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Neurological Changes Associated With Behavioral Activation Treatment For Depression (BATD) Using A Functional MRI Reward Responsivity Paradigm

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I am submitting herewith a dissertation written by Michael John Gawrysiak entitled "Neurological Changes Associated With Behavioral Activation Treatment For Depression (BATD) Using A Functional MRI Reward Responsivity Paradigm." I have examined the final electronic copy of this dissertation for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, with a major in Psychology.

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NEUROLOGICAL CHANGES ASSOCIATED WITH BEHAVIORAL ACTIVATION TREATMENT FOR DEPRESSION (BATD) USING A FUNCTIONAL MRI REWARD RESPONSIVITY PARADIGM

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DEDICATION

I dedicate this dissertation to my mother, father, sister, and wife who have been a continual source of inspiration, encouragement, and support.

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ABSTRACT

Functional magnetic resonance imaging (fMRI) was used to examine functional brain activity in two demographically matched depressed women following their participation in a Behavioral Activation Treatment for Depression (BATD; Hopko & Lejuez, 2007) or Pragmatic Psychodynamic Psychotherapy (PPP; Summers & Barber, 2010). A reward responsiveness pleasurable music listening scanner paradigm was employed during brain scanning to assess reward responsivity prior to and following treatment. Both women responded positively to treatment, evidenced reductions in depression, and exhibited changes in their blood oxygenation level dependence (BOLD) response as measured by fMRI following treatment. BOLD response changes were not observed in either patient in subcortical regions implicated in reward responsiveness following treatment. However, BOLD response changes were observed for both patients in regions of the dorsolateral and medial orbital prefrontal cortex and subgenual cingulate following treatment, with each treatment affecting these areas. These findings support the notion that when BATD and PPP are implemented effectively they are associated with functional brain changes in areas implicated in the pathophysiology of depression.

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CHAPTER 1

INTRODUCTION

Understanding the relationship between neurobiological processes and effective treatments for clinical depression is an important and burgeoning area of research. Indeed, major depressive disorder is now beginning to be understood as a systems level disorder affecting distributed regions in the cortical, subcortical, and limbic regions that in turn contribute to the pathophysiology and symptom presentation of the condition (Davidson Pizzagalli, Nitschke, & Putnam, 2002; Drevets, Price, & Furey, 2008; Mayberg et al., 1997, Mayberg, 2003). Much of the aberrant functional brain activity that characterizes depression has been normalized following recovery from depression (Brody et al., 2001; Mayberg et al., 1999, 2000, 2005). Understanding the putative mechanisms of change facilitated by psychosocial treatments for depression may enhance our understanding of the pathophysiology of the disorder, lead to treatment refinement and development, and eventually facilitate patient-treatment matching (Mayberg, 2006). Initial studies evaluating associative changes that psychosocial treatments have on the neurobiological basis of depression hold promise toward achieving these objectives.

Studies examining neurobiological changes associated with Interpersonal Psychotherapy (IPT) for depression have found increased metabolic changes in the left temporal lobe and anterior insula during resting state PET scans following treatment (Brody et al., 2001), and increases in blood flow in the right basal ganglia and limbic right posterior cingulate during resting state SPECT scans after six weeks of treatment (Martin, Martin, Rai, Richardson, & Royall, 2001). Additional findings entailed decreases in the right middle frontal gyrus (including both VLPFC and DLPFC) left

middle anterior cingulate, and right dorsal caudate nucleus during resting state PET scan (Brody et al., 2001). In terms of methodological limitations, results reported by Martin et al. (2001) are somewhat limited due to the second scan occurring at 6-weeks into treatment, mid-way through treatment completions, and because SPECT methodology produces resolution without the precision required to evaluate activity in striatal subregions. Nonetheless, these studies were pioneering works insofar as being among the first to demonstrate functional brain changes corresponding to psychotherapeutic treatments for depression.

Studies examining neurobiological changes following Cognitive Behavioral Therapy (CBT) for depression have found increases in metabolic activity in the hippocampus and dorsal anterior cingulate cortex (Goldapple et al., 2004), as well as increases in the right inferior occipital cortex, left inferior temporal cortex, and anterior portions of the subgenual/ventromedial frontal cortex during resting state PET scans (Kennedy et al., 2007). At post-treatment, these same studies found attenuation of depressive symptoms and decreased activations in the dorsolateral, medial, and ventrolateral prefrontal regions, orbital frontal regions, posterior cingulate, inferior parietal and temporal regions (Goldapple et al., 2004), as well as decreases in the bilateral orbital frontal cortex, left medial prefrontal cortex, left dorsomedial, posterior cingulate, and thalamus during resting state PET scans (Kennedy et al., 2007).

One study employed an affective facial processing task during fMRI scanning to assess blood oxygenation level dependence (BOLD) prior to and following CBT for depression, and observed elevated amygdala-hippocampal activity (relative to healthy individuals) that was observed to normalize following treatment (Fu et al., 2008). Fu et

al., (2008) also observed increases in BOLD response in the dorsal anterior cingulate following treatment. Examining reward responsiveness using a Wheel-Of-Fortune task prior to and following Behavioral Activation Treatment for Depression (BATD; Hopko, Lejuez, Ruggiero, & Eiffert 2003; Lejuez, Hopko, Acierno, Daughters, & Pagoto, 2011) it was shown that simultaneous with depression symptom reduction, left planum temporale, right superior lateral occipital cortex, and right posterior temporal fusiform cortex functioning increased during reward feedback (Dichter et al., 2009). Following BATD, decreases in the left posterior cingulate, left caudate, left postcentral gyrus, and left paracingulate gyrus also were observed during reward feedback (Dichter et al., 2009). Importantly, this was the first study using a scanner paradigm to assess neurobiological changes directly corresponding to the aim of the treatment. Specifically, BATD was designed to increase exposure to rewarding stimuli (Hopko et al., 2003) and the scanner paradigm assessed for neurobiological response to rewarding feedback.

Initial findings generally suggest that positive treatment outcome among depressed patients treated with BATD, IPT, and CBT are associated with changes in brain regions that have been implicated in the pathophysiology of depression. Such brain changes have been thought to reflect improved problem-solving, reductions in negative affect and associated cognitions, decreased rumination, and improved affect regulation and self-perception (Cabeza & Nyberg, 2000; Duncan & Owen, 2000; Northoff et al., 2006; Ochsner & Gross, 2005). While these findings are salient to understanding the pathophysiology of depression and the role that psychotherapeutic treatments may have in modulating aberrant brain activations, the assumptions made about functional brain changes are mostly based on resting state brain scans. Only two studies incorporated

functional tasks during brain scans to more clearly assess activations associated with features of depression. In particular, processing affectively salient facial features (Fu et al., 2008) and reward feedback (Dichter et al., 2009) directly relate to behavioral models of depression and targets of intervention. Utilizing functional tasks during scanning has been encouraged as it more clearly delineates specific neurobiological components of depression and how treatments may or may not specifically target relevant brain regions (Frewen, Dozois, & Lanius, 2008). Ideally, functional brain data acquired during scanning would entail a task that is relevant to the psychiatric disorder as well as the mechanisms of change the treatment of interest purports to be predicated upon.

Investigating neurobiological networks of reward is warranted given the relevance of behavioral inhibition, withdrawal, avoidance, and limited behavioral activation among depressed individuals (Jacobson, Martell, Dimidjian, 2001; Kasch, Rottenberg, Arnow & Gotlib, 2002). Plausibly, these behavioral correlates are due to decreased reward responsiveness as the brain activity of healthy and depressed patients are distinguishable by differential responsiveness to rewarding stimuli. Lower activation of the mesolimbic regions in depressed individuals is observed in response to positive stimuli such as happy faces or pleasant autobiographical narratives (Epstein et al., 2006; Keedwell, Andrew, Williams, Brammer, & Phillips, 2005; Schaefer, Putnam, Benca, & Davidson, 2006). Brain regions observed to be active during passive listening to pleasurable music (Blood & Zatorre, 2001; Menon & Levitin, 2005) have similarly been observed to be active in response to other reward inducing stimuli such as food, sex, and drugs of abuse (Bardo, 1998; Pfaus, Damsma, Wenkstern, & Fibiger, 1995; Schilström, Svensson, Svensson, &

Nomikos, 1998; Carelli, Ijames, & Crumling, 2000) and have distinguished brain functioning between healthy and depressed individuals (Osuch et al., 2009).

Osuch et al., (2009) utilized a pleasurable music listening paradigm during fMRI scanning to assess differential responsiveness to rewarding stimuli among depressed individuals and healthy controls. Depressed individuals exhibited significantly weaker activations in the medial orbital prefrontal cortex (moPFC) and nucleus accumbens/ventral striatum, regions implicated in reward processing (Osuch et al., 2009). Moreover, self-reported pleasure ratings were positively correlated with left medial prefrontal activity and negatively correlated with the middle temporal cortex and globus pallidus. Examining the neurobiological activity associated with reward responsiveness is an important advancement in clarifying the pathophysiology of depression. However, only one study has examined how such aberrant functional brain activity associated with both diminished reward response and depressive symptoms corresponds to changes induced by psychotherapy (Dichter et al., 2009).

