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Behavioral, Neural, and Psychiatric Correlates of Responses to Social Feedback

Brent Rappaport Washington University in St. Louis

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WASHINGTON UNIVERSITY IN ST. LOUIS

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Behavioral, Neural, and Psychiatric Correlates of Responses to Social Feedback

by

Brent Ian Rappaport

A dissertation presented to The Graduate School of Washington University in partial fulfillment of the requirements for the degree of Doctor of Philosophy

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Brent I. Rappaport

Washington University in St. Louis August 2022

ABSTRACT

Problems responding to peer feedback and disrupted interpersonal relationships arise in numerous psychiatric disorders; yet heterogeneity and homogeneity across disorders suggests both common and unique mechanisms of impaired social function. Identifying brain correlates of these disruptions could help explain diagnostic comorbidities as well as unique pathways, thus informing more individualized treatments. However, studies seeking to understand the link between psychological and neural mechanisms often have to rely on reverse inference assumptions to match psychological processes to brain activity. One hypothesis is that social feedback is processed similar to other forms of feedback (e.g., monetary). Thus, we aimed to test such assumptions by examining the correspondence between the brain's response to social acceptance and rejection and behavioral performance on a separate reward and loss task, as well as examine the relationship between these brain responses and depression and social anxiety severity. The sample consisted of 113 16–21-year-olds who received virtual peer acceptance or rejection feedback in an event-related potential (ERP) task. We used temporospatial principal component analysis to identify the reward positivity (RewP) and feedback negativity (FN) ERP components and measured the mean amplitude. Hypotheses were tested using multiple regression models, including covariates. Structural equation modeling was used to test the overall fit of all proposed hypotheses to the data. We did not find that the RewP to social acceptance was related to reward bias nor that the FN to social rejection related to loss avoidance, thus not supporting reverse inference assumptions. Moreover, we found a relationship between the RewP and depression severity that, while non-significant, was of a similar magnitude to prior studies. Finally, exploratory analyses showed a statistically significant relationship between socioeconomic status (SES) and the RewP, as well as between SES and loss

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avoidance, and to a smaller extent SES and reward bias. These findings call into question reverse inference based assumptions of the function of the brain's response to social feedback, while also suggesting a novel pathway for further study, whereby poverty may lead to depression via social and reward learning mechanisms.

1. Introduction

Problems forming and maintaining interpersonal relationships are associated with physical health problems and increased mortality risk (House et al., 1988). Such problems arise in numerous psychiatric disorders (American Psychiatric Association, 2013; Kennedy & Adolphs, 2012). Responding properly to social feedback is a key element of effective social function. Here, *social feedback* is used to refer to the receipt of socially relevant information (e.g., being accepted or rejected by a conspecific). Individuals must use such feedback to learn and alter their behavior, and respond in a prosocial manner that elicits the desired response in another person. Clinically, patients with different disorders often present with complaints of dysfunction in their interpersonal relationships, resulting in, for example, withdrawal or avoidance of social situations and thus reduced contact with others (Brown et al., 2007; Rubin et al., 2009). This has led to an exciting recent increase in interest of the psychological and neural processes involved in responding to social feedback (i.e. acceptance and rejection), as well as about shared and unique disruptions across disorders. Thus, one aim of the current study was to assess shared and dissociate responses to social feedback in depression and anxiety.

Recent studies of social feedback have suggested that the brain responds to acceptance much like monetary rewards (Distefano et al., 2018; Gu et al., 2019; Wake & Izuma, 2017). A long literature has used monetary rewards to study reward processes such as reward learning (e.g., Delgado, 2007; Haber & Knutson, 2010), since it is universal and easy to titrate. However, it remains unclear how this translates to other types of rewards. In fact, other studies have shown weak relationships between brain responses to social and monetary rewards (Ethridge et al., 2017), differential responses depending on participants' age (Rademacher et al., 2014), or

differential relationships as a function of prior peer victimization (Rappaport et al., 2019). Although some researchers have suggested that the brain responds to rejection much like physical pain—due to BOLD signal in the dorsal anterior cingulate cortex (Eisenberger, 2012; Eisenberger et al., 2003; Eisenberger & Lieberman, 2004; Lieberman & Eisenberger, 2015) this precise proposition has recently been called into question by two independent meta-analyses (Cacioppo et al., 2013; Vijayakumar et al., 2017), among others (Somerville et al., 2006; Woo et al., 2014). An alternative interpretation consistent with the above findings is that rejection is akin to loss. As defined in the Research Domain Criteria matrix, loss refers to: *"a state of deprivation of a motivationally significant con-specific, object, or situation. Loss may be social or non-social and may include permanent or sustained loss of…loved ones, or relationships"* (*NIMH Definitions of the RDoC Domains and Constructs*). In fact, Cacioppo et al. (2013) found greater BOLD signal in the insula to social exclusion and Vijayakumar et al. (2017) found greater BOLD signal in the ventral striatum—both of which are regions implicated in processing negative affect (Hamilton et al., 2011; Palaniyappan, 2012) and loss (Canessa et al., 2013; Dugré et al., 2018; Liu et al., 2011; Oldham et al., 2018; Tom et al., 2007). Thus, a hypothesis that is compatible with both the pain theories of rejection and recent meta-analyses is that social rejection is processed similarly to other forms of loss.

