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Neural Responsiveness to Reward as an Index of Depressive Symptom Change following Cognitive-Behavioral Therapy and Selective Serotonin Reuptake Inhibitor Treatment

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Abstract

Objective: The reward positivity (RewP), a neurophysiological index of reward responsivity, is consistently reduced in participants with depression, and to a lesser extent anxiety. It remains unknown, however, whether the RewP can be altered as psychiatric symptoms change with treatment. The current study addressed this question by examining differences in RewP within

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[1]Pearson correlation coefficients revealed moderate to high stability of the ERP-Gain and ERP-Loss variables from T1 to T2 among both patients (ERP-Gain $r = .59$, $p < .001$; ERP-Loss $r = .63$, $p < .001$) and healthy controls (ERP-Gain $r = .61$, $p < .01$; ERP-Loss $r = .72$, $p < .001$). The stability of the RewP was low among both groups (lowest $p = .50$).

[2]Post-hoc analyses were conducted to determine whether changes in the ERP-Gain and/or ERP-Loss variables correlated with changes in symptoms of depression and/or anxiety pre-to-post treatment. None of these analyses reached significance (lowest $p = .09$).

[3]Post-hoc analyses were conducted to determine whether the ERP-Gain and/or ERP-Loss variables predicted changes in symptoms of depression and/or anxiety pre-to-post treatment. None of these analyses reached significance (lowest $p = .18$).

patients before and after twelve weeks of a selective serotonin reuptake inhibitor (SSRI) or cognitive-behavioral therapy (CBT). We also examined the utility of the RewP as a predictor of symptom change during CBT and SSRI treatment.

Methods: Participants were recruited between 2014 and 2017 and included adults with a primary anxiety or depressive disorder (n=63) and healthy controls (n=25). At baseline and twelve weeks, participants completed a monetary award task while EEG (electroencephalogram) was recorded. Between EEG sessions, patients completed CBT or SSRI treatment.

Results: At baseline, higher depressive symptoms were associated with a more attenuated RewP. We found no significant differences between patients and healthy controls in the degree of RewP change across the twelve weeks; however, among patients, the extent of increase in the RewP robustly correlated with the extent of decline in depressive (t=−2.21, p=.03) and anxiety (t=−2.57, p=.02) symptoms following CBT and SSRI treatment. Additionally, a more reduced RewP at baseline predicted a greater reduction in depressive symptoms following SSRIs (t=−2.04, p<.05), but not after CBT.

Conclusions: These findings highlight neural responsiveness to reward as both a mechanism and predictor of depressive symptom change that may be used serve as an objective index of symptom improvement.

Keywords

depression; reward positivity; cognitive-behavioral therapy; selective serotonin reuptake inhibitors; anxiety

Introduction

Internalizing psychopathologies, encompassing anxiety and depressive disorders, are characterized by deficits in several aspects of reward processing, including effort valuation, reward outcome, and decision-making processes in the context of reward (1,2). The Research Domain Criteria (RDoC) initiative of the National Institute of Mental Health (NIMH) has identified a number of reward-related biologically based constructs within the Positive Valence System (PVS) to promote better ways of classifying psychiatric disorders and identifying treatment targets. Initial responsiveness to reward attainment is one construct within the PVS that is consistently linked to depressive disorders (3), and to a lesser extent anxiety (2), and refers to the mechanisms associated with hedonic responses (e.g., behavioral, physiological, and neurological responses to pleasurable or positive stimuli) and culmination of reward seeking.

There is substantial evidence at self-report and behavioral levels that depressive disorders, particularly when accompanied by anhedonia, are characterized by diminished hedonic responses and an inability to modulate behavior as a function of rewards (4). There is some evidence that deficits in reward responsiveness also extend to anxiety disorders. For instance, even when controlling for depression history, social anxiety is characterized by diminished positive experiences, infrequent positive events, and fear responses to overtly positive experiences (5). Diminished hedonic responses have also been documented among individuals with posttraumatic stress disorder (PTSD, 6) and generalized anxiety disorder

(GAD, 7), albeit with mixed evidence. Specifically, there is also evidence for intact reward responses among individuals with anxiety disorders at self-report and behavioral levels (8). It has been suggested that the relationship between anxiety and reward responsiveness might vary as a function of self-regulatory abilities (5) or the presence of anhedonia (1) among individuals.

To capture individual differences in reward responsiveness at the psychophysiological level, researchers have utilized the event-related potential (ERP) component, the reward positivity (RewP). The RewP, also referred to as the feedback negativity (FN) or feedback-related negativity (FRN), appears as a frontocentral ERP component occurring approximately 250–350 ms following the receipt of a reward, and is thought to reflect the processing of positive feedback for reward relative to feedback for non-reward or losing (9). Studies have consistently documented a negative relationship between the RewP and depressive symptoms and diagnoses across development (10–14). A decreased RewP has been also observed to prospectively predict future depressive symptoms (15) and diagnoses (16) in youth. Fewer studies have examined the association between the RewP and anxiety, and findings have been less consistent relative to studies with depression. For instance, whereas some studies have found a relationship between an attenuated RewP and anxiety symptoms in youth (17) and adults (18), others have failed to find a significant relationship (10,11).