Examining brain regions implicated in reward responsiveness is a pressing need, especially given models of depression that implicate decreased behavioral activation and minimized exposure to reward as being primary causal factors associated with the onset and maintenance of clinical depression (Ferster, 1973; Lewinsohn, 1974; Lewinsohn & Graf, 1973). Behavioral activation is a therapeutic process that emphasizes structured attempts at engendering increases in overt behaviors likely to bring patients into contact with reinforcing environmental contingencies and corresponding improvements in thoughts, mood, and quality of life (Hopko et al., 2003). Behavioral activation interventions largely have been used to treat depressive disorders and symptoms, with

three meta-analyses supporting their efficacy such that behavioral activation is now considered an empirically validated treatment for depression (Cuijpers van Straten, & Warmerdam, 2007; Ekers, Richards, & Gilbody, 2008; Mazzucchelli, Kane, & Rees, 2009; Sturmey, 2009). In one of the more compelling studies, behavioral activation was comparable to antidepressant medication and superior to cognitive therapy in treating severe depression (Dimidjian et al. 2006), results that were maintained at 2-year follow-up (Dobson et al., 2008). Behavioral activation also has been effectively used with depressed patients in community mental health centers (Lejuez, Hopko, LePage, Hopko, & McNeil, 2001; Porter, Spates, & Smitham, 2004), in a primary care setting as administered by previously untrained mental health nurses, (Ekers, Richards, McMillan, Bland, & Gilbody, 2011), an inpatient psychiatric facility (Hopko, Lejuez, LePage, Hopko, & McNeil, 2003), a representative community outpatient sample (Jacobson et al., 1996), for smokers and drug users with elevated depressive symptoms (Daughters et al., 2008; MacPherson et al., 2010), as a single session intervention with depressed college students (Gawrysiak, Nicholas, & Hopko, 2009), for depressed patients with obesity (Pagoto et al., 2008) and as a supplemental intervention for patients with co-existent Axis I (Hopko, Hopko, & Lejuez, 2004; Jakupak et al., 2006; Mulick & Naugle, 2004) and Axis II disorders (Hopko, Sanchez, Hopko, Dvir, & Lejuez, 2003). Perhaps most relevant to the current study, behavioral activation also has been effective with depressed cancer patients in a medical care setting (Hopko et al., 2005, 2008, 2011), an important finding given the high rates of depression in patients with co-existent medical problems (Welch, Czerwinski, Chimire, & Bertsimas, 2009).

Given the efficacy of behavioral activation in treating depression and its purported mechanism of change being increased behavioral activation and reward exposure, the following study was designed to evaluate whether treatment of a depressed woman corresponded to changes in relevant functional brain activity. To examine this question, a novel reward responsiveness paradigm (pleasurable music listening) was used to explore regional brain activations following BATD. We first posited that music listening was an appropriate fMRI paradigm to evaluate neurobiological reward responsiveness given the relevant literature speaking to the relationship between music and neurobiological activity related to reward (Blood & Zatorre, 2001; Menon & Levitin, 2005; Osuch et al., 2009). It was hypothesized that exposure to preferred as opposed to neutral music passages at pre- and post-treatment would elicit increased activation in the nucleus accumbens, orbital, medial, and dorsolateral prefrontal regions, ventral striatum, and the dorsal anterior cingulate cortex, and/or reductions in the globus pallidus, the caudate, the anterior cingulate cortex, paracingulate, posterior and subgenual cingulate cortical regions. The second hypothesis was that following treatment these regional changes would correspond with reduced depression severity and behavioral inhibition, and increased environmental reward and behavioral activation.

To assess whether BATD uniquely affected regions implicated in depression and reward responsiveness, we included a demographically matched control patient. This patient underwent identical procedures to the patient receiving BATD with the exception that the control patient received Pragmatic Psychodynamic Psychotherapy (PPP; Summers & Barber, 2010), a semi-structured therapeutic intervention that utilizes psychoanalytic principles as the primary mechanism of change (see Shedler, 2010 for a

review). This treatment was selected because psychodynamic treatment is garnering increased support as an evidence-based practice that relies on mechanisms of change quite distinct from those purported by BATD (Shedler, 2010). Accordingly, it was predicted that functional brain changes in the control patient treated with PPP would be distinct from those observed in the patient treated with BATD.

CHAPTER 2

METHODS

Patients

Both patients were recruited from the University of Tennessee Medical Center's Cancer Institute from an on-going randomized controlled study examining the efficacy of BATD and Problem Solving Therapy for depressed women with breast cancer (Hopko et al., 2011). Participants for this study were recruited through physician and medical staff referral. Eligibility criteria to participate in the present study was consistent with the larger study and was contingent upon a primary diagnosis of major depression made by a trained masters level clinician who administered the Anxiety Disorder Interview for DSM-IV (ADIS-IV; Brown, Di Nardo, & Barlow, 1994). Additional eligibility requirements included no current or former history of spinal or brain cancer, right hand dominance as indicated by the Edinburgh Handedness Inventory (Oldfield, 1971), no surgical metal implants, and no co-morbid Axis-I or II diagnoses other than anxiety secondary to depression. At pre- and post-treatment evaluations, patients completed the Behavioral Inhibition and Activation Scale (BIS/BAS; Carver & White, 1994) to assess activity and inhibition, the Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996), to assess depression, and the Environmental Reward Observation Scale (EROS; Armento & Hopko, 2007) to assess environmental reward. The BDI-II and EROS also were completed after each therapy session. Clinicians completed the Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960) at pre and post-treatment.

A total of 5 patients were screened for inclusion, with two declining participation due to time commitments and one withdrawing after inclusion due to scanner-induced

claustrophobia during the initial scan. This study involved inclusion of 2 patients, one assigned to BATD and one to PPP. Both patients provided informed consent as approved by both the University of Tennessee Graduate School of Medicine and the University of Tennessee Institutional Review Boards.

The first patient who received BATD was a 64 year-old, right-handed, married, Caucasian female, with two years of graduate level education. She was diagnosed with breast cancer four months prior to her pre-assessment evaluation for study inclusion. She received cancer treatment in the form of a lumpectomy, one month following her diagnosis, and chemotherapy that began one month prior to study enrollment that persisted through the course of psychotherapy. Her medication regimen was consistent throughout therapy and was limited to allergy, migraine, and sleep prescriptions. This patient reported no prior history of psychiatric problems other than depression and anxiety that emerged six months prior to her cancer diagnosis due to psychosocial stressors (i.e. death of dog, marital problems, job dissatisfaction). Her depression significantly exacerbated upon her breast cancer diagnosis and manifested as sleep disturbances, feelings of guilt, worthlessness and low self-esteem. Her generalized anxiety manifested as restlessness, fatigue, difficulty concentrating, irritability, muscle tension, and minor insomnia. At the time of inclusion in this study she was diagnosed with major depressive disorder with generalized anxiety disorder.

The second patient who received PPP was a 68 year-old, right-handed, married, Caucasian female, with four years of graduate school education. She was diagnosed with breast cancer two years prior to enrollment in the study. She received cancer treatment in the form of a left radical mastectomy approximately two years prior to study enrollment,

which was followed by 6 months of chemotherapy. She also received hormone treatment (i.e., Tamoxifen) for breast cancer that persisted from one year prior to study enrollment through mid-way through psychotherapy. Her medication regimen consisted of prescriptions for cholesterol, hypertension, Edema, allergies, asthma, and breast cancer, and was consistent throughout the study with the exception of Tamoxifen, which she discontinued following consultation with her physician. This patient reported no prior history of psychiatric problems. Her depression emerged approximately two years prior to participation in the study and surfaced in conjunction with her cancer diagnosis and her husband suffering a stroke. Her depression manifested as decreased energy, fatigue, listlessness, agitation, and feeling like a failure. At the time of study inclusion she was diagnosed with major depressive disorder.

Outcome Measures

The *Hamilton Rating Scale for Depression* (HRSD; Hamilton, 1960) is a 24-item semi-structured interview designed to measure symptom severity in patients diagnosed with depression. The instrument is the most widely used and accepted outcome measure for the evaluation of depression and has become the standard outcome measure in clinical trials (Kobak & Reynolds, 1999; Wolf & Hopko, 2008).

The *Beck Depression Inventory-II* (BDI-II; Beck et al. 1996) consists of 21 items, each of which is rated on a 4-point Likert scale. The instrument has been demonstrated to have excellent reliability and validity with depressed younger and older adults (Beck et al., 1996; Dozois, Dobson, & Ahnberg, 1998). The psychometric properties of the BDI-II have been studied in cancer patients as well as a diverse primary care sample, with the instrument having strong predictive validity as it pertains to diagnoses of clinical

depression, strong internal consistency (α = .94), and adequate item-total correlations (*R* = .54-.74; Arnau, Meagher, Norris, & Bramson; 2001; Katz, Kopek, Waldron, Devins, & Thomlinson, 2004).

The *Environmental Reward Observation Scale* (EROS; Armento & Hopko, 2007) is a 10-item measure (1 to 4 point Likert Scale) that assesses environmental reward and response-contingent positive reinforcement (RCPR; Lewinsohn, 1974). Scores range from 10 to 40, with higher scores suggesting increased environmental reward. Sample items include "the activities I engage in usually have positive consequences," and "lots of activities in my life are pleasurable." Based on psychometric research with three independent college samples, the EROS has strong internal consistency (α = .85-.86) and excellent test-retest reliability (r = .85), and correlates strongly with other commonly administered and psychometrically sound self-report measures of depression (r = -.63 to -.69) and anxiety (Armento & Hopko, 2007).