1.1 Social Feedback Processing in Depression and Anxiety

As noted above, different types of psychopathology involve disruptions in interpersonal relationships and reduced social engagement. However, these same endpoints may be due to different underlying mechanisms across individuals. For instance, individuals may withdraw because they experience less pleasure from interacting with other people or negative self-esteem, out of fear of rejection (or negative evaluation more generally), or for both reasons (see Rubin et

al., 2009 for a review). Such heterogeneity and homogeneity across disorders suggests both common and unique mechanisms of impaired interpersonal relationships. Homogeneity is exemplified by multiple disorders sharing a deficit. For example, both depression and social anxiety are associated with heightened sensitivity to social rejection (Burklund et al., 2017; Cohen et al., 2016; Gao et al., 2017; Groschwitz et al., 2016; Harrewijn et al., 2017; Heeren et al., 2017; Hsu et al., 2015; Kujawa et al., 2014; Malejko et al., 2018; Silk et al., 2014), but only depression, not social anxiety (Kujawa et al., 2017; Pegg et al., 2019), is associated with blunted neural responses to social acceptance and inclusion (Davey et al., 2011; Kujawa et al., 2017; Zhang et al., 2020; Zhang et al., 2017).

Studying the neural processes at play in responding to social feedback can help us understand whether these similar behavioral outcomes (i.e. reduced time spent with others) are due to common or distinct psychophysiological mechanisms. That is, although these two dimensions of psychopathology are related to deficits in responding to social feedback, they may do so via both shared and distinct mechanisms, necessitating more individualized treatments. Although such deficits could be evaluated in a clinical interview, using self and informant reports, they carry limitations such as method bias, self-presentation biases, and reliance on reporter insight (Campbell & Fiske, 1959; Podsakoff et al., 2003). Furthermore, brain measures can tap into implicit differences in individuals' response to social feedback, such as attentional biases (Silk et al., 2012). Thus, neural measures may serve to complement other measures of symptoms to inform more individualized treatments (e.g., exposure and habituation to social rejection, pairing reinforcements with social acceptance). To test such hypotheses, transdiagnostic studies are needed to distinguish common from unique neural and behavioral deficits in social feedback response across psychiatric disorders.

1.1 Using Event-Related Potentials (ERP) to study Social Feedback

Neural systems that process reward and loss involve a host of brain regions that work in a coordinated fashion, just as any other social function (Amodio, 2010) or complex behavioral function, to process and respond to social feedback. FMRI studies have begun to identify regions active in response to social exclusion (Cacioppo et al., 2013; Vijayakumar et al., 2017). In complementary research, event-related potentials (ERPs)—EEG signals time-locked to a stimulus onset—provide a robust way to understand the timing of neural responses associated with social feedback by examining specific ERP components thought to reflect brain activity to acceptance (reward positivity [RewP]) and rejection (feedback negativity [FN]; Luck & Kappenman, 2012; Proudfit, 2015; Regan, 1989). Given the complexity of brain responses to social feedback, the temporal resolution of ERP may be well suited to identifying individual differences in brain responses as compared to methods with worse temporal but better spatial resolution (Amodio et al., 2014). Moreover, ERPs directly measure brain activity (Gratton & Fabiani, 2001), rather than its indirect consequence with a hemodynamic response in fMRI. Furthermore, ERP allows participants to sit upright rather than still and supine in a scanner, lending it greater ecological validity (Amodio et al., 2014). These factors together suggest that ERP is an excellent method for measuring individual differences in brain responsivity to social feedback.

1.2 The Reverse Inference Problem

To test such hypotheses about the psychological function of processes implicated in the response of social feedback, studies thus far have typically relied on *affirmation of the consequent* (Cacioppo et al., 2003) or *reverse inference*: *"the inference of a psychological process from an observed pattern of brain activity"* (Amodio, 2010). For example, despite

suggestions that similar brain regions are activated to social acceptance and monetary reward, drawing the conclusion that the reward system is implicated in responding to social acceptance from such findings is problematic since similar patterns of brain activation could reflect different psychological processes. As such, studies are needed that test whether the brain's response to such feedback is associated with behavioral measures (Poldrack, 2006)—in this case indexing response to reward or loss—providing converging evidence of dysfunction in the hypothesized psychological process. If so, it suggests a function of that brain activity in reward/loss responsivity; if not it calls into question prior conclusions made using reverse inference. Thus, the current proposal aims to test whether the brain's reward/loss system responds to social acceptance and rejection feedback.

1.3 Current study

The current study aims to address the key questions outlined above. Specifically, first we test reverse inference assumptions by analyzing the relationship between individual differences in RewP and FN magnitude to social acceptance and rejection feedback and separate behavioral individual differences of bias towards rewards and away from losses. Testing whether individual or group differences in brain activity are also related to a converging behavioral measure constrains the interpretation of the brain activation (Poldrack, 2006). The hypotheses for this aim are that individual differences in the RewP to social acceptance will be positively related to behavioral reward bias, and similarly that individual differences in the FN to social rejection will be positively related to behavioral loss avoidance. Second, we test diagnostic homogeneity and heterogeneity by analyzing the relationship between individual differences in RewP and FN magnitude to social acceptance and rejection feedback and severity of depression and social anxiety symptoms. The specific hypotheses are that the RewP to acceptance will be negatively

related to depression severity, and that the FN to rejection will be positively related to depression and social anxiety severity. Third, we test for the presence of a relationship between behavioral bias towards rewards and away from losses and severity of depression and social anxiety, aiding in the interpretation of the previous analyses. This would provide converging evidence of our proposed nomological network between the ERP, behavioral, and psychopathology measures. Thus, the specific hypotheses are that behavioral reward bias will be negatively related to depression severity, and that behavioral loss avoidance will be positively related to depression and social anxiety severity.