Taken together, extant data indicate an attenuated RewP response in depressive disorders across development, with some mixed evidence in individuals with anxiety. In one study, the significant negative relationship between the RewP and depressive symptoms was maintained at a separate testing point two years later among a sample of adolescents (15), suggesting that the RewP indexes a trait-like vulnerability factor for depression. Providing additional support for this notion, studies have found evidence for a blunted RewP among adults in remission from depression (19,20). No studies to date, however, have examined the malleability, or lack thereof, of the RewP in these populations as it pertains to treatment. Specifically, it remains unknown whether the RewP can be altered as psychiatric symptoms change over time and is therefore a candidate treatment target.

Functional magnetic resonance imaging (fMRI) studies provide some evidence that neural responsiveness to reward is improved following behavioral activation and selective serotonin reuptake inhibitors (SSRIs) treatments (21,22). For instance, Stoy et al. (22) found that depressed patients exhibited hypoactivation of the ventral striatum, an area linked to the RewP (23), during reward processing at baseline and this deficit was normalized after SSRIs use. This suggests that the RewP may dynamically change along with symptom improvement and thus serve as an objective marker of treatment progress. Addressing whether the RewP is disrupted in internalizing disorders and is malleable with treatment is critical in advancing the NIMH RDoC Initiative, which seeks to develop objective dimensional assays that align with brain circuits and, in turn, enable quantification of treatment response (24).

The current study examined the malleability of the RewP to standard treatments in a heterogeneous treatment-seeking sample with anxiety and depressive disorders. We first sought to replicate previous findings demonstrating a negative relationship between the

RewP and depressive symptomatology among patients and healthy controls at baseline. We examined whether the RewP is amenable to change after twelve-weeks of either cognitive behavioral therapy (CBT) or SSRI treatment. Consistent with the fMRI literature (21,22), we predicted that the RewP would be enhanced after twelve weeks of treatment. We also evaluated whether pre-to-post treatment-related change in the RewP would correlate with change in depressive symptoms in patients. For healthy controls, we suspected that the RewP would remain relatively stable over the same time period given the previously documented stability of the RewP among healthy adults (25).

In addition to examining whether the RewP increases after treatment, we explored whether individual differences in pre-treatment RewP predicted symptom change following treatment. Specifically, response rates to CBT and SSRIs vary, with a range of 38%–87% across anxiety and depressive disorders (26,27). Identifying predictors of symptom reduction following CBT and/or SSRIs has the potential to inform clinical decision making and precision medicine. Indeed, recent evidence highlights the advantage of utilizing ERPs, versus self-report and behavioral measures, to identify which individuals respond to prevention (28) and intervention (29) programs. We recently showed, in a separate cohort of patients with comorbid anxiety and depression, that an attenuated RewP response at baseline predicted a greater reduction in depressive symptoms after 12 weeks of CBT (30). Findings from this previous study suggest that individuals who exhibit preexisting deficits in reward processing may respond better with this form of treatment. In the current study, we sought to extend this previous finding to examine whether a similar prediction pattern would be observed for both CBT and SSRI treatment response.

We explored whether treatment type moderated the predictive power and malleability of the RewP; however, we did not have specific hypotheses as both forms of treatment have been shown to be effective at reducing internalizing symptoms of psychopathology (26,27). We also investigated whether the RewP served as a mechanism or predictor of anxiety symptom change following treatment.

Methods

Participants and Procedure

The current study was designed to be consistent with, and funded by, the NIMH RDoC Initiative (RFA-MH-13–080) and therefore enrolled a treatment-seeking community sample of adults with a wide range of internalizing symptoms. Potential participants were recruited from the community through a variety of means (e.g., mass e-mails, referrals, flyers at local businesses and outpatient clinics) between 2014 and 2017. To be included as a patient, participants were required to have all of the following: a current full-threshold or sub-threshold DSM-5 depressive or anxiety disorder, a Global Assessment of Functioning (GAF; 31) score of ≤ 60, and report a total score of ≥ 23 on the Depression, Anxiety, and Stress Scale [DASS-21 (32)]. Healthy controls were required to have no lifetime diagnosis of a psychiatric disorder as determined by the Structured Clinical Interview for DSM-5 Disorders [SCID-5 (33)]. Exclusionary criteria for both groups included an inability to provide consent and read and write in English; a major active medical or neurological problem; a history of mania, psychosis, an intellectual disability or pervasive developmental disorder; current

substance dependence; any contraindication to receiving SSRIs; being currently enrolled in psychiatric treatment; a history of traumatic brain injury; and being pregnant. This study was approved by the UIC Institutional Review Board and informed consent was obtained from all participants. The study was registered on ClinicalTrials.gov (Identifier: NCT01903447).