The *Beck Anxiety Inventory* (BAI; Beck & Steer, 1993) is a 21-item questionnaire designed specifically to distinguish cognitive and somatic symptoms of anxiety from those of depression. Good psychometric properties have been demonstrated among community, medical, and psychiatric outpatient samples (de Beurs, Wilson, Chambless, Goldstein, & Feske, 1997; Morin et al., 1999; Wetherell & Areán, 1997).

The *Behavioral Inhibition and Behavioral Activation Scale* (BIS/BAS; Kasch, Rottenberg, Arnow & Gotlib, 2002) is a 20-item self-report questionnaire that assesses how people typically react to certain situations. The scale is subdivided into four subscales: Behavioral Inhibition, Behavioral Activation-Reward Responsiveness, Behavioral Activation-Drive, and Behavioral Activation-Fun-Seeking. Internal

consistencies of all subscales are high (BIS = .78; BAS-RR = .80; BAS-Drive = .83; BAS-Fun = .69). The BIS/BAS scales also have good convergent and discriminant validity, with scores on the BAS scales typically relating to positive affect and extraversion and scores on the BIS scale generally being related to anxiety symptoms, negative affect and neuroticism (Carver & White, 1994; Jorm et al., 1999).

Treatments

BATD was derived from an 8-session protocol and consisted of 45–50 minute sessions administered over 10 weeks (Hopko & Lejuez, 2007; Lejuez, Hopko & Hopko, 2001). Initial sessions consisted of assessing the function of depressed behavior, efforts to weaken access to positive and negative reinforcement for depressed behavior, and introduction of the treatment rationale. A systematic activation approach was then initiated to increase the frequency and subsequent reinforcement of healthy behaviors. The patient began with a weekly self-monitoring exercise that served as a baseline assessment of daily activities, oriented her to the quality and quantity of her activities, and generated ideas about activities to target during treatment. Based on a subsequent value-based goal assessment, approximately 15 overt behaviors were identified that would increase environmental reward and response-contingent positive reinforcement. The overt behaviors identified in this treatment entailed increasing such things as exercise and intimate and meaningful activities with her husband. Subsequent treatment sessions focused on increasing engagement in rewarding activities and monitoring progress.

PPP was derived from a psychodynamic psychotherapy guide outlining case formulations and treatment techniques (Summers & Barber, 2010), and consisted of 8 45-50 minute, sessions administered over 13 weeks. PPP approach for treating depression

suggests two treatment goals, which are ideographically modified to meet patient characteristics, which include: (1) decreasing vulnerability to abandonment, and (2) decreasing harsh self-criticism (Summers & Barber, 2010). The initial phase of treatment can be brief (e.g. 1 – 2 sessions) and in the present study was comprised of taking a history of her depression and deciding on treatment goals: 1) working through multiple losses and related resentment, and 2) recovering a sense of pride, resilience, and "toughness." Therapy proceeded in the second phase (sessions 3 - 6), toward working to identify key themes of abandonment and loss, resentment about such loss, and conflict over self-worth. A Core Conflictual Relational Theme (CCRT; Luborsky, 1977) was developed, per PPP guidelines, which concretely conceptualize patient's maladaptive intra- and inter-personal style of relatedness. Specific discussion focuses on personal experiences and relationships, with attention to how the past informs the present, and in this specific treatment, how cancer and medical treatment influenced her sense of self. The final phase of treatment draws to a close by helping the patient to consolidate new understandings they have made.

Patients received treatment on an outpatient basis at the Cancer Institute within the University of Tennessee Medical Center. Two advanced male clinical psychology graduate students, similar in age and experience in their respective theoretical orientations, conducted the therapies. Patients were scanned within one week prior to beginning therapy and within one week following completion of therapy.

Task Design

The music listening reward responsiveness paradigm was adapted from previous neuroimaging studies on music listening, reward, and depression (Menon & Levitin,

2005; Osuch et al., 2009). The paradigm was approximately 30 minutes and involved listening to two music tracks, each of which was 7.5 minutes, followed by a 7.5-minute period of silence to collect "resting state" data (Greicius et al., 2007). The first track was comprised of 50 seconds of preferred music, 50 seconds of neutral music, then 50 seconds of silence. This sequence repeated twice more proceeding through the respective songs in 50-second segments totaling 7.5 minutes for the first track. The second track was identical with the exception of the order of preferred and neutral music being reversed (see Figure 1 for visual representation of block design). Track order was reversed for time 2 such that tracks began with the neutral stimulus if the previous scan began with the preferred stimulus. Patients were also counterbalanced to order such that for the first scan one patient heard her preferred passage first where the other heard the neutral first.

Selection of preferred and neutral music passages was based on previously established methodology (Osuch et al., 2009) whereby prior to the day of the scan, patients listened to numerous instrumental music passages that they rated on a likert scale ranging from -100 (disliked completely) to 0 (neither liked nor disliked) to +100 (liked completely). Rankings were obtained in intervals of 20 and considered neutral if rated between -40 through +40 and preferred if rated 60 or higher. The neutral music passage served as the control condition for brain activity associated with a non-rewarding stimulus. Volume and clarity of music was assessed prior to scanning to ensure each patient could hear music passages. Patients were given no instructions during scanning other than to stay focused and remain still.

Functional MRI Acquisition

Imaging was performed on a 1.5-T Siemens MRI scanner with a standard head coil at the University of Tennessee Department of Radiology. In each condition, 150 whole-brain functional T2*-weighted echo planar images were acquired, each comprising 35 slices parallel to the intercommissural (AC-PC) line: repetition time (TR) 3000 ms; echo time (TE) 50 ms; flip angle 90º; slice thickness 3.75 mm; matrix 64 x 64; field of view (FOV) 220mm x 220mm for a voxel size of 3.44 x 3.44 x 3.75 mm^3.

Functional MRI Pre-Processing

Data processing took place using Statistical Parametric Mapping (SPM8) methods (Wellcome Department of Cognitive Neurology, London, United Kingdom). High-resolution anatomical images were registered nonlinearly to the ICBM atlas space using the MNI-152 templates. Each volume of the fMRI image series was aligned to the first using rigid body registration to correct for head motion. Then the high-resolution anatomical image was rigidly registered with the first functional, and the nonlinear transformation to atlas space was applied to all functional images. Images were subsequently smoothed using a 6 mm FWHM Gaussian kernel.

Functional MRI Statistical Analysis

Statistical parametric mapping was also performed using SPM8 software. Pre- and post-treatment scans were included in a single massively univariate general linear model. Regressors were included for each condition (neutral or preferred) to indicate music listening for each run of each session. These images consist of appropriate boxcar functions convolved with a canonical hemodynamic response shape. Within each session the contrast of BOLD signal during the preferred music relative to the neutral music run

was used as a measure of brain response to reward. This measure was compared between sessions using relevant contrasts to examine the effect of treatment.

The SPM T maps of the contrast of interest were set at a threshold of T=2.58 (voxelwise $p<0.005$). The statistical significance of the resulting clusters was calculated using the approach of random field theory (Worsley, 1994; Friston, Worsley, Frackowiak, Mazziotta, & Evans, 1994). With knowledge of the search volume (number of total voxels) and the smoothness of the T map images, this methodology allows for calculating the probability of a suprathreshold cluster of a particular size occurring by chance. To improve sensitivity, this statistical analysis was limited to an a priori region of interest using small volume correction methodology (Friston, 1997). By limiting the volume searched to only part of the brain, the statistical corrections applied can be less stringent, allowing better sensitivity to small changes at the cost of missing activations outside the a priori region. The regions of interest included brain areas related to reward responsiveness and depression treatment outcome and was defined as the union of caudate, putamen, pallidum, accumbens, anterior cingulate, paracingulate, orbital frontal cortex, subcallosal, medial frontal, posterior cingulate, middle, inferior (opercularis, triangularis), and superior frontral gyrus, and the frontal pole, from the Harvard-Oxford probabilistic atlas implemented in FSLView v3.0 (http://www.fmrib.ox.ac.uk/fsl/fslview/index.html). Clusters that showed significant responses at the uncorrected cluster-level p-value of 0.05 were tabulated and reported along with p-values corrected for multiple comparisons at the whole brain level.

CHAPTER III

RESULTS

Clinical Data

Clinically relevant changes were observed in both treatments as evidenced by reductions in behavioral measures from pre- to post-treatment assessment (see Table 1). The patient treated with BATD exhibited depressive symptom reduction based on a change in her BDI-II score from 24 (moderate depression) to 2 (no depression), a reduction on her HRSD from 26 to 0, and increased environmental reward on the EROS (21 to 26). The patient receiving PPP also demonstrated clinically significant reductions in depression [BDI-II scores from 31 (severe depression) to 3 (no depression), HRSD from 21 to 3] and increased environmental reward on the EROS (18 to 30). Both patients exhibited an increase in environmental reward and a decrease in depressive symptoms throughout the course of treatment as evidenced by self-report measures completed at pre-treatment assessment, at each therapy session, and at post-treatment assessment (see Figures 2-5). Minimal symptom change was observed on self-report measures of anxiety or BIS/BAS scores, however, as indicated in Table 1.