2. Methods

Participants were drawn from the Preschool Depression Study (PDS), a prospective longitudinal investigation of young children and their families conducted at a midwestern university in the United States (Luby et al., 2009). Details of recruitment have been previously reported (Luby et al., 2014, 2009). To briefly summarize, 3- to 6-year-old children were recruited from primary care practices and preschools/daycares throughout the St. Louis metropolitan region using a validated screening checklist (Preschool Feelings Checklist [PFC]; Luby et al., 2004) to oversample preschoolers with symptoms of depression, externalizing disorders, and healthy controls (i.e. those whose caregivers endorsed no items on the PFC, two or more internalizing items, and/or two or more externalizing items). Children were excluded if they presented with chronic illness, marked speech and/or language delays and/or neurologic or autism spectrum disorders. Parental written consent and child assent were obtained before participation and the local Institutional Review Board approved all procedures. These 306 children have participated in up to 10 in person clinical and behavior assessments and five neuroimaging assessments. An additional 40 healthy controls (i.e. without a prior history of psychiatric disorders) were added at school age and have participated in up to five clinical and behavior assessments and five neuroimaging assessments. Participants completed all measures of the current study during the tenth and most recent assessment wave of the PDS. Of those, 175 participated in the most recent wave, with 118 participants completing the social feedback task. Of those, one participant was excluded due to technical errors during the social feedback task, and two participants were excluded due to intelligence quotients (IQ) below 70. Of those 115 remaining participants, 100 had participated since preschool age, and 15 were recruited as healthy controls at the later wave of the study. Furthermore, 111 had completed and had usable

data for the behavioral reward task and 110 for the loss task, 110 had completed a self-report measure of depression, and 115 had completed a self-report measure of social anxiety. The final analytical sample contained 113 after 2 participants were excluded as outliers (see below). See Table 1 for demographic characteristics of the study sample.

Note. $N=9$ missing recent psychotropic medication use.

Mean (SD) for continuous variables or N (%) for

categorical variables presented.

Table 1. Demographics of study sample

2.1 Measures

Depression severity

Depression severity was measured using the Child Depression Inventory–2 (CDI-2;

Kovacs, 1992) for participants less than 18 years-old and Beck Depression Inventory–II (BDI–II;

Dozois et al., 1998) for participants 18 years-old and older. The CDI-2 includes 28 items scored

on a three point Likert scale. The BDI-II includes 21 items scored on a four point Likert scale. Both measures assess self-reported depression symptoms in the past 2 weeks and have excellent internal consistency in the current sample (CDI-2: $\alpha = 0.90$; BDI-II: $\alpha = 0.92$) and test-retest reliability in prior studies (CDI-2: $r = 0.89$; BDI-II: $r = 0.93$) (Beck et al., 1996; Dozois et al., 1998; Kovacs, 1992). See Table 2 for means and standard deviations.

Social anxiety severity

Social anxiety severity was measured using the Social Interaction Anxiety Scale (SIAS-6) and Social Phobia Scale (SPS-6; Peters et al., 2012)—a scale that combines the two scales and was developed as an abbreviated version of the full SIAS/SPS (Mattick & Clarke, 1998) using Item Response Theory modeling. This scale includes six items rated on a five point Likert scale from each of the SIAS-6 and SPS-6, comprising one total 12 item scale. The SIAS/SPS-6 assesses self-reported current symptoms of social anxiety/phobia (with no specific time frame given) and has excellent internal consistency in the current sample (α = 0.89) and test-retest reliability in prior studies (*r* > 0.91; Mattick and Clarke, 1998; Osman et al., 1998). See Table 2 for means and standard deviations.

Covariates

Covariates in multiple regression models included age at time of task, sex, race (Caucasian, African American, or Multiracial), Hispanic ethnicity, and socioeconomic status, operationalized as income-to-needs ratio (i.e. total family income divided by the federal poverty level, based on family size). Income-to-needs ratio from the most recent available assessment wave was used. Supplemental analyses also included recent psychotropic medicine use as a covariate, however nine participants were missing this data and thus were excluded from

analyses when this covariate was included. All categorical variables (i.e., sex, race, Hispanic ethnicity, and psychotropic medicine use) were dummy coded and all continuous variables (i.e. reward bias, loss avoidance, RewP, FN, depression severity, social anxiety severity, age, socioeconomic status) were standardized to aid in interpretation of regression estimates.

2.2 Procedure

Social Feedback ERP Task

The Island Getaway task was used to measure brain responses to social feedback. In the task, participants are told they are playing a game with 11 co-players in which they are traveling in the Hawaiian Islands, and at each island, vote whether they want each co-player to continue on with them to the next island, followed by feedback on how co-players voted for them. Participants review information about each co-player (e.g., gender, location, personal preferences) and enter information that they are told is similarly reviewed by each co-player. Participants complete 6 rounds of "voting," during which they vote whether to "keep" or "kick" out" each co-player, and following each vote receive feedback as to whether that co-player voted to accept ("keep") or reject ("kick out") them (Figure 1A). After each round, participants are told that one of the co-players had been sent out, and after completing the sixth round, participants are informed that they made it to the "Big Island." Participants receive 51 trials of feedback: 25 acceptance and 25 rejection, and one randomly selected trial—a unique strength of this particular task (over tasks of only social rejection or exclusion) that yields reliable measurements of brain activity to social acceptance and rejection feedback (Ethridge & Weinberg, 2018). Co-players are randomly assigned a voting pattern for each participant such that 2 co-players reject the participant on most rounds, 2 co-players accept the participant on most rounds, and the remaining 7 co-players are equally likely to accept or reject the participant. Following the task,

participants complete a brief post-task questionnaire assessing engagement in the task. This task has been validated in early adolescent, late adolescent, and young adult samples (Ethridge et al., 2017; Ethridge & Weinberg, 2018; Kujawa et al., 2017; Pegg et al., 2019).