A total of 50 healthy controls and 168 patients initially enrolled in the study. For the healthy controls, 4 were deemed ineligible and withdrawn from the study, 4 dropped out prior to the baseline assessment, 2 were lost to follow-up, 11 discontinued, and 4 had poor quality EEG data at either baseline or follow-up (i.e., having fewer than 15 artifact-free trials per condition), resulting in a final sample of 25 controls. For the patients, 39 were deemed ineligible, 35 dropped out prior to baseline, 13 were lost to follow-up, and 18 had poor quality EEG data at either baseline or follow-up, resulting in a final sample of 63 patients.

Assessment of Psychopathology

Psychiatric diagnoses were assessed via the SCID-5 (33) by a trained masters-level assessor, PhD-level psychologist, or psychiatrist. The breakdown of *current* diagnoses was 73.0% (*n*=46) generalized anxiety disorder, 57.1% (*n*=36) social anxiety disorder, 54.0% (*n*=34) major depressive disorder, 27.0% (*n*=17) panic disorder, 19.0% (*n*=12) persistent depressive disorder, 19.0% (*n* = 12) specific phobia, and 14.3% (*n* = 9) posttraumatic stress disorder. The breakdown of *primary* diagnoses was 41.2% (*n*=26) generalized anxiety disorder, 27.0% (*n*=17) social anxiety disorder, 20.1% (*n*=13) major depressive disorder, 6.0% (*n*=4) panic disorder, 3.2% (*n* = 2) posttraumatic stress disorder, and 1.5% (*n*=1) persistent depressive disorder. The patients had a high rate of comorbid diagnoses, which is reflected by 59.1% of the adults having co-occurring anxiety and depressive disorders and participants having an average of 3.6±1.19 internalizing psychopathology diagnoses.

At pre- treatment, trained clinical research assessors blinded to treatment randomization administered healthy controls and patients the Hamilton Anxiety Rating Scale (HAM-A; 34), a 14-item interview-based measure of broad anxiety and somatic symptoms, and the Hamilton Depression Rating Scale (HAM-D; 35), a 17-item interview-based measure of broad depressive and somatic symptoms. Participants also completed the Beck Depression Inventory (36) and Beck Anxiety Inventory (37) self-report measures, each of which include 21-items to capture common symptoms of depression (e.g., sadness, anhedonia, worthlessness, suicidal ideation, psychomotor complaints) and anxiety (e.g., physical/panic sensations, nervousness, fear of bad things happening), respectively. Patients also completed these measures at post-treatment.

Treatment Procedures

Participants were randomized to either 12-weeks of CBT (*n*=34) or SSRI (*n*=29) treatment. For participants randomized to SSRIs (sertraline, fluoxetine, paroxetine, escitalopram or citalopram), the dosing schedule was flexible depending on tolerability and aimed to reach target dose by week 8. Patients receiving SSRIs attended medication management sessions that lasted approximately 20–30 mins with their study psychiatrist at 0, 2, 4, 8 and 12-weeks. For participants randomized to CBT, treatment was delivered through 12, once-weekly 60-minute sessions led by a PhD-level clinical psychologist under the supervision of a licensed

clinical psychologist with expertise in clinical trials with CBT. Evidence-based manuals were used based on the patient's principal diagnosis and predominant symptoms (38,39,40). As per the manualized protocol, sessions began with psychoeducation and cognitive restructuring and then expanded to include strategies such as behavioral change (e.g., exposures, behavioral activation) and relapse prevention.

Reward Task

Participants completed a well-validated computerized guessing task (10,11,16) that consisted of 40 trials. On each trial, participants were asked to choose one of two doors shown side by side on a computer monitor; the graphic remained visible until a choice was made. A fixation mark then appeared for 1000 ms, followed by feedback screen for 2000 ms. Feedback consisted of either a green "↑", indicating a gain of $0.50, or a red "↓", indicating a loss of $0.25; these amounts were chosen to give gains and losses equivalent subjective values. After receiving feedback, a fixation mark was presented for 1500 ms, followed by a screen reading "Click for the next round," which remained onscreen until participants responded. Participants received 20 trials each of gain and loss feedback, presented in a random order.