To further assess changes observed in measures of depression and environmental reward, a cross-correlation analyses (CCA) was conducted using the Simulation Modeling Analysis software (SMA; Borckardt, 2006) to determine the extent to which changes in weekly session measures were related to one another throughout therapy. CCA determines the degree that two variables are related to each other at a specified interval. For both cases, the two measures were most highly correlated at lag 0, meaning that BDI-II scores were most strongly related to EROS scores on a session-by-session

basis. CCA statistics for the patient receiving BATD showed that the BDI-II and EROS scores were statistically significant at lag 0 ($r = -0.92$, $p = 0.000$; see Figure 6) likewise the patient receiving the PPP treatment was statistically significant at lag 0 ($r=-0.90$, $p = 0.001$; see Figure 7).

Functional MRI Data

To assess changes in BOLD response following treatment, contrasts were run with a basic subtraction method where an uncorrected p-value (≤ 0.05) was applied. Assessment of BOLD responses was done through two types of contrast. The first contrast was time (pre-treatment, post-treatment) by music (preferred, neutral) to assess responsiveness to preferred relative to neutral music. The second contrast examined time (pre-treatment, post-treatment) by music, disregarding preference (music, silence) to assess responsiveness to music relative to silence. Examination of both contrasts revealed no changes in any of the sub-cortical regions implicated in reward responsiveness hypothesized to change following treatment. Neither contrast revealed significant BOLD responses within the nucleus accumbens, caudate nucleus, ventral striatum, anterior cingulate, the posterior cingulate, or the globus pallidus in either patient.

Contrasts examining music valence, preferred and neutral, did not result in significance at the p-corrected level for any regions but did evidence significance in several regions at the p-uncorrected level (See Tables 2 & 3). Contrasts that resulted in significance at the p-corrected value examined music and silence and evidenced significant changes in two different brain regions (See Tables 2 & 3). Common to both treatments were changes observed within the subgenual cingulate. The patient receiving BATD exhibited elevated subgenual cingulate BOLD response during silence at pre-

treatment and reduced BOLD response at post-treatment, where activity was not distinguishable between music and silence (See Figure 9). The PPP condition also exhibited changes in the subgenual cingulate region such that BOLD response here was observed to be elevated during music at pre-treatment, and to become elevated during silence at post-treatment (See Figure 11). The PPP condition was also associated with post-treatment significance, at the p-corrected level, within the superior frontal gyrus. BOLD response here was observed to be elevated during music at pre-treatment and was reduced during music at post-treatment, or rather, elevated BOLD response during silence at post-treatment (See Figure 11).

Contrasts examining music preference over neutral did not result in significance at the p-corrected level for any regions. However, several regions evidenced significance at the p-uncorrected level and are reported here. While these data are not significant at the p-corrected level, they may be suggestive of certain patterns of activation relevant to the pathophysiology of depression and treatment and are therefore reported. Common to both treatments, changes were observed in bilateral dorsolateral prefrontal regions (dlPFC), and the medial orbital prefrontal regions (moPFC), with each treatment differentially affecting these regions (see Tables 2 & 3). Within the BATD condition, pre- to post-treatment responses during the preferred relative to neutral music contrast resulted in increased BOLD response activations in the bilateral moPFC and right dlPFC/frontal eye field (see Figure 8). When comparing the interaction between pre- and post-treatment with music and silence, the BATD condition resulted in BOLD response increases in the right moPFC and deactivations in the left lateral anterior frontal cortex (see Figure 9).

BOLD responses in the left dlPFC were deactivated during music at pre-treatment and indistinguishable between music and silence at post-treatment (see Figure 9).

Within the PPP condition, pre- to post-treatment responses during the preferred relative to neutral music contrast resulted in increased BOLD response activations in the right moPFC and deactivations in left and right dlPFC relative to neutral music passages. (see Figure 10). When comparing the interaction between pre- and post-treatment with music and silence, the PPP condition resulted in BOLD response deactivations in the left, lateral orbital PFC and the dlPFC/frontal eye field (see Figure 11).

CHAPTER IV

DISCUSSION

This study explored changes in depression symptom severity and functional brain activation following 8 sessions of two psychosocial treatments for clinical depression. Both patients responded favorably to respective treatments, as reflected on both clinician and self-report measures of depression. A direct inverse relation between self-reported depression and environmental reward, with depression attenuation associated with increased environmental reward supports predominant behavioral models of depression (Carvalho & Hopko, 2011; Lewinsohn, 1974; Manos, Kanter, & Busch, 2010). Neither patient evidenced substantial changes in self-reported behavioral inhibition or behavioral activation, however, providing no support for the hypothesis that functional brain changes would correspond to changes on behavioral inhibition and activation.

Our first hypothesis was unsupported as the music listening fMRI paradigm did not sufficiently elicit activity in subcortical regions implicated in reward. No contrast revealed significant changes in the several hypothesized regions implicated in reward responsiveness and depression. To speculate on this finding, either the rewarding music paradigm was insufficient to elicit reward responsiveness and corresponding neural underpinnings or the small sample size restricted the power necessary to observe changes in these subcortical areas. The latter explanation is suspected as very similar scanner paradigms have been previously employed and demonstrated efficacy in eliciting reward responsiveness neural activity in both healthy controls and depressed individuals (Osuch et al., 2009). A third possibility is that BATD and PPP do not exert their neurobiological mechanism of change via direct effect on subcortical neural circuits of reward, and that

these regions are affected as a secondary consequence of frontal cortical regions being engaged during psychotherapy.

Regarding the contrast examining music and silence, statistically significant changes at the p-corrected level emerged in two different regions. First, activity in regions within, or in close proximity to, the subgenual cingulate was significant for both patients. BOLD signal response for the BATD patient was observed to be elevated during silence relative to music at pre-treatment, and was observed to attenuate and become indistinguishable between music and silence at post-treatment. Elevated activity here has been observed to be a hallmark for neurobiological models of depression (Mayberg et al., 1999, 2000, 2005; Mayberg 2006), and generally is abnormally elevated among depressed individuals during resting-state scans (Greicius et al., 2007). Data from numerous studies utilizing neuroimaging modalities to evaluate differing mood states implicate the subgenual cingulate as a brain region crucial to emotion processing and to the pathophysiology of mood disorders (Mayberg et al., 2005; Greicius, et al., 2007). The attenuation of subgenual cingulate activity following BATD taken in conjunction with other cortical findings may reflect a biological mechanism of change where the patient was better able to modulate her emotional experiences, thereby enhancing her capacity to enjoy pleasurable stimuli. In either case, subgenual cingulate activity is elevated in depressed states (Drevets, Bogers, & Raichle, 2002; Kennedy et al., 2001) and tends to decline in activity in depressed patients who respond to treatment (Kennedy et al., 2001; Mayberg et al., 2000). A seemingly opposite pattern was observed within the subgenual cingulate for the PPP patient. BOLD response was elevated during music relative to silence at pre-treatment, and was deactive during music relative to neutral at post-

treatment. Simply stated, BOLD response within the subgenual cingulate increased during neutral music following PPP treatment. This is difficult to interpret in lieu of the patient's reduction in depressive symptoms and requires experimental replication.

Significance, at the p-corrected level, was also observed in the superior frontal gyrus for the PPP condition. This area evidenced elevated BOLD response during music compared to silence at pre-treatment and attenuated BOLD response at post-treatment during music, such that it was elevated during silence. This region has been observed to play a role in executive functioning, affect regulation, self-reference, and laughter among other things (Fried, Wilson, MacDonald, & Behnke, 1998; Goldberg, Harel, Malach, 2006; Koenigs & Gragman, 2009). Interestingly, regional decreased activity within this region and in immediately surrounding regions, is associated with depression (Koenigs & Grafman, 2009) where increased metabolism here has been associated with recovery from depression (Mayberg et al., 1997). The fact that this region increased BOLD signal during silent conditions may reflect increased cognitive processes that was adaptive and consistent with reduction in depression.

Of note, several other brain regions evidenced BOLD response that was interesting and deserving of speculation despite their not achieving statistical significance at the p-corrected level. We feel compelled to report additional results that were observed at the p-uncorrected level as these regions were part of our a priori predictions, BOLD response changes were observed within similar regions for both patients, and because these regions are implicated in the pathophysiology of depression (Mayberg 2003, 2006). While these results are speculative, we suspect that, with a larger sample size, many of these regions would have reached statistical significance at the p-corrected level.

Contrasts examining music preference over neutral resulted in significance at the p-uncorrected value in several regions which, although highly speculative, may be suggestive of certain patterns of activation relevant to the pathophysiology of depression and our treatment. Both treatments evidenced differential changes within similar regions of interest. For example, BOLD response in the right dlPFC was observed to increase activation during preferred relative to neutral music in the BATD condition, where bilateral dlPFC was observed to trend towards deactivation during preferred music in the PPP condition. Similar findings were observed with music and silence for left sided dlPFC where increased BOLD response was observed in the BATD condition in response to music where it was observed to attenuate in response to music for the PPP condition. These findings suggest that bilateral dlPFC increases in BOLD response for preferred music relative to neutral and silence conditions for the BATD patient, where the opposite pattern was observed for the PPP patient.