Figure 1. A) Depiction of Island Getaway (IG) ERP task trial and B) schematic of Probabilistic

Incentive Learning Task (PILT)

Behavioral reward bis and loss avoidance task

To measure reward bias and loss avoidance we used the Probabilistic Incentive Learning Task (PILT), specifically two modified versions (Heerey et al., 2008; Pizzagalli et al., 2005), here termed PILT-Positive and PILT-Negative, to assess reward bias and loss avoidance respectively. These tasks have been used in adult and pediatric samples (Heerey et al., 2008; Luking et al., 2016b, 2015; Luking, Neiman, et al., 2015; Pizzagalli et al., 2005, 2008). In each trial, participants perform a perceptual discrimination and indicate whether a long or short stimulus was briefly presented (Figure 1B). For the PILT-P, a portion of correct responses receive gain feedback while, for the PILT-N, a portion of incorrect responses receive loss feedback. For both tasks, one of the two responses (i.e. short or long, termed the RICH response) is scheduled to receive three times the amount of feedback as the alternative (LEAN) response. This leads to preferentially selecting the RICH response in the PILT-P (reward bias) and avoiding the RICH response in the PILT-N (loss avoidance; Luking, Pagliaccio, et al., 2015; Luking, Neiman, et al., 2015; Pizzagalli et al., 2005, 2008).

Participants complete 20 practice trials, followed by two blocks of 60 trials each. Feedback was presented in a pseudo-random order, so that no more than three trials in a row could receive feedback. As in prior studies, individual trials with reaction times (RT) faster than 150ms or slower than 2500ms, or greater than or less than 3 standard deviations from the participant's mean RT were excluded. Response bias (log b) assesses behavioral responsiveness to feedback. Responses were coded such that more positive values on the PILT-P task indicate a greater propensity to select the RICH (i.e. rewarded) stimulus and more positive values on the PILT-N task indicate a greater propensity to select the LEAN (i.e. non-punished) stimulus. Per prior studies, 0.5 was added to each cell (i.e. *Richcorrect*, *Leanincorrect*, *Richincorrect*, *Leancorrect*) to account for cases when one of these cells was zero (Hautus, 1995; Pizzagalli et al., 2008).

Reward bias/Loss avoidance $(log b) = \frac{1}{2} log \frac{Rich_{correct} * Lean_{incorrect}}{Rich_{incorrect} * Lean_{correct}}$

EEG Acquisition and Processing

Continuous EEG was recorded using the BrainVision ActiChamp, 32 channel active channel amplifier system (BrainVision LLC, Morrisville, NC, USA). Electrodes were mounted in an elastic cap using a subset of the International $10/20$ System sites (FP1, F3, F7, FC1, FC5, FT9, C3, T7, CP1, CP5, TP9, P3, P7, O1, Fz, Cz, Pz, Oz, FP2, F4, F8, FC2, FC6, FT10, C4, T8, CP2, CP6, P4, P8, TP10, O2), with a ground electrode located at FPz. The electrooculogram (EOG) generated from blinks and eye movements was recorded from five facial electrodes. The EEG was sampled at 500 Hz and all signals digitized on a computer. All data was re-referenced to the average of Tp9 and Tp10 and band-pass filtered from 0.1 to 30 Hz. The EEG was corrected for EOG artifacts (Gratton et al., 1983) and physiological artifacts removed using an automatic procedure with a maximum allowed voltage step of 50 μ V within a 400 ms interval length, maximum absolute difference between any two points of $175 \mu V$, and a minimum allowed activity of 0.50μ V within a 100 ms interval length. The EEG was segmented into 1000 ms epochs, beginning 200 ms before and ending 800 ms after feedback onset. ERPs were averaged for acceptance and rejection feedback, and baseline corrected to activity 200 ms prior to feedback.

2.3 Data Analysis

Data analysis plans were preregistered following data collection but prior to data analysis (osf.io/x8rdh). Those analyses that were not preregistered are included in the exploratory analyses section of the results. Code for analyses is available in the same OSF repository.

PCA

Temporospatial principal component analysis (PCA) was conducted with the EP Toolkit (Dien, 2010b) and data from all 117 participants with usable ERP data. A temporal PCA was conducted first, using a Promax rotation to rotate a simple structure in the temporal domain (Dien, 2010a, 2012; Dien et al., 2007) and included time points from each participant's averaged data as variables and participants, recording sites, and trial types as observations. To identify factors accounting for substantial variance, a Scree plot (Cattell, 1966) was generated and a parallel test (Horn, 1965) conducted comparing a Scree of the dataset to that of a fully random dataset. We identified 15 temporal factors (TF) that accounted for a larger proportion of variance than the random dataset, and thus were retained. Next, a spatial PCA was conducted using Infomax rotation to rotate the spatial factors to independence (Dien, 2010a) and included all recordings sites as variables and participants, trial types, and temporal factor scores as observations. We identified 3 spatial factors (SF), resulting in 45 factor combinations accounting for a total 34.8% of the variance. Factor scores were converted to voltages and robust analysis of variance was conducted on factors that accounted for greater than 1% of variance to identify those that meaningfully distinguish acceptance and rejection feedback, yielding 11 factors. Peak latency and electrode location were used to identify the RewP/FN component at temporal factor 2–spatial factor 1 (TF2/SF1). Data was imported from Brain Vision Analyzer to R (R Core Team, 2020) for all further computations.

ERP activity in the RewP significantly differed between the acceptance and rejection conditions ($M_d = 1.45$, 95% CI [0.81,2.10], $\tau(114) = 4.49$, $p < .001$). The RewP was calculated as the mean activity 50ms before and 50ms after the peak latency (344ms, time

window of 294-394ms) at the peak electrode (FC2; Figure 2B). In line with previous work and recommendations (Meyer-Lindenberg & Tost, 2012), residual scores for the RewP response to acceptance accounting for the response to rejection were calculated, producing scores uncorrelated with the response to rejection. Likewise, residual scores for the FN response to rejection accounting for the response to acceptance were calculated, producing scores uncorrelated with the response to acceptance. This produces RewP and FN scores that are highly correlated ($\mathbf{r} = 0.83$) but not inverses of one another and isolates mean amplitude in the ERP unique to acceptance or rejection. A non-difference score measure (e.g., mean amplitude to acceptance without accounting for activity to rejection) is confounded by activity throughout the brain unrelated to the acceptance stimulus. Results of the PCA also suggested the presence of the P2 (peak latency: 212ms, time window of 162-262ms at Cz electrode; Figure 2C) and N1 (peak latency: 174ms, time window of 124-224ms at Cz electrode; Figure 2D) components, both of which also significantly differed between the acceptance and rejection conditions (P2: $M_d = 1.43$, 95% CI $[0.83, 2.02]$, $\frac{t(114)}{14} = 4.72$, $p < .001$; N1: $M_d = 1.54$, 95% CI $[0.99, 2.10], \, \frac{t(114)}{5.49}, \, \frac{p}{6.001}.$