EEG Data Acquisition and Processing

Continuous EEG was recorded during the task using an elastic cap and the ActiveTwo BioSemi system (BioSemi, Amsterdam, Netherlands). Thirty-four standard electrode sites were used. The data were digitized at 24-bit resolution with a Least Significant Bit (LSB) value of 31.25nV and a sampling rate of 1024Hz, using a low-pass fifth order sinc filter with a −3dB cutoff point at 204.8Hz. Off-line analyses were performed using Brain Vision Analyzer 2 software (Brain Products, Gilching, Germany). Data were re-referenced to the average of the two mastoids and high-pass (0.1 Hz) and low-pass (30 Hz) filtered. Standard eyeblink and ocular corrections were performed utilizing the Gratton & Coles algorithm which corrects ocular artifacts by using a regression based approach (41). Semiautomated artifact rejection procedures removed artifacts with the following criteria: voltage step of more than 50 μV between sample points, a voltage difference of 300 μV within a trial, and a maximum voltage difference of less than 0.5 μV within 100 ms intervals. Additional artifacts were removed using visual inspection. Data were baseline corrected using the 200 ms interval prior to feedback. ERPs were averaged across gain and loss trials, and the RewP was scored as the mean amplitude 250–350 ms following feedback at a pooling of FCz and Fz, where the gain minus loss difference was maximal (see Figure 1). Consistent with previous research (9), analyses focused on the gain minus loss difference score (RewP); more positive values for the difference score indicate greater reactivity to reward.

Statistical Analyses

To reduce the number of statistical analyses conducted, composite depression (HAM-D and BDI) and anxiety (HAM-A and BAI) scores were created by summing standardized Z scores. A series of planned within-subjects and between-subjects analysis of variance (ANOVA) tests were conducted to verify that SSRIs and CBT were successful in reducing depressive and anxiety symptoms. We also conducted a series of bivariate correlations to examine relations between depressive and anxiety symptoms and the RewP at baseline.

Next, to assess mean level RewP changes from T1 to T2, we conducted a time (2; T1 and T2) x group (3; controls, SSRI, CBT) omnibus ANOVA. To examine whether change in the RewP corresponded to changes in symptoms among patients only, a series of hierarchical linear regression analyses were conducted with change (pre- minus post-treatment) of anxiety and depressive symptoms serving as the dependent variables. For all models, baseline symptoms, RewP change (centered), and treatment arm (CBT, SSRI) were entered in Step 1, and the two-way interaction between RewP change and treatment arm was entered in Step 2.

Finally, to examine whether the RewP at T1 predicted change in symptoms during treatment with CBT and/or SSRIs within patients, hierarchical linear regression analyses were conducted. For all models, baseline symptoms, RewP at T1 (centered), and treatment arm (CBT, SSRI) were entered in Step 1, and the two-way interaction between T1 RewP and treatment arm was entered in Step 2.

Results

Descriptive and Clinical Characteristics

Table 1 provides demographic and clinical characteristics of the sample separated by group. Within patients, depressive [$t(63)=4.27$, $p<.001$] and anxiety [$t(63)=3.86$, $p<.001$] symptoms decreased pre- to post-treatment. Neither baseline measures nor the extent of reduction in internalizing symptoms differed based on treatment modality (SSRI versus CBT; $p_s > .18$).

Bivariate correlations revealed that participants with higher depressive symptoms exhibited a more attenuated RewP at baseline ($r = -.27$; $p = .01$). However, the relationship between baseline anxiety symptoms and the RewP was non-significant ($r = -.13$, lowest $p = .20$).

RewP Before and After Treatment

An omnibus ANOVA, controlling for age and sex, was conducted to examine whether group (controls, SSRI, CBT) influenced the extent to which the RewP changed from T1 to T2. These analyses revealed no significant main effects of Group or Time, nor a significant Group by Time interaction (lowest $p = .09$).

Association between Change in RewP and Change in Symptoms among Patients

As shown in Table 2, changes in RewP correlated with changes in symptoms of depression (Figure 2a) and anxiety (Figure 2b) pre-to-post treatment. Specifically, decreases in symptoms were associated with an increase in the RewP pre-to-post treatment. The association between RewP change and depressive and anxiety symptom change was not moderated by treatment arm (Table 2).

Pre-Treatment RewP as a Predictor of Symptom Reduction among Patients

Finally, we examined whether the RewP at baseline predicted symptom change following treatment (Table 3). For change in anxiety symptoms, findings revealed no main effects of T1 RewP or two-way interactions. However, results revealed a significant T1 RewP × Arm interaction for change in depressive symptoms (Figure 3). Follow-up analyses indicated that

within patients who received SSRIs, a more attenuated T1 RewP was associated with greater reduction in depressive symptoms ($\beta = -.39$, $t = -2.04$, $p < .05$). Meanwhile, within patients who received CBT, T1 RewP was not associated with change in depressive symptoms ($\beta = .14$, $t = .75$, $p = .46$). We also probed this interaction utilizing the Johnson-Neyman technique (42), which gives a value of the moderator at which the significance of the predictor on outcome changes. The result of this procedure suggested a RewP cutoff of −4.71 ($p < .05$) and thus confirmed that patients assigned to SSRIs were more likely to exhibit depressive symptom reduction if they exhibited a blunted RewP at baseline.