The dlPFC has commonly been associated with "cognitive" or "executive" functions where hypoactivity has been commonly observed in depressed individuals with increased activity reflecting attenuations in depressive symptoms (Koenigs & Grafman, 2009). One interpretation, while highly speculative, might be that BATD resulted in reduced depression severity, thereby allowing the BATD patient to more effectively and efficiently utilize cognitive resources to more effectively cope with depression (Eysenck & Calvo, 1992). This increased dlPFC activation was seemingly not at the expense of experiencing pleasureable music stimuli, as post-treatment scans revealed elevated BOLD responses in the moPFC for preferred relative to neutral music.

Interestingly, while hypoactivity in the dlPFC is observed in depression, decreased glucose metabolism has been observed following CBT and IPT treatment for depression (Brody et al., 2001; Goldapple et al., 2004). Therefore, one speculation of the dlPFC deactivations observed in the PPP patient might be that treatment resulted in a reduction in ruminative depressive affect during passive experiences whereby in the patient's ability to enjoy pleasureable music was enhanced. This is one plausible interpretation as the post-treatment assessment revealed BOLD signal response within the moPFC to increase, while the dlPFC decreased. In either case, both treatments resulted in symptom reduction, and increased activation in the moPFC during preferred music passages at post-treatment. The moPFC is a region that has shown to be correlated with pleasure ratings of music (Osuch et al., 2009). These disparate findings may plausibly reflect differential neural mechanisms of change induced by different treatment approaches.

Consistent with a priori hypotheses, activity within bilateral regions of the medial orbital frontal cortex increased during preferred music following BATD treatment. Right-sided activations in this region also became more active for music relative to silence at post-treatment. This region has been implicated in models of depression (Mayberg 2003, 2006), and distinguishes depressed and healthy individuals during music listening tasks (Osuch et al., 2009). Change observed in the BATD patient might plausibly reflect an increased capacity to experience reward as the moPFC plays a role in relative rather than absolute reward (Elliott, Agnew & Deakin, 2008). These bilateral elevations in the moPFC may reflect a greater ability of the BATD patient's capacity to experience pleasure as this region has been implicated in a conscious regulation of emotional states

(Phillips, Drevets, Rauch, & Lane, 2003). The PPP patient also experienced a somewhat similar activation pattern of right sided medial orbital activity that involved increased BOLD signal response for preferred relative to neutral music at post-treatment. We speculate that these regional activations might reflect an increased capacity to experience affectively arousing music during scanning. It is difficult to state this with confidence, however, as our results are interpreted based of p-uncorrected values and are derived from a sample size of 1 patient per treatment.

Importantly, within all contrasts examined, similarities were not noted with those reported in other studies examining BOLD responses to reward responsiveness following BATD (Dichter et al., 2009). Our interpretation of the distinct findings observed is that we employed a relatively simple reward response paradigm that assessed a more passive pleasurable experience, rather than a more sophisticated reward paradigm that required engagement in tasks to elicit components related to reward selection, feedback and response (Smoski et al., 2009). Moreover, this study assessed BOLD response change and depression symptom attenuation among two patients, a very small sample size that might have restricted power to detect changes in sub-cortical regions implicated in reward responsiveness.

Although this study demonstrated functional brain changes assessed by fMRI BOLD response, several limitations must be addressed. First, due to the small sample size, this study requires replication to assess external validity. Second, changes were assessed between two patients receiving disparate interventions for depression, with neural changes interpreted based on intervention characteristics. In addition to a larger sample size, a stronger research design would include a no-treatment control group to

control for the passage of time in the attenuation of depressive symptoms or changes in functional brain activity. Furthermore, neither treatment was independently evaluated to measure and assess therapist competence or treatment adherence. Third, although both treatments demonstrated efficacy in ameliorating depression, the PPP patient data may be somewhat confounded by the discontinuation of Tamoxifen, a hormone treatment for breast cancer that has depression listed as a side-effect for 15% of women (Demissie, Silliman, & Lash, 2001). It can therefore not be ruled out that attenuation in depressive symptoms and corresponding changes in neurobiological activity observed from pre- to post-treatment was due in some part to hormone fluctuation. Likewise, it is not clear to what extent the consistent regimen of allergy and sleep medication constitutes and artifact for each patient's depression, their respective treatments, or the results of their brain scans. Finally, while attempts were made to include participants that matched as close as possible, important differences deserve mention. Patient differences included co-morbid psychiatric diagnosis of generalized anxiety disorder for the BATD patient who evidenced slightly elevated BAI at pre-treatment that did not attenuate following treatment. Moreover, both patients were also in substantially different stages of the cancer treatment and recovery such that the patient receiving PPP was two years cancer remised where the BATD patient was in the midst of her chemotherapy treatment.

While the music paradigm used in this study did not effectively elicit subcortical activations associated with reward responsiveness, it did effectively elicit cortical activations, at the p-uncorrected level, implicated in reward, affect regulation, and executive function. It is therefore a viable scanner paradigm that should be employed in future studies using larger samples of depressed individuals. Moreover, this is the second

study demonstrating that when BATD is associated with positive treatment outcome, functional brain changes are identified. This was also the first study assessing PPP and associated functional brain changes. While these results are preliminary, this study may be suggestive that while two treatment approaches may effectively attenuate symptoms of depression, they may do so through distinct neurobiological mechanisms. This bares relevance as the pathophysiology of depression is hypothesized to be a neural network distributed through cortical and subcortical regions of the brain with differential components of the network playing roles in subtypes of depression (Mayberg, 2003, 2006). Future studies might consider evaluating how different treatment approaches differentially target specific neural components of depression. The future treatment of psychiatric disorders may greatly benefit from basing treatment selections on neurobiological features that are known to respond more to one treatment relative to other available options.

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APPENDIX

Table 1
Symptom Measures At Pre-assessment and Post-treatment

	BATD		PPP	
Measures	Pre	Post	Pre	Post
BDI-II	24	2	31	3
EROS	21	27	18	30
HAM-D	26	0	21	3
BAI	16	17	5	2
BIS	9	10	12	16
BAS-Drive	9	10	15	15
BAS-Fun	7	7	11	12
BAS-Reward Response	7	7	12	11

Note. BATD = Behavioral Activation Treatment for Depression; PPP = Pragmatic Psychodynamic Psychotherapy. All scores listed are raw scores.

Table 2
BOLD response between pre- and post-treatment for BATD condition.

Region	Side	MNI x	MNI y	MNI z	size	p(cor)	p(unc.)	T-Value
Pre > Post (Pref. > Neu.)								
Middle Frontal Gyrus Frontal eye field/Dorsolateral PFC	R	42	17	31	35	.219	**.016***	4.48
Inferior Frontal Gyrus Medial orbital frontal	L	-27	35	-8	38	.178	**.013***	4.09
Inferior Frontal Gyrus Medial orbital Frontal	R	24	32	-20	18	.663	.070	4.23
Post>Pre (Music > Slience)								
Subgenual cingulate/moPFC		-3	35	-20	79	**.012****	**.001***	4.73
Inferior Frontal Gyrus Dorsolateral PFC	L	-51	38	16	36	.204	**.015***	4.37
Middle Frontal Gyrus Medial orbital frontal	R	21	32	-20	27	.379	**.031***	4.73
Pre>Post (Music > Slience)								
Middle Frontal Gyrus Lateral Anterior frontal PFC	L	-36	44	19	46	.102	**.007***	4.32

Note. MNI corresponds to Montreal Neurological Institute coordinates. Size corresponds to the number of voxels within a given activation cluster, where T-Value denotes peak T-Value activation within that cluster. Significance at the p-corrected level of .05 is denoted by ** where significance at the p-uncorrected level of .05 is denoted by *.

Table 3
BOLD response between pre- and post-treatment for PPP condition

Region	Side	MNI x	y	z	size	p(cor)	p(unc.)	T-Value
Pre>Post (Neu. > Pref)								
Medial Frontal Gyrus Medial orbital frontal	R	9	41	-20	21	.546	**.05***	4.05
Pre>Post (Pref. > Neu.)								
Middle Frontal Gyrus Dorsolateral PFC	L	-33	56	-2	33	.241	**.017***	3.85
Middle Fontal Gyrus Dorsolateral PFC	R	36	47	25	36	.194	**.014***	3.60
Pre>Post (Music – Slience)								
Superior Frontal Gyrus	L	-3	53	13	103	**<.001****	**.003***	3.67
Middle Frontal Gyrus Lateral orbital frontal PFC	L	-24	29	-17	27	.367	**.029***	3.61
Middle Frontal Gyrus Frontal eye field/Dorsolateral PFC	L	-48	11	46	21	.546	**.05***	3.47
Subgenual Cingulate		0	29	-23	167	**<.001****	**<.001***	4.91

Note. MNI corresponds to Montreal Neurological Institute coordinates. Size corresponds to the number of voxels within a given activation cluster, where T-Value denotes peak T-Value activation within that cluster. Significance at the p-corrected value of .05 is denoted by ** where significance at the p-uncorrected value of .05 is denoted by *.