Figure 2. ERP waveforms to acceptance and rejection feedback. A) Grand average ERP activity at Cz electrode; B-D: ERP activity at PCA components that significantly different between

acceptance and rejection feedback, including B) RewP: temporal factor (TF) 2 and spatial factor (SF) 1 at electrode FC2, C) P2 component: TF 4 and SF 1 at electrode Cz, and D) N1 component: TF 7 and SF 1 at electrode Cz.

Table 6. Temporospatial factors that differed between social acceptance and rejection feedback. *Note.* t values derived from robust ANOVA; TF = temporal factor; SF = spatial factor.

Multivariate outliers

Mahalanobis distance was calculated among all measures used in confirmatory analyses (i.e. reward positivity, feedback negativity, reward bias, loss avoidance, depression severity, social anxiety severity) and used to identify and exclude multivariate outliers with a threshold of p <0.001 ($N = 2$). This resulted in a final sample of $N = 113$.

Multiple imputation of missing data

MCAR analyses showed that there was not significant evidence to reject the hypothesis that the variables of interest (i.e. depression severity, social anxiety severity, reward positivity, feedback negativity, reward bias, and loss avoidance, and covariates [age, sex, SES, race, ethnicity]) were missing completely at random (MCAR; $p = 0.22$). 4 had missing data for the behavioral reward task and 5 for the loss task, 5 had missing data for depression severity, and there was no missing data for social anxiety severity. There was no missing data for the covariates, except for psychotropic medication use, which 9 subjects were missing. Thus, multiple imputation was conducted using the 'MICE' package (van Buuren & Groothuis-Oudshoorn, 2011) in R. Ten imputations were generated using predictive mean matching of the variables of interest and covariates, and other measures that were collected concurrently and a priori considered to inform missing data in depression severity (e.g., major depressive disorder diagnosis on the Kiddie Schedule for Affective Disorders and Schizophrenia [K-SADS], social anxiety disorder diagnosis on the KSADS, behavioral approach system [BAS] child drive, BAS child fun seeking, BAS child reward responsiveness–revised, behavioral inhibition system [BIS] child–revised, and the Pleasure Scale for Children) and behavioral reward bias/loss avoidance (accuracy on the PILT-P and PILT-N, National Institutes of Health Toolbox list sorting, pattern completion, picture sequencing, picture vocabulary, flanker). Of note, psychotropic medication use was not imputed.

Multiple regression models

Following multiple imputation, measures were standardized in each of the 10 imputations. Multiple regression models were conducted and estimates were pooled across the imputations using the 'miceadds' package (Robitzsch & Grund, 2020).

Multiple regression models were used to test all three primary hypotheses. For example, two models tested the first hypothesis. In one model, reward bias and loss avoidance were included as predictors, along with covariates, and the RewP as the outcome (see equation 1 below). The other model included the same predictors but included the FN as the outcome (see equation 2 below). These models allow for estimation of the amount of unique variance in the ERP component activity accounted for by reward bias and loss avoidance, controlling for covariates.

[1]
$$
RowP = b_0 + b_1
$$
 $Reward bias + b_2Loss Avoidance + b_3Age$
+ b_4 $hccone$ $to needs ratio + b_5Sex + b_6 Race_1 + b_7 Race_2 + b_8Hispanic$

[2]
$$
FN = b_0 + b_1
$$
 Reward bias + b_2 *Loss Avoidance* + b_3 *Age* + b_4 *Income to needs ratio* + b_5 *Sex* + b_6 *Race*1 + b_7 *Race*2 + b_8 *Hispanic* An identical structure

was used to test the second and third hypotheses. That is, in models testing the second hypothesis, depression and social anxiety severity were included as predictors and the RewP as the outcome in the first model, and the FN as the outcome in the second model. The RewP and FN were not included in any models as simultaneous predictors due to multicollinearity concerns. In models testing the third hypothesis, depression and social anxiety severity were included as predictors and reward bias as the outcome in the first model, and loss avoidance as the outcome in the second model. Finally, exploratory Bayesian estimation and Bayes Factor analyses were conducted when a relevant prior was present in the extant literature to guard against potential Type II (false negative) errors.

Structural equation model of hypotheses

A structural equation model (SEM) of all three hypotheses was modeled using the 'lavaan' package version 0.6.7 (Rosseel, 2012) to determine whether the hypotheses demonstrated an overall improvement in model fit over a null model (i.e. one that assumed that all of the hypothesized relationships were null). By simultaneously testing the predicted associations between all variables, this model accounts for within-subject shared variance across, for example, ERP components (i.e. $RewP \& FN$), while testing its predicted associations with reward bias and loss avoidance and with the psychopathology measures. Model fit was assessed two ways. First, measures of absolute model fit—root mean square error of approximation (RMSEA) and standardized root mean square residual (SRMR)—were compared to established guidelines (RMSEA & SRMR < 0.08) to determine goodness of fit (Hooper et al., 2008). Second, measures of relative model fit—chi-square difference $(\Delta \chi^2)$ test, comparative fit index (CFI), Akaike Information Criteria (AIC), and Bayesian Information Criteria (BIC)—were compared to a reduced model (with higher CFI and lower AIC and BIC indicating better model fit; Hooper et al., 2008).