Discussion

The current study examined whether the RewP, an objective neurophysiological marker of reward responsiveness, served as a biological target of depressive and anxiety symptom change following CBT and SSRI treatment. Replicating previous studies (10–16,19,20), greater depressive symptoms were associated with a more attenuated RewP at baseline. Contrary to our initial hypothesis, patients and controls did not differ in the degree of RewP change over the course of 12-weeks. Although some studies highlight changes in neural structures implicated in reward as a result of treatment for depression (21,22), our finding is somewhat consistent with other studies showing that reward responsiveness at the behavioral and neural levels continues to be reduced among individuals in remission from depression (19,20,43,44). Importantly, the current study did demonstrate that the RewP may be a novel, objective psychophysiological indicator of depressive symptom change following CBT and SSRI treatment. Specifically, within patients, the more that the RewP increased, the more that depressive symptoms improved following both treatments. These initial findings provide initial support for the RewP serving as an objective marker of treatment success for depressive symptom reduction.

In a distinct set of results, the current study also found that a more attenuated RewP at baseline predicted greater reduction in depressive symptoms following SSRIs, but not following CBT. Notably, this is in slight contrast to our previous study using a separate clinical sample where we found that a more blunted pre-treatment RewP is associated with greater depressive symptom change following CBT among adults with comorbid anxiety and depression (30). Although the precise reason for this discrepant finding is unclear, differences in study population and design may account for the different pattern of findings across studies. For instance, the current study included a more severe patient population with a greater number of comorbid diagnoses, relative to the previous reported study. Alternatively, the monetary award tasks used to elicit the RewP may be influencing the different results across studies. In our previous study, the reward task included an anticipation phase in which participants received feedback regarding whether the condition was a gain (versus breaking even) or loss (versus breaking even) condition. As a result, the consumption phase, where RewP was measured, tended to reflect sustained reward responsiveness, whereas the current task is more representative of initial reward reactivity. Although speculative, this may mean that individuals who exhibit attenuated sustained reward responses may perform better with CBT, whereas SSRIs may more directly target initial reward responsiveness. Future, larger studies are needed to test this hypothesis. If replicated, the RewP may have an important role in the application of precision medicine,

and the mission of RDoC, especially considering it is as a more time- and cost-effective option than other brain measures, such as neuroimaging, and has the potential to be utilized in psychiatric clinics.

The current set of findings appeared to be specific to depressive, versus, anxiety symptoms. That is, consistent with previous research (18) we found no evidence for a relationship between the RewP and anxiety symptoms at baseline, nor the RewP acting as a predictor of anxiety symptom change following treatment. However, change in RewP did correlate with change in anxiety symptoms following CBT and SSRI treatment, providing some evidence for the RewP exhibiting transdiagnostic features. Given the high content overlap of the scales utilized to assess anxiety and depressive symptoms, it is possible that the correlation with anxiety is more of a reflection of the RewP's association with depression. Alternatively, the current findings may have been driven by high levels of anhedonia, which is common to both anxiety and depressive disorders (1). It will be important for future studies to examine how diagnostic subgroups (e.g., anhedonia or low positive affect, mixed anxiety/depression) influence the current pattern of findings.

There were several limitations to the current study. First, due to the RDoC strategy of enrolling patients with comorbid internalizing psychopathologies, we were unable to examine whether specific psychiatric diagnoses (i.e., major depressive disorder) moderated any of the above findings because of the high comorbidity rates. Though this was never the intention of the RDoC approach, future studies may benefit from examining whether these effects are specific for certain diagnostic groups. Similarly, future studies with larger sample sizes are needed to determine if other factors (i.e., sex, age) influence the pattern of findings. In addition, the current study only included two assessments of the RewP and was unable to statistically demonstrate that changes in RewP lead to subsequent change in depression. An alternative explanation may be that changes in depressive symptoms lead to subsequent changes in reward responding at the neural level. To rule out this possibility and in order to accurately model state and trait influences, additional assessment points of these measures are needed. Next, the healthy control participants were not administered symptom measures at the follow up assessment. Future studies are needed to determine if the relation between change in symptoms and change in RewP is specific to patients or is also observed for healthy individuals not receiving treatment. It will be also important for future studies to include positive valence measures (e.g., anhedonia, well-being) as clinical outcome measures to determine if the current findings are specific to changes in positive affect or depression more broadly. Similarly, the inclusion of other measures of reward responsiveness [e.g., behavioral responses from the probabilistic reward task, (4)] in future studies will be important to determine the incremental validity of the RewP as a predictor of symptom improvement following treatment. Finally, although change in RewP correlated with change in depressive symptoms, the lack of a waitlist "treatment control" group makes it difficult to rule out whether the primary findings may have been influenced by general effects related to symptom change over time.