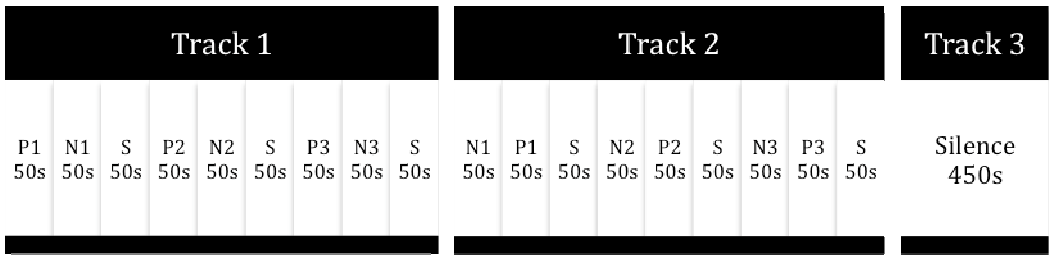

Figure 1. Visual Representation of Block Design completed by participants during their 30 minute functional MRI scan prior to an following their treatment. P1 denotes the first 50 seconds of the preferred music passage where P2 and P3 denotes 51 through 1.40 seconds and 1.41 through 2.30 seconds of that preferred song. N denotes neutral music passages, S to silence, and s to seconds.

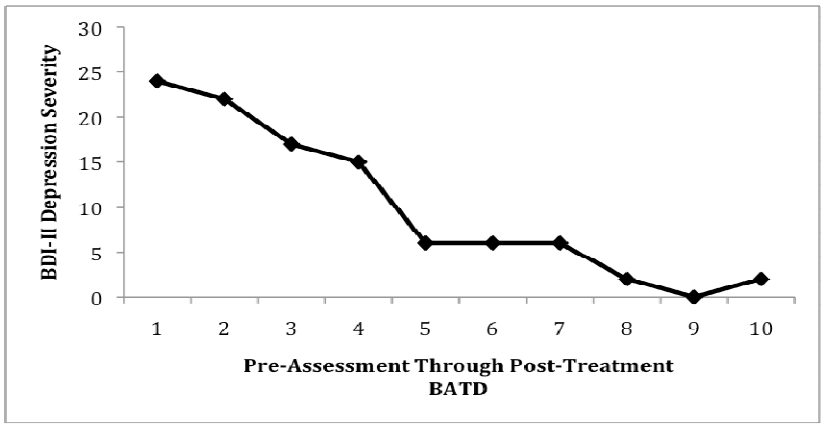

Figure 2. BDI-II scores completed at pre-assessment, during each of the 8 therapy sessions, and following completion of BATD.

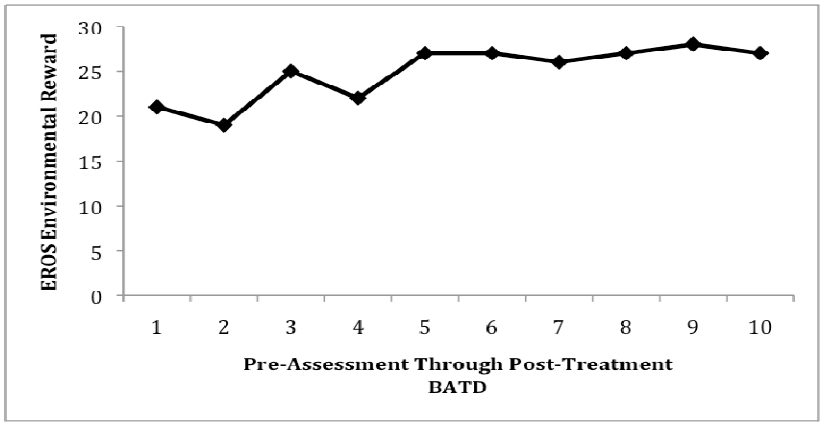

Figure 3. EROS scores completed at pre-assessment, during each of the 8 therapy sessions, and following completion of BATD.

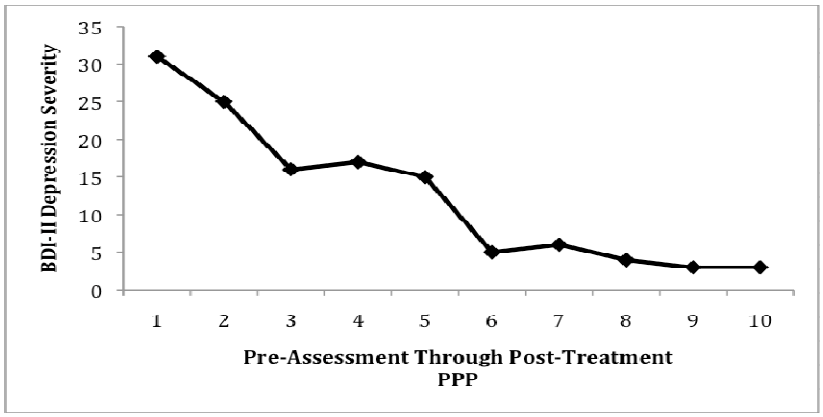

Figure 4. BDI-II scores completed at pre-assessment, during each of the 8 therapy sessions, and following completion of PPP.

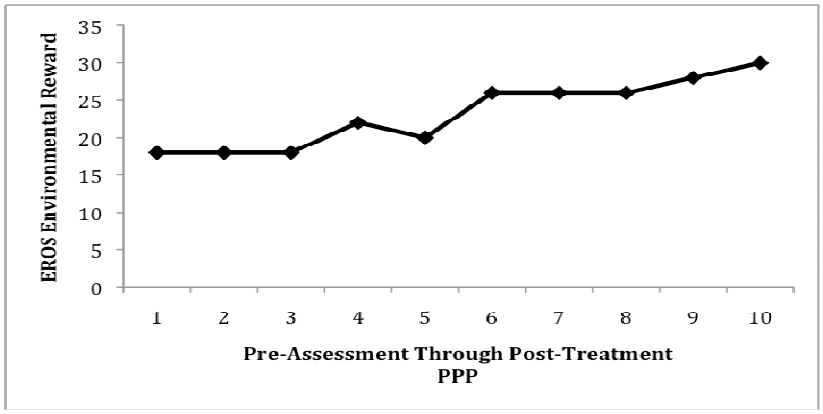

Figure 5. EROS scores completed at pre-assessment, during each of the 8 therapy sessions, and following completion of PPP.

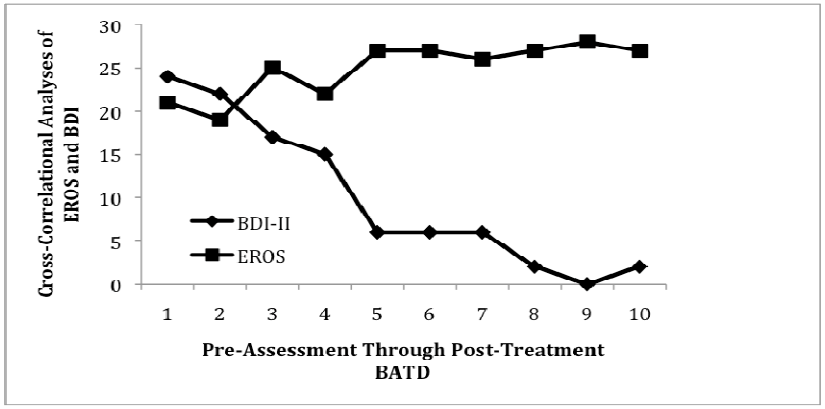

Figure 6. Cross-correlational analyses of EROS and BDI-II from pre-assessment, though each of the 8 therapy sessions, and following completion of BATD. CCA statistics for the patient receiving BATD showed that the BDI-II and EROS scores were statistically significant at lag 0 ($r = -0.92$, $p = 0.000$).

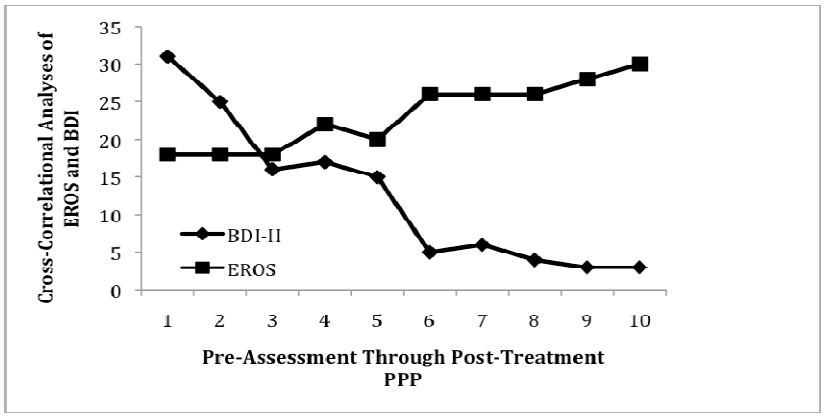

Figure 7. Cross-correlational analyses (CCA) of EROS and BDI-II from pre-assessment, though each of the 8 therapy sessions, and following completion of PPP. CCA statistics for the patient receiving PPP showed that the BDI-II and EROS scores were statistically significant at lag 0 ($r=-0.90$, $p = 0.001$).