3. Results

3.1 Confirmatory Analyses

Association between RewP/FN and reward bias and loss avoidance

Multiple regression models showed that the RewP to social acceptance feedback was not significantly associated with behavioral reward bias, nor was the FN to social rejection significantly associated with behavioral loss avoidance (Table 3). Zero order correlations further confirmed this pattern of results (Table 2). Results from supplemental analyses including recent psychotropic medication use were consistent (Table 7).

Association between RewP/FN and depression and social anxiety severity

Multiple regression models showed that the RewP to social acceptance feedback was not significantly associated with depression severity, nor was the FN to social rejection feedback significantly associated with depression or social anxiety severity (Table 3). Zero order correlations further confirmed this pattern of results (Table 2), however, the effect size of the correlation between the RewP and depression severity ($r = -0.09$, 95% CI [-0.28 , 0.10], $p = 0.35$) was comparable to three large prior studies using independent samples ($r_{pooled} = -0.11$, total $N =$ 760; Kujawa et al., 2017; Pegg et al., 2019, 2021). Results from supplemental analyses including recent psychotropic medication use were consistent (Table 7).

Note. Correlations coefficients (r) are presented in the upper diagonal, while relative standard errors (rse) are presented in the lower diagonal

Table 2. Correlations between variables of interest

Table 3. Multiple regressions of RewP/FN predicted by behavioral reward bias and loss avoidance and psychopathology

Bayesian analyses

Bayesian analyses were used to test for the strength of the alternative hypothesis relative to the null hypothesis given the presence of a null effect and availability of an informed prior (Kujawa et al., 2017; Pegg et al., 2021, 2019). The relative standard error was estimated using the pooled sample size $(N = 760)$ and correlation of the three studies, and was included as the standard deviation of the prior for all analyses. Thus, the Bayesian linear regression with an informed prior of -0.11 (standard deviation 0.036) showed a similar estimate to the results above $(\beta = -0.11, 95\% \text{ CI}$ [-0.18, -0.04]) and resulted in a Bayes Factor of 2.58, suggesting anecdotal support for the alternative hypothesis (Wetzels et al., 2011).

Association between reward bias/loss avoidance and depression and social anxiety

Multiple regression models showed that reward bias was not significantly associated with depression severity, nor was loss avoidance significantly associated with depression or social anxiety severity (Table 4). Zero order correlations further confirmed this pattern of results (Table 2). Results from supplemental analyses including recent psychotropic medication use were consistent (Table 8).

Predictors		Reward bias		Loss avoidance			
	β	СI	\boldsymbol{p}	β	СI	\boldsymbol{p}	
Intercept	-0.04	$(-0.35, 0.28)$	0.81	0.13	$(-0.19, 0.44)$	0.43	
Depression	0.15	$(-0.1, 0.39)$	0.23	0.08	$(-0.16, 0.32)$	0.51	
Social Anxiety	-0.21	$(-0.45, 0.03)$	0.08	0.04	$(-0.18, 0.27)$	0.69	
Age	-0.12	$(-0.31, 0.07)$	0.20	-0.05	$(-0.24, 0.14)$	0.60	
Sex	-0.13	$(-0.5, 0.25)$	$0.51\,$	-0.11	$(-0.49, 0.27)$	0.57	
Black or AA	0.16	$(-0.32, 0.64)$	$0.50\,$	-0.08	$(-0.56, 0.4)$	0.74	
Multiracial	0.73	(0.05, 1.41)	0.04	-0.43	$(-1.1, 0.24)$	0.20	
Hispanic	-0.84	$(-2.06, 0.37)$		$0.17 - 0.10$	$(-1.29, 1.09)$	0.87	
SES	0.22	(0, 0.43)	0.05	-0.37	$(-0.59, -0.16)$	0.00	

Table 4. Multiple regressions of Reward bias/loss avoidance predicted by psychopathology

Predictors	Reward bias			Loss avoidance			
	β	СI	\boldsymbol{p}	β	СI	\boldsymbol{p}	
Intercept	-0.07	$(-0.41, 0.27)$	0.69		0.13 $(-0.21, 0.47)$	0.45	
Depression	0.13	$(-0.13, 0.38)$	$0.32\,$	0.10	$(-0.14, 0.35)$	0.41	
Social Anxiety	-0.22	$(-0.47, 0.04)$	0.09	0.03	$(-0.21, 0.27)$	0.79	
Age	-0.13	$(-0.33, 0.07)$	0.21		-0.07 $(-0.26, 0.13)$	0.49	
Sex	-0.22	$(-0.62, 0.18)$			$0.27 -0.14$ $(-0.54, 0.26)$	0.48	
Black or AA	0.14	$(-0.38, 0.67)$			$0.59 -0.17$ $(-0.7, 0.35)$	0.51	
Multiracial	0.80	(0.08, 1.53)			$0.03 -0.34$ $(-1.04, 0.37)$	0.35	
Hispanic	-0.81	$(-2.04, 0.42)$			$0.19 -0.16$ $(-1.36, 1.03)$	0.79	
SES	0.21	$(-0.01, 0.44)$			$0.07 -0.37$ $(-0.6, -0.15)$	0.00	
Psychotropic medication use		0.37 $(-0.25, 0.98)$ 0.24		0.00	$(-0.6, 0.6)$	1.00	

Table 8. Multiple regressions of Reward bias/loss avoidance predicted by psychopathology covarying for recent psychotropic medication use

Structural equation modeling of hypotheses

Structural equation models, modeling all hypotheses simultaneously, supported the pattern of results reported above. The hypothesized model showed good fit according to absolute model fit indices (RMSEA=0.06, SRMR=0.03), but it did not show significant improvement in model fit over the simplified model (Table 5; Figure 3).