In summary, these findings highlight neural responsiveness to reward as both a mechanism and predictor of depressive symptom change that may be used to not only serve as an objective index of symptom improvement but also to help guide treatment selection.

Although previous fMRI studies have provided evidence for changes in neural structures implicated in reward following treatment (26,27), this is the first study to examine this question using ERPs. Future mechanistically-based interventions aimed at directly enhancing the reward positivity may prove to be most useful in reducing depression symptoms for patients who demonstrate preexisting deficits in this area.

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Clinical Points

1. The reward positivity (RewP), a neurophysiological index of reward responsivity, is consistently reduced among individuals with depression. It is unknown, however, whether the RewP can be altered as depressive symptoms change with treatment and/or serve as a marker of treatment success.
2. Findings suggest that initial responsiveness to reward at the neural level may serve as a novel, objective psychophysiological indicator of depressive symptom improvement following cognitive behavioral therapy (CBT) and selective serotonin reuptake inhibitor (SSRI) treatment. Findings from the current study also highlight neural responsiveness to reward as a predictor of SSRI treatment response.
3. This is the first study to suggest event-related potentials (ERPs), which are cost-effective and have potential to be utilized in clinical settings, can track treatment effects for depressive symptom reduction.

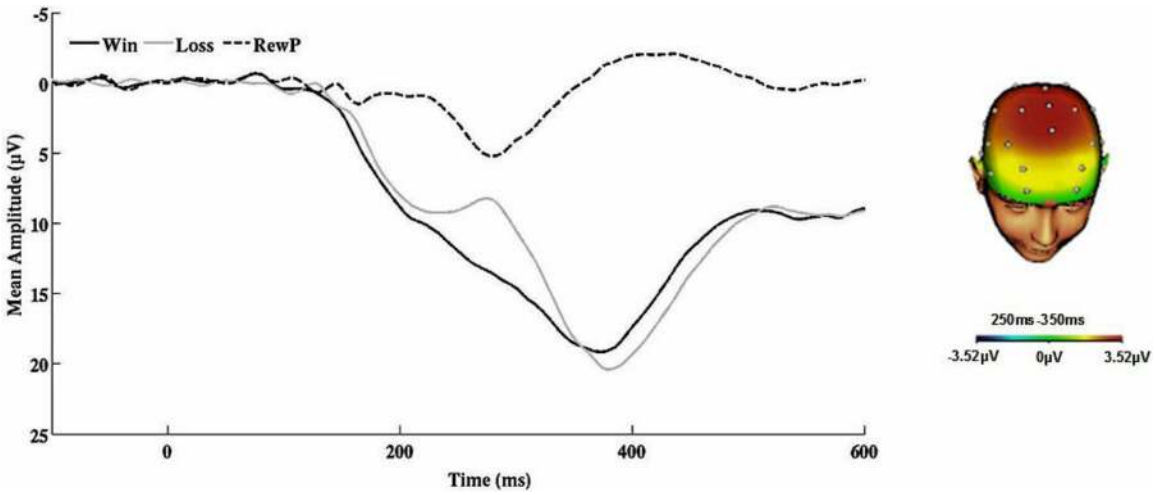

Figure 1.

Response-locked ERP waveforms (pooling of FCz and Fz) following gain, loss, and the gain minus loss difference wave (RewP) across the entire sample ($n = 82$) at Time 1 (pre-treatment). Topographic scalp map of neural activity depicting the gain minus loss difference 250–350ms after the response.

