyrus could not be explained by retrieval of autobiographical memories. This finding again confirmed the significant
emotional valence of the BPD compared to NC stimuli (Bodner et al., 2010; Ivanoff et al., 2007; James & Cowman, 2007; Woollaston & Hixenbaugh, 2008).

*Sensory processing:* In the current study, the enhancement of activation in visual cortex (e.g. cueneus and lingual gyrus) was only observed during the reading the symptom I screen of vignettes. The enhanced parietal activities were evident throughout the presentation of the whole vignette. Regions in visual (occipital) and parietal cortex have been described in association with the neural processing of visually presented negatively valenced words (Herbert et al., 2009; Isenberg et al., 1999; Tabert et al., 2001). The facilitated sensory processing of emotional stimuli in the visual cortex were often accompanied by activation in amygdala and documented as “re-entrant processing” by many authors (e.g. Lane et al., 1997; Morris et al., 1998; Thielscher & Pessoa, 2007). The BPD related amygdala activation, as discussed previously in this thesis, was only significant during the presentation of the diagnosis screen. This specific finding is not surprising because human amygdala rapidly habituates to repeated complex emotionally stimuli after the initial response (Breiter et al., 1996; Fisher et al., 2003). The increased activity in visual cortex was, however, accompanied by activation in other regions involved in emotion processing (e.g. bilateral posterior cingulate gyrus, left caudate, and left cerebellum).

Besides the activation in occipital and parietal cortex during the symptom I screen, there were also regions significantly activated in the temporal and parietal cortex during the presentation of the diagnosis and symptom II screens. Specifically, they were fusiform and parahippocampal gyrus in temporal cortex and inferior parietal lobule, angular gyrus in parietal cortex.
The lateralized activations in the left fusiform gyrus, middle and superior temporal gyrus, inferior parietal lobule, and angular gyrus during the diagnosis screen are most likely associated with word/object identification (Cohen et al., 2002; Gaillard et al., 2006; Petersen et al., 1990; Posner & Abdullaev, 1999; Simon et al., 2002) and semantic analysis (Bookheimer et al., 1995; Demonet et al., 1992; Pugh et al., 1996). The significant activation related to BPD stimuli in these regions are in line with the findings in previous studies that emotional stimuli elicit stronger activity in the brain regions related to processing semantic stimuli (Canli et al., 2004; Herbert et al., 2009; Luo et al., 2004; Maddock et al., 2003).

**Decision making:** The cortical activations in the symptom II screen, especially activations in the temporal and parietal cortex, were either pronounced in the right hemisphere (right fusiform gyrus and PHG) or shown bilaterally (bilateral IPL and AG) compared to the left lateralization during the diagnosis screen. The frontal activations were more inferior (bilateral IFG, MFG, and insula) compared to the frontal activation in the diagnosis screen. In addition, the amplitude of BOLD signal change in these regions was not only increased during reading of with BPD stimuli but also predicted the participants’ self-efficacy ratings in the scanner. The general pattern was very similar to the study reported by Thielscher & Pessoa (2007) in which they presented fearful, disgust and neutral face to participants and asked them to perform a challenging fear-disgust, two-choice discrimination task while their brains were scanned. They found that voxels whose signals predicted fearful responses were observed in superior parietal gyrus, anterior insula, ACC, middle frontal gyrus, inferior frontal gyrus, orbitofrontal cortex, and thalamus. The linear relationship between participants rating and cortical activity was
also reported in Zeki and Romayas’ study (2008) on neural correlates of hate. In their study, participants reported hate scores toward stimuli and the parameter estimates for the contrast of interest (hated face versus neutral faces) were positively correlated in right insula, premotor cortex and fronto-medial gyrus. The results indicated that a decision making process involving multiple distributed regions were carried out during the system II screen (Thielscher & Pessoa, 2007) and more BPD related activities showed in these regions.