Note. $\Delta \chi^2$ =9.89, *p*=0.27

Table 5. Model fit of SEM model of hypotheses

Figure 3. SEM model of all hypotheses. Note: Values are beta coefficients (p values)

3.2 Exploratory analyses

Socioeconomic status

Multiple regression models showed that income-to-needs ratio was significantly positively associated with the RewP (not the FN) when reward bias and loss avoidance were included as predictors (β = 0.24, 95% CI [0.01, 0.47], p = 0.04), and that the association was trending when current depression and social anxiety severity were included as predictors (β = 0.21, 95% CI $[-0.01, 0.42]$, $p = 0.06$; Table 3). Follow up analyses showed that income-to-needs was indeed positively associated with the RewP, and not the FN, in zero-order correlations (Figure 4; RewP: *r* = 0.24, 95% CI [0.05, 0.42], *p* = 0.01; FN: *r* = 0.11, 95% CI [-0.07, 0.30], *p* = 0.23). Because 1) income-to-needs significantly differed between races in our sample (*F*(2,110)

 $= 16.27$, $p < .001$) and 2) there has been recent discussion in the field about the imperfectness of reports on participants' race in identifying risk factors and equity gaps (Ioannidis et al., 2021), we also examined models in which race was omitted as a covariate. In these models, income-toneeds was significantly positively associated with the RewP covarying for reward bias, loss avoidance, depression severity, and social anxiety severity (β = 0.25, 95% CI [0.05, 0.46], p = 0.02).

Multiple regression models also showed that income-to-needs ratio was significantly positively associated with behavioral reward bias (β = 0.22, 95% CI [0.00, 0.43], p = 0.05) and significantly negatively associated with loss avoidance (β = -0.37, 95% CI [-0.59, -0.16], *p* < 0.01; Table 4). That is, reduced income-to-needs ratio was related to reduced bias towards rewarding stimuli and greater avoidance of the punished response. Zero order correlations further confirmed a significant association with loss avoidance ($r = -0.35$, 95% CI [-0.53 , -0.17], $p <$ 0.01), but not reward bias (*r* = 0.15, 95% CI [-0.04, 0.34], *p* = 0.13) . These results were consistent when accuracy (i.e. participants' ability to correctly discriminate between the stimuli) and recent psychotropic medication use was included in the model, though at trend levels for the association with reward bias (Table 9).

Figure 4. Relationship between behavioral loss avoidance and income to needs ratio with histograms

Table 9. Multiple regressions of behavioral reward bias and loss avoidance covarying for accuracy

Other ERP components

We also examined exploratory ERP components. The temporospatial PCA yielded one component similar to the P2 and one similar to the N1. Exploratory analyses revealed that neither the P2 nor N1 were significantly associated with reward bias or loss avoidance, nor with depression or social anxiety severity (Table 10).

Predictors	P ₂			N1		
	β	$_{\rm CI}$	\boldsymbol{p}	β	CI	\boldsymbol{p}
Reward bias and loss avoidance						
Intercept	0.13	$(-0.18, 0.44)$	0.41	0.10	$(-0.21, 0.42)$	0.52
Reward bias	-0.08	$(-0.28, 0.12)$	0.43	-0.05	$(-0.25, 0.16)$	0.65
Loss avoidance	0.07	$(-0.14, 0.27)$	0.52	0.01	$(-0.19, 0.22)$	0.89
Age	0.09	$(-0.11, 0.28)$	0.38	0.06	$(-0.13, 0.26)$	0.53
Sex	-0.27	$(-0.65, 0.11)$	0.16	-0.28	$(-0.67, 0.1)$	0.15
Black or AA	-0.07	$(-0.55, 0.41)$	0.76	0.05	$(-0.44, 0.54)$	0.84
Multiracial	0.05	$(-0.64, 0.74)$	0.89	0.11	$(-0.58, 0.81)$	0.75
Hispanic	0.63	$(-0.61, 1.86)$	0.32	0.35	$(-0.91, 1.61)$	0.59
SES	0.23	(0, 0.46)	0.05	0.19	$(-0.04, 0.42)$	0.11
Psychopathology						
Intercept	0.13	$(-0.18, 0.44)$	0.41	0.09	$(-0.23, 0.42)$	0.56
Depression	-0.03	$(-0.28, 0.21)$	0.79	-0.06	$(-0.31, 0.2)$	0.67
Social anxiety	-0.12	$(-0.35, 0.11)$	$0.29\,$	-0.01	$(-0.25, 0.22)$	0.90
Age	$0.07\,$	$(-0.12, 0.26)$	0.47	0.06	$(-0.14, 0.25)$	0.58
Sex	-0.24	$(-0.61, 0.14)$	0.21	-0.26	$(-0.65, 0.12)$	0.18
Black or AA	-0.12	$(-0.6, 0.36)$	0.61	0.04	$(-0.45, 0.53)$	0.87
Multiracial	0.03	$(-0.65, 0.72)$	0.93	0.12	$(-0.58, 0.83)$	0.72
Hispanic	0.71	$(-0.52, 1.94)$	$0.26\,$	0.41	$(-0.84, 1.67)$	0.52
SES	0.18	$(-0.03, 0.4)$	0.09	0.17	$(-0.04, 0.39)$	0.12

Table 10. Multiple regressions of P2/N1 predicted by behavioral reward bias and loss avoidance and psychopathology

4. Discussion

As the first to assess the relationship between ERP responses to social feedback and behavioral performance on reward/loss tasks, the current study sought to test hypotheses that a) the RewP and FN ERP components observed in response to social feedback reflect reward and loss system function respectively, b) depression and social anxiety have shared and distinct mechanisms of interpersonal relationship problems, and c) that depression and social anxiety have shared and distinct mechanisms of dysfunction in responding to rewards and losses.