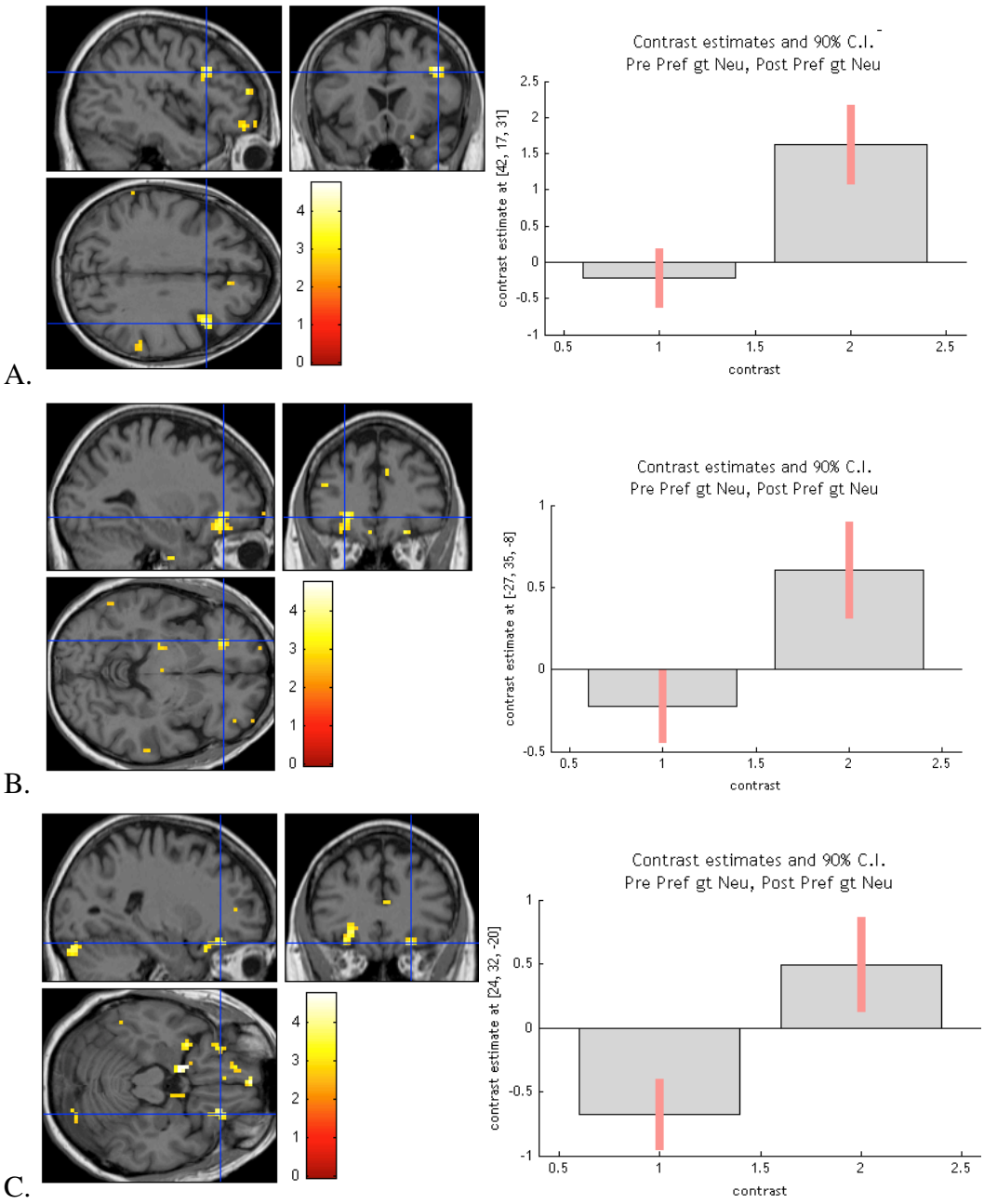

Figure 8. T-Maps and plots denoting BOLD response for interaction contrast of treatment (pre, post) by music (preferred, neutral) for BATD. Contrasts denote that BOLD response was indistinguishable between preferred and neutral pre-treatment in the (A) right dorsolateral cortex (42 17 31) and (B) left medial orbital frontal cortex (-27 35 -8) where each region evidenced elevated BOLD response during preferred, relative to neutral, at post-treatment. BOLD response was deactive in the (C) right medial orbital frontal cortex (24 32 -20) during preferred music, relative to neutral, at pre-treatment, and evidenced elevated BOLD response during preferred, relative to neutral, at post-treatment. Neurological convention (right on right) is used and coordinates are in Montreal Neurological Institute space.

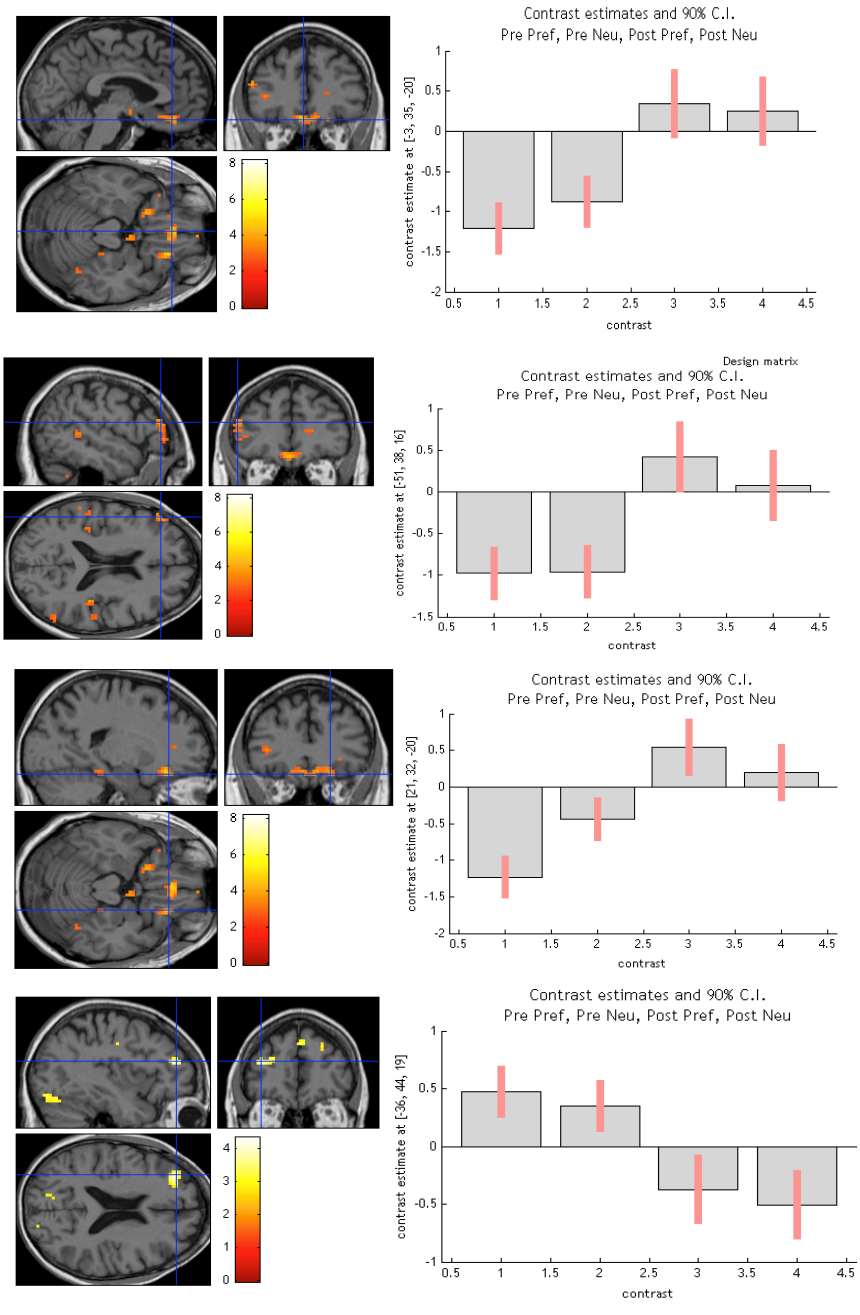

Figure 9. T-Maps and plots denoting BOLD response for interaction contrast of treatment (pre, post) by music, agnostic to valence (music, silence) for BATD. Contrasts denote that pre-treatment BOLD responses were deactive for music, relative silence, within the (A) subgenual cingulate (-3 35 -20), the (B) left dorsolateral prefrontal cortex (-51 38 16), and the (C) right medial orbital frontal cortex (21 32 -20), and, at post-treatment, these regions trended towards higher BOLD response for music, relative to silence, though, the activations evidenced little distinctiveness between music and silence at post-treatment. BOLD response was slightly elevated in the (D) left lateral anterior frontal cortex (-36 44 19) during music, relative silence, at pre-treatment and was deactive during music, relative to silence, at post-treatment.