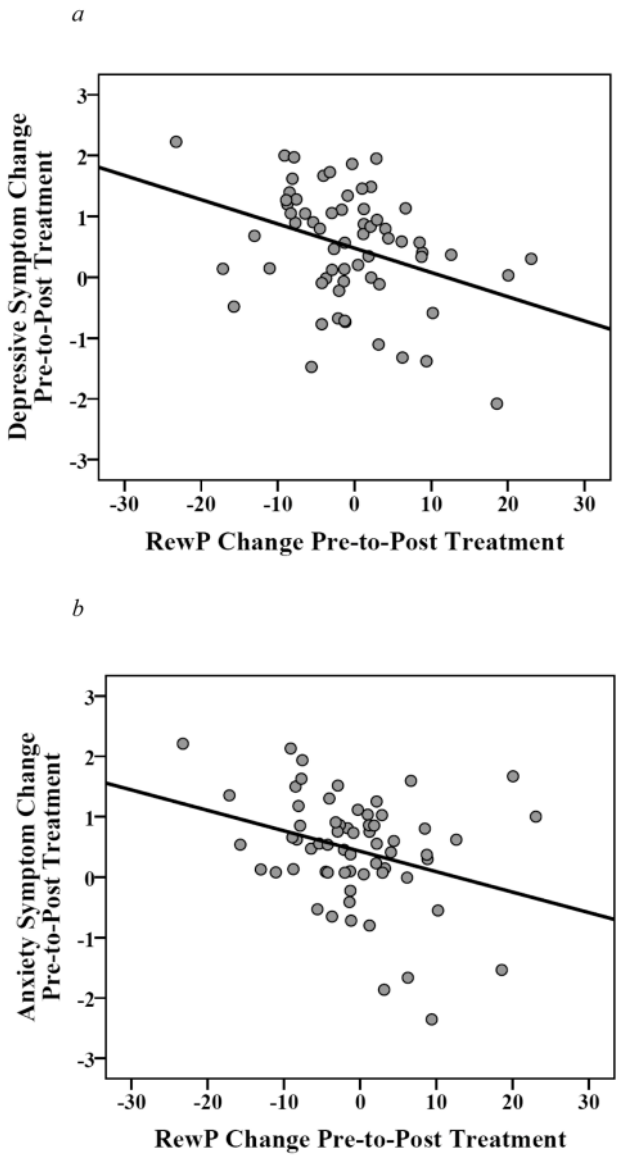

Figure 2.

Scatter plots reflecting the association between RewP change (non-centered) and change in a) depressive (composite HAM-D and BDI Z-scores) and b) anxiety (composite HAM-A and BAI Z-scores) symptoms following cognitive-behavioral therapy and selective serotonin reuptake inhibitors treatment.

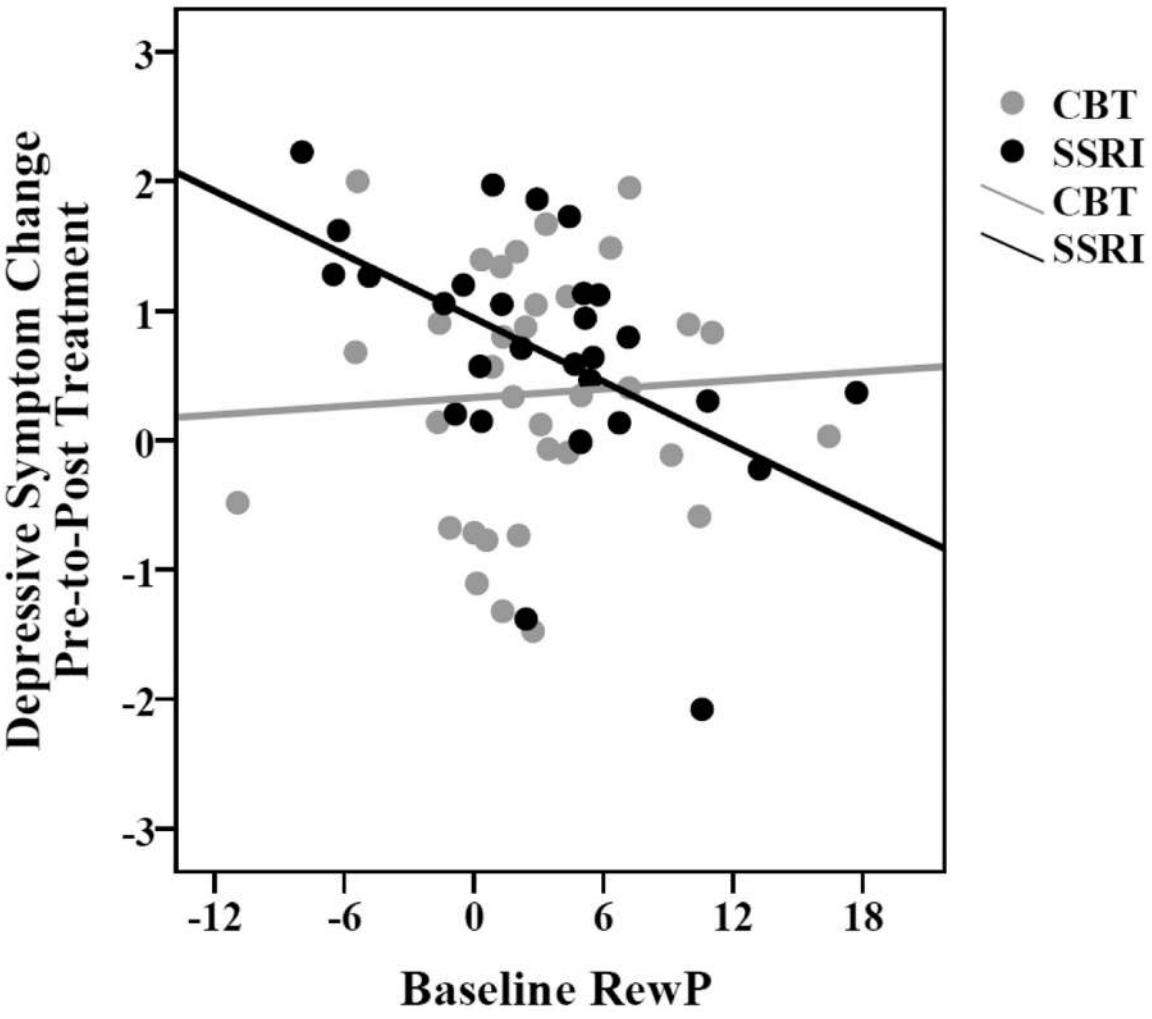

Figure 3.