**Activation Summary**

Reading BPD compared to NC stimuli activated many cortical, subcortical, and cerebellar brain regions involved in emotion processing, sensory processing and decision making. More specifically, reading the name of “borderline personality disorder” activated subcortical regions. As more information were presented, subcortical regions habituated to the BPD stimuli while emotion processing related cortical and cerebellar regions showed more responses. In addition, the emotionally valenced BPD stimuli activated brain regions which were related to sensory processing and decision making. The brain activities in regions involved decision making also predicted the participants’ behavioral ratings of their self-efficacy in treating clients with BPD. Taken together, the brain activation results confirmed that “borderline” and the symptoms of BPD had a strong emotional charge to clinicians (Fraser & Gallop, 1993; Krawitz & Watson, 2003). The results could also explain why clinicians often are hesitating or reluctant to see client with BPD (Bodner et al., 2010; Cleary et al., 2002; James & Cowman, 2007; Fraser & Gallop, 1993; Krawitz & Watson, 2003; Woollaston and Hixenbaugh, 2008).
Deactivation

Patterns of deactivation (NC > BPD) were observed in reading of the symptoms but not diagnostic information. The deactivated regions involved right postcentral gyrus, precentral gyrus, left superior frontal gyrus and a restricted area in visual cortex (lingual gyrus/cuneus). The left superior frontal gyrus, right precentral gyrs, and right postcentral gyrus are involved in motor preparation and execution (e.g. Menon et al., 2001; Simon et al., 2002) while the visual cortex is responsible for sensory processing.

The deactivations in these four clusters in the symptom II screen were accompanied activation related to the decision making. Thus, regions involved in decision making might inhibit the activity in these regions to limit the sensory input and suppress the response to press the keypad. It is also important to note that all the participants in the present thesis were highly trained professionals with many years of experience. They were trained to respect their clients and maintain a professional manner even when facing difficult patients. They might not express their fear toward a BPD patient but instead inhibit the sensory input and unprofessional responses. I hypothesize that the deactivation could be associated with participants’ professional experience. The deactivation in the sensor and motor related cortex was accompanied by activations in many decision making related foci in the prefrontal cortex (e.g. Knight et al., 1999). In addition, in participants who had no need to inhibit their emotion, these sensor and motor related regions were reported active in response to negative stimuli (Herbert et al., 2009; Zeki & Romaya, 2008). This inhibition/experience hypothesis could be tested by adding participants who have knowledge about BPD but do not have working experience with
patients with BPD (e.g. graduate students who have 3-5 years training in clinical psychology program) as a control group in the next step of the study.

The BPD related activity in the superior frontal gyrus showed an interesting dynamic change in response on the stimuli across the three screens of vignettes: the activity of BPD was significantly higher, comparable, and significantly lower than the activity of NC stimuli during the presentation of diagnosis, symptom I, and symptom II screen, respectively. The dynamic pattern might be related to the superior frontal cortex’s role in self-awareness processing (Goldberg et al., 2006). In a recent study Goldberg et al. (2006) reported that the superior frontal cortex was associated with self-awareness and its activity could be modulated by demanding sensory/perceptual task. Specifically, when stimuli were shown slowly and emotional responses were required, the participants would have a sense of self-awareness and the superior frontal gyurs showed enhanced activity. But when the stimuli sequences were rapid and participants were too busy to pay attention to self, there was no activity in the superior frontal gyrus. In the current study, there were generally more words in the symptom screens and thus more demanding in terms of perceptual and semantic processing. In addition, a self-related response was required after the symptom II screen thus the symptom II screen was then more demanding than the symptom I screen. When emotionally valence BPD stimuli was not very complex (e.g. in diagnosis screen), participants might be able to related the stimuli to self and resulted the self-awareness related activation in the superior frontal gyrus. The activation vanished and even suppressed when more complex stimuli plus task were involved in the symptom screen I and II.
Furthermore, the left superior frontal cortex was also deactivated in Zeki and Romayas’ study (2008) when their participants were processing hated face in contrast neutral faces. The authors argued that the activity in this area was negatively correlated with obsessive-compulsive states (McGuire et al., 1994). Specifically, lower level of anxiety was associated with higher activity in superior frontal cortex. The perception of emotional stimuli would attract attention to extrapersonal space and induce more anxiety, and the neutral stimuli would trigger a shift of attention back to internal space and reduce anxiety. In case of the present study, reading BPD symptoms was more demanding and could induce more anxiety than reading only the diagnosis information of BPD or reading those in the NC conditions. The deactivation in the superior frontal cortex reflected the participants’ mental state in response to the task complexity and emotion load of the stimuli.