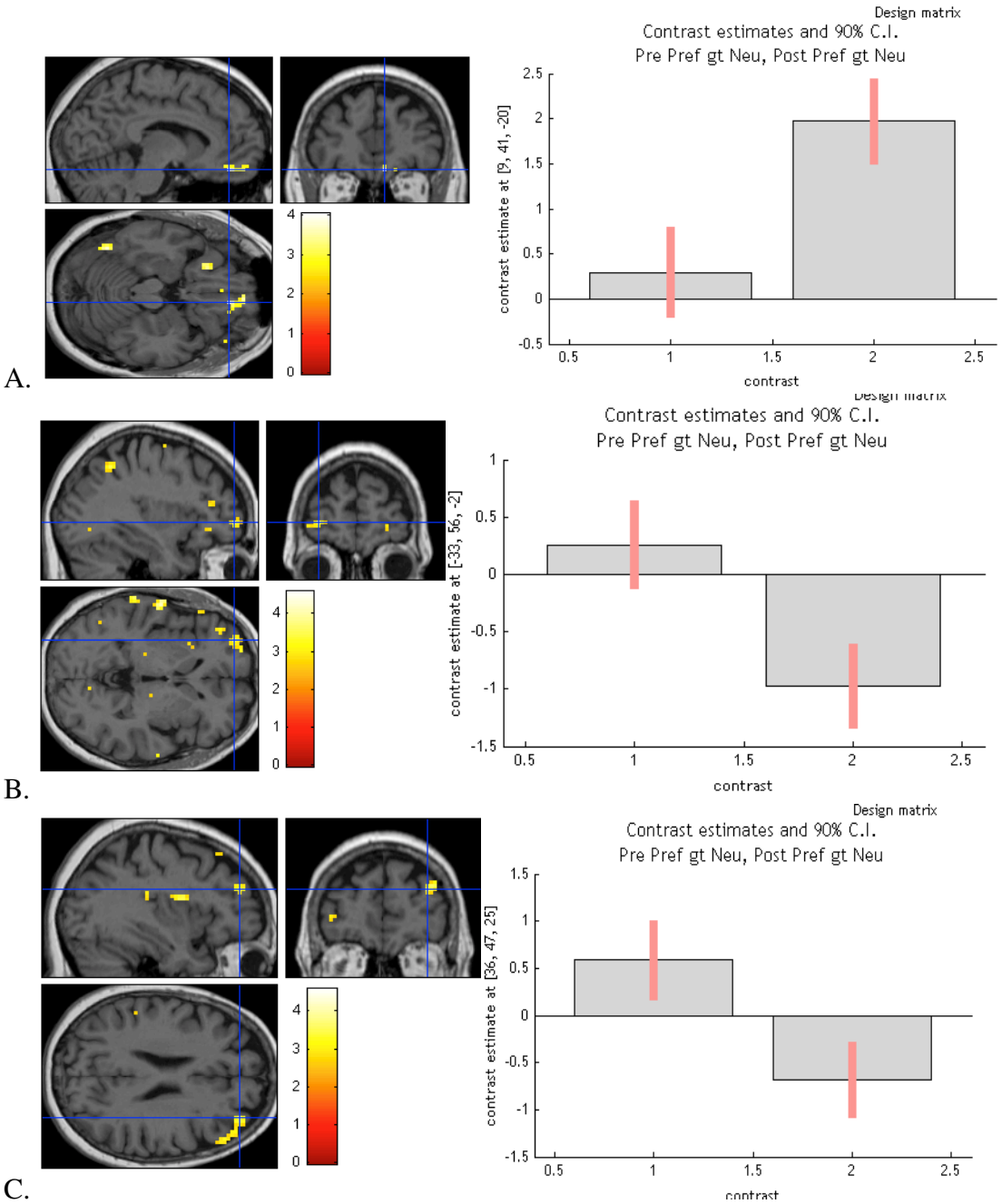

Figure 10. T-Maps and plots denoting BOLD response for interaction contrast of treatment (pre, post) by music (preferred, neutral) for PPP. Contrasts denote that BOLD response was indistinguishable between preferred and neutral pre-treatment in the (A) right medial orbital (9 -41 -20) and (B) left lateral anterior PFC (-33 56 -2) where it evidenced elevated BOLD response and decreased BOLD response, relative to neutral, in these respective areas at post-treatment. BOLD response was slightly elevated in for preferred music, relative to neutral, at pre-treatment, and was deactive during preferred, relative to neutral, at post-treatment in the (C) right dorsolateral prefrontal cortex (36 47 25).

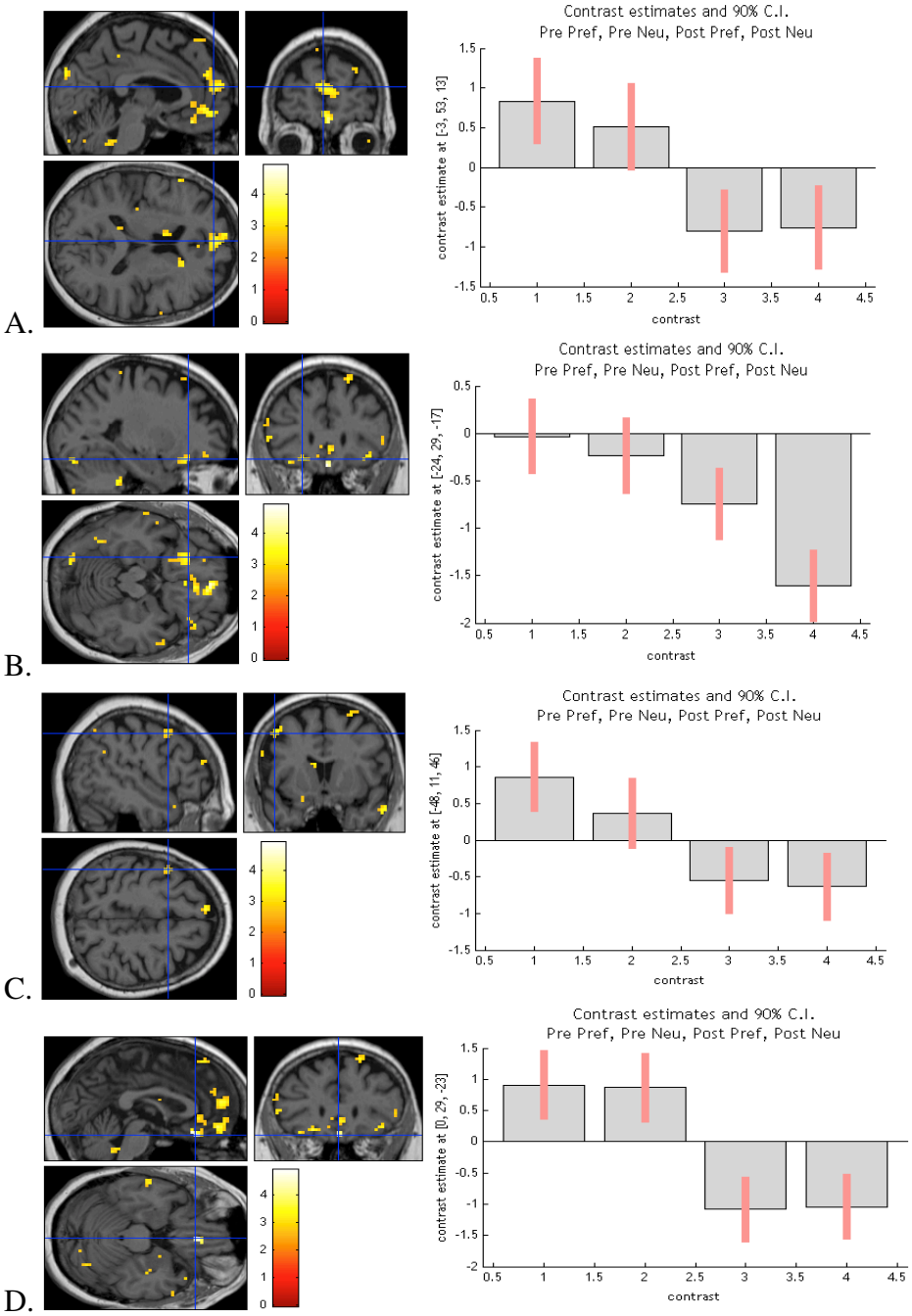

Figure 11. T-Maps and plots denoting BOLD response for interaction contrast of treatment (pre, post) by music, agnostic to valence (music, silence) for PPP. Contrasts denote that BOLD response elevated for music, relative silence, at pre-treatment within the left sided (A) medial anterior frontal (-3 53 13), the (C) dorsolateral PFC (-48 11 46), and the (D) subgenual cingulate (0 29 -23), and was deactive in these regions, during music relative silence, at post-treatment. BOLD response was indistinguishable between music and silence at pre-treatment within the (B) left ventral medial frontal cortex (-24 29 13) and was more deactive during music, relative silence, at post-treatment.

VITA

Michael Gawrysiak was born in Geneseo, Illinois on January 6th, 1983 to Michael and Lourdine Gawrysiak. He studied Philosophy and Psychology at Southern Illinois University, Carbondale, where he graduated in 2005. He completed his Masters Degree, under the mentorship of Dr. Derek Hopko, in 2008. In June of 2011 he completed his pre-doctoral internship in clinical psychology at Jesse Brown VA Medical Center. He also graduated with his Ph.D. in Psychology in 2011 at the University of Tennessee. He is continuing his career interests through a post-doctoral fellowship where he will work jointly at the University of Pennsylvania as well as the Philadelphia VA Medical Center.