Scatter plot reflecting the association between RewP change (non-centered) and change in depressive symptoms (composite HAM-D and BDI Z-scores) following CBT and SSRI treatment (separate colors). CBT = cognitive-behavioral therapy; SSRI = selective serotonin reuptake inhibitors.

Table 1.

Demographics and clinical characteristics of the sample.

	Patients M (SD)	**HCs M (SD)**	***t-value***	**CBT M (SD)**	**SSRI M (SD)**	***t-value***
Age	28.70 (9.55)	23.56 (8.20)	2.36*	28.68 (8.90)	28.72 (10.43)	−0.02
BDI Symptoms at T1	25.21 (8.42)	1.12 (1.81)	14.14***	24.85 (8.09)	25.62 (8.90)	−0.36
BDI Symptoms at T2	8.16 (6.75)	-	-	8.85 (7.25)	7.34 (6.14)	0.88
BAI Symptoms at T1	20.71 (10.18)	0.96 (1.54)	9.63***	22.15 (10.70)	19.03 (9.47)	1.22
BAI Symptoms at T2	7.39 (8.08)	-	-	7.45 (6.99)	7.32 (9.27)	0.61
HAM-D Symptoms at T1	11.97 (3.96)	0.48 (0.65)	14.38***	10.94 (2.81)	12.17 (4.76)	−1.44
HAM-D Symptoms at T2	5.11 (3.66)	-	-	5.12 (3.83)	5.10 (3.52)	0.02
HAM-A Symptoms at T1	17.67 (6.82)	1.24 (1.76)	11.85***	16.50 (5.48)	19.03 (8.00)	−1.48
HAM-A Symptoms at T2	6.70 (5.26)	-	-	6.09 (4.35)	7.41 (6.16)	−0.99
	Patients N (%)	**HCs N (%)**	**χ^2**	**CBT N (%)**	**SSRI N (%)**	**χ^2**
Female	47 (74.6%)	11 (44.0%)	7.46**	25 (73.5%)	22 (75.9%)	0.05
Caucasian	43 (68.3%)	12 (48.0%)	3.13	23 (67.6%)	20 (68.9%)	0.01
Hispanic/Latino	9 (14.2%)	2 (8.0%)	0.65	5 (14.7%)	4 (13.8%)	0.01

Note: HCs = Healthy Controls ($n = 25$); Patients ($n = 63$); CBT = Cognitive Behavioral Therapy ($n = 34$); SSRI = Selective Serotonin Reuptake Inhibitors ($n = 29$); BDI = Beck Depression Inventory; BAI = Beck Anxiety Inventory; HAM-D = Hamilton Depression Rating Scale; HAM-A = Hamilton Anxiety Rating Scale;

* = $p < .05$;

** = $p < .01$;

*** = $p < .001$.

Table 2.

Hierarchical linear regression analyses examining whether change in RewP predicts change in depressive and anxiety symptoms pre-to-post treatment.

	Change in Depression (Composite Z Score)			Change in Anxiety (Composite Z Score)		
	β	***t***	***p*-value**	***B***	***t***	***p*-value**
Step 1						
Baseline Symptoms	.19	1.45	.15	.31	2.47	**.02**
Arm	.16	1.28	.21	.02	0.16	.87
Change in RewP	–.29	–2.21	**.03**	–.30	–2.57	**.02**
Step 2						
RewP Change × Arm	–.59	–1.54	.13	–.29	0.73	.47

Note: Arm = medication or cognitive behavioral therapy; Baseline symptoms = depression composite Z score for change in depression model or anxiety composite Z score for change in anxiety model; RewP Change = pre minus post change in Reward Positivity.

Table 3.

Hierarchical linear regression analyses examining whether baseline RewP predicts change in depressive and anxiety symptoms pre-to-post treatment.

	Change in Depression (Composite Z Score)			Change in Anxiety (Composite Z Score)		
	β	***t***	***p*-value**	***B***	***t***	***p*-value**
Step 1						
Baseline Symptoms	.28	2.03	**<.05**	.29	2.35	**.02**
Arm	.12	0.94	.35	.00	−0.02	.98
Baseline RewP	−.10	−0.71	−.48	−.11	−0.89	.38
Step 2						
Baseline RewP × Arm	−.76	−1.98	**<.05**	−.68	−1.76	.09

Note: Arm = medication or cognitive behavioral therapy; Baseline symptoms = depression composite Z score for change in depression model or anxiety composite Z score for change in anxiety model; RewP = reward positivity.