Similar to Zeki and Romayas’ explanation to the deactivation in the superior frontal cortex, previous studies have also shown that the postcentral gyrus is involved in self versus other perspective taking (Ruby & Decety, 2001, 2003). Activation was observed in the postcentral gyrus when participants taking a first-person perspective. As argued above, less demanding emotional and neutral stimuli would shift attention to internal space so that the participant would focus on self and take a 1st-person perspective. In addition, performing a demanding task which involves emotional processing might attract participants’ attention to extrapersonal task or stimuli (McGuire et al., 1994) and change participants’ perspective to a 3rd-person perspective. The deactivation in postcentral gyrus in response to the BPD stimuli, according to the
perspective taking theory and self-awareness hypothesis, supports our hypothesis that BPD stimuli have emotional charge.

Conclusions

The goal of the current study was to investigate neural activity associated with BPD among experienced clinicians. It was hypothesized that the BPD related stimuli would induce emotional response in clinicians’ brain and the neural activity would affect their behavioral performance on self-reported efficacy measures on treating BPD. The results of current study show that BPD related stimuli were associated with increased brain activities in the limbic system (e.g. amygdala, thalamus, and posterior cingulate cortex) and many other cortical and subcortical regions which were related to the processing of negative valenced stimuli. BPD, either the name of the disorder or its symptoms, has emotional valence to experienced clinicians. Brain activities, compared to self-reported questionnaires, are more accurate in predicting clinicians’ self-rated efficacy in the treating of BPD. Further studies are required to determine whether modulation of clinicians’ experience with BPD patients or training in more effective treatment program will affect the brain activities associated with emotional processing of BPD related stimuli.
REFERENCES


APPENDIX
Clinical Questionnaire

Background Information:

1. Please list your age:

2. Sex (click on the box that applies): Male ☐ Female ☐

3. Race (click the box next to all that apply):
   a. American Indian or Alaska Native ☐
   b. Asian ☐
   c. Black or African American ☐
   d. Native Hawaiian or Other Pacific Islander ☐
   e. White ☐

4. What is your current marital status (click on the box that applies):
   a. Single (never married) ☐
   b. Married (first marriage) ☐
   c. Remarried ☐
   d. Separated ☐
   e. Divorced ☐
   f. Widowed ☐
   g. Long-term domestic partner (at least one year) ☐

5. Your average yearly income (click on the box that applies):
   a. < $20,000 ☒
   b. $20,000 - $30,000 ☐
   c. $30,000 - $40,000 ☐
   d. $40,000 - $50,000 ☐
   e. $50,000 - $60,000 ☐
   f. $60,000 - $70,000 ☐
   g. $70,000 - $80,000 ☐
   h. >$80,000 ☐

6. Click on the box next to your highest degree:
   a. Clinical Ph.D. ☐
   b. Counseling Ph.D. ☐
   c. Psy.D. ☐

7. Where did you receive your highest degree (i.e. what school/university)?

8. What was the orientation of your program (e.g., Behavioral, Cognitive, Cognitive-Behavioral, Psychodynamic)?
9. Click the box next to the training model of your graduate program:
   a. Boulder model (equal weight to clinical and research)
   b. Vail model (more clinically weighted)
   c. Other (please specify)

Using the scale below, answer the following two questions:

1  2  3  4  5  6  7
Very Clinical Focused Very Research-Focused

10. How would you describe the focus of your graduate program?

11. Aside from your program’s focus, what was your focus in graduate school?

________________________________________________________________________

12. How many years have you been a licensed psychologist?

13. How many years have you been an independently (i.e. not requiring supervision) practicing clinician?

**Treatment**

Using the scale below, how much training (e.g., graduate coursework/training, seminars, intensive supervision, etc.), if any, do you have with the following:

1  2  3  4  5  6  7
No Training Extensive

**Training**

1) Cognitive Behavioral Therapy
2) Dialectical Behavior Therapy
3) Interpersonal Therapy
4) Parent-Child Interaction Therapy
5) Psychodynamic Therapy
6) Play Therapy
7) Exposure and Response Prevention
8) Parent Training
9) Behavioral activation

Using the scale below, rate your experience (e.g., use in grad school, internship, private practice, etc.) with the following:

1  2  3  4  5  6  7
No Experience Extensive Experience

10) Cognitive Behavioral Therapy
11) Dialectical Behavior Therapy
12) Interpersonal Therapy
13) Parent-Child Interaction Therapy
14) Psychodynamic Therapy
15) Play Therapy

\[
\begin{array}{cccccc}
\text{No Experience} & 1 & 2 & 3 & 4 & 5 & 6 & 7 \\
\text{Extensive Experience} & & & & & & &
\end{array}
\]

16) Exposure and Response Prevention
17) Parent Training
18) Behavioral activation

**Client/Patient Experience**
Approximately **how many clients have you treated** with the following *DSM-IV* diagnoses in your career (e.g., grad school, internship, private practice, etc.) and in the past two years? **We realize that this may be difficult to accurately report, but please give your best estimate**

<table>
<thead>
<tr>
<th>Career</th>
<th>Past 2 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Major Depressive Disorder</td>
<td></td>
</tr>
<tr>
<td>2) Dysthymia</td>
<td></td>
</tr>
<tr>
<td>3) Bipolar Disorder</td>
<td></td>
</tr>
<tr>
<td>4) Obsessive-Compulsive Disorder</td>
<td></td>
</tr>
<tr>
<td>5) Generalized Anxiety Disorder</td>
<td></td>
</tr>
<tr>
<td>6) Panic Disorder</td>
<td></td>
</tr>
<tr>
<td>7) Schizophrenia</td>
<td></td>
</tr>
<tr>
<td>8) Schizoaffective Disorder</td>
<td></td>
</tr>
<tr>
<td>9) Paranoid Personality Disorder</td>
<td></td>
</tr>
<tr>
<td>10) Borderline Personality Disorder</td>
<td></td>
</tr>
<tr>
<td>11) Avoidant Personality Disorder</td>
<td></td>
</tr>
</tbody>
</table>

Using the scale below, rate your **level of comfort** when treating patients/clients with the following *DSM-IV* diagnoses:

\[
\begin{array}{cccccc}
\text{Not at all} & 1 & 2 & 3 & 4 & 5 & 6 & 7 \\
\text{Very Comfortable} & & & & & & &
\end{array}
\]

12) Major Depressive Disorder
13) Dysthymia
14) Bipolar Disorder
15) Obsessive-Compulsive Disorder
16) Generalized Anxiety Disorder
17) Panic Disorder
18) Schizophrenia
19) Schizoaffective Disorder
20) Paranoid Personality Disorder
21) Borderline Personality Disorder
22) Avoidant Personality Disorder

Using the scale below, indicate how successful you have been when treating patients/clients with the following *DSM-IV* diagnoses:

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not at all Successful</td>
<td>Very Successful</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

23) Major Depressive Disorder
24) Dysthymia
25) Bipolar Disorder
26) Obsessive-Compulsive Disorder
27) Generalized Anxiety Disorder
28) Panic Disorder
29) Schizophrenia
30) Schizoaffective Disorder
31) Paranoid Personality Disorder
32) Borderline Personality Disorder
33) Avoidant Personality Disorder

Using the scale below, indicate how much you enjoy treating patients/clients with the following *DSM-IV* diagnoses:

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do Not Enjoy At All Enjoy Very Much</td>
<td></td>
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</tbody>
</table>

34) Major Depressive Disorder
35) Dysthymia
36) Bipolar Disorder
37) Obsessive-Compulsive Disorder
38) Generalized Anxiety Disorder
39) Panic Disorder
40) Schizophrenia
41) Schizoaffective Disorder
42) Paranoid Personality Disorder
43) Borderline Personality Disorder
44) Avoidant Personality Disorder
Using the scale below, indicate how likely you would be to **accept a referral** for a patient/client with the following diagnosis (assuming that you were currently accepting referrals):

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not At All</td>
<td>Likely</td>
<td>Very Likely</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

45) Major Depressive Disorder  
46) Dysthymia  
47) Bipolar Disorder  
48) Obsessive-Compulsive Disorder  
49) Generalized Anxiety Disorder  
50) Panic Disorder  

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not At All</td>
<td>Likely</td>
<td>Very Likely</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

51) Schizophrenia  
52) Schizoaffective Disorder  
53) Paranoid Personality Disorder  
54) Borderline Personality Disorder  
55) Avoidant Personality Disorder