4.1 Brain responses to social feedback and behavioral reward bias and loss avoidance

We did not find significant associations between the RewP to social acceptance feedback and behavioral reward bias, and the FN to social rejection feedback and behavioral loss avoidance. This calls into question potential assumptions that the RewP and FN to social feedback reflect reward and loss related processes. Indeed, a prior study found weak relationships between brain responses to social and monetary rewards (i.e. RewP) in emerging adults ($r(46) = 0.16$, $p = 0.27$) and early adolescents ($r(37) = 0.28$, $p = 0.09$; Ethridge et al., 2017), and a subset of the current sample showed weak correlations as well $(r(54) = 0.04, p =$ 0.76; unpublished data, see Rappaport et al., 2019 for methods). However, differences in the structure of the social reward task have led to a more correlated social and monetary RewP $(r(114) = 0.26, p<0.01;$ Distefano et al., 2018). These studies however compare patterns of brain activity, subjecting them to reverse inference biases. Thus, further studies using convergent behavioral measures of reward and loss processing and brain measures of neural response to social acceptance and rejection are needed to establish the conditions under which brain responses to social and other types of feedback are similar and different.

One potential and intriguing explanation for the lack of correspondence between the RewP/FN and behavioral reward bias/loss avoidance is that there are a number of psychological processes that occur when one experiences social feedback, with the reward or loss system as just one of those processes. For example, one review proposed that there is a period of attentional orienting to feedback, followed by emotional appraisal of feedback, and finally resulting in emotion regulation (Wang et al., 2017). Such theories are supported by the presence of different ERP components identified in the current study (i.e. N1, P2, RewP/FN), and another review supporting the presence of multiple processes in response to rewards (Glazer et al., 2018). However, such conclusions again rely on reverse inference. Thus, future studies will need to assess the relationship between these brain signals and converging behaviors to better determine their function.

4.2 Brain responses to social feedback and depression and social anxiety severity

We did not find support for significant relationships between the RewP and FN and depression and social anxiety symptoms. One possibility is that blunted RewP and heightened FN responses may reflect risk factors for future depression and/or social anxiety (Kujawa & Burkhouse, 2017; Masten et al., 2011) rather than indicators of a current depressive or socially anxious state. In fact, prospective studies have found that the RewP interacts with stressful life events to predict later depression (Burani et al., 2021; Goldstein et al., 2020; Mackin et al., 2019; Olino et al., 2015; Pegg et al., 2019). The clinical literature supports different forms of social rejection (e.g., peer victimization, romantic breakups, parental rejection) as risk factors for depression (Copeland et al., 2013; Kendler et al., 2003; Monroe et al., 1999; Rapee, 1997; Slavich et al., 2009) and social anxiety (Moore et al., 2017; Pickard et al., 2018; Reijntjes et al.,

2010; Storch et al., 2005). Therefore, greater sensitivity (i.e. heightened FN) to rejection, in combination with greater experiences of interpersonal rejection, may lead to depression and/or social anxiety.

4.3 Reward bias/loss avoidance and depression and social anxiety severity

Finally, we did not find that depression and social anxiety severity were related to behavioral reward bias or loss avoidance. This was surprising given previous evidence that these constructs are affected, particularly in depression (Luking, Pagliaccio, et al., 2015; Luking, Neiman, et al., 2015; Pizzagalli et al., 2008; Vrieze et al., 2013; Whitton et al., 2016). One possibility is that the prior literature may reflect false positives. Another is that rather than being related cross-sectionally to depression or social anxiety severity, impaired reward processing may be a trait associated with risk of future psychopathology. This is supported by studies showing that history of depression is related to impaired reward processing (Pechtel et al., 2013; Rappaport et al., 2020), history of social anxiety is related to enhanced reactivity to losses (Kessel et al., 2015), and that reward processing dysfunction predicts depressive symptoms (Gotlib et al., 2010; Luking et al., 2016a; McCabe et al., 2012; Stringaris et al., 2015). Although the PDS study includes data about past psychopathology of the current sample, we were concerned that such exploratory analyses would require too many comparisons. Further, past assessments of social anxiety were limited, since the SIAS/SPS was not collected prior to the current wave.

4.4 Socioeconomic status and brain responses to social acceptance

The results also suggested some interesting avenues for further exploration. We had not predicted a priori that SES (as operationalized as income-to-needs ratio) would be associated

with the RewP and FN. In fact, the only prior literature we are aware of would suggest that lower SES might be associated with improved reward learning and brain responses to monetary rewards (Tobler et al., 2007), with no evidence in regards to social feedback. We chose to include this in the multiple regression models to control for the established relationship between income-to-needs and psychopathology (Barch et al., 2016; Gilman, 2002). Thus, it is intriguing that we found a positive relationship between SES and RewP to social acceptance. We are not aware of any prior literature examining relationships between socioeconomic status and brain response to social feedback, making this a highly novel finding. There is robust literature indicating that low SES is related to greater risk for psychopathology (Leung $\&$ Shek, 2011; Lorant, 2003; Peverill et al., 2021). Given that lower SES was associated with a reduced RewP to acceptance, one possibility is that poverty confers risk for psychopathology at least partially through social anhedonia. This could lead to social withdrawal and greater social isolation which is already exacerbated in impoverished youth (Eckhard, 2018; Sletten, 2010)—and subsequently depression (Bruce & Hoff, 1994). If blunted responses to acceptance is in fact a risk factor for future depression, then this illustrates a potential causal pathway whereby poverty leads to blunted responses to acceptance, which in turn leads to depression. However, since this was an exploratory finding, replication is necessary to support such propositions.

4.5 Socioeconomic status and behavioral reward bias and loss avoidance

Another novel finding was that lower SES was associated with less behavioral reward bias and greater loss avoidance on the PILT (with a larger effect size for the latter). That is, the lower the SES of the adolescent's family, the less they were biased towards the rewarded response, and the more they were biased against the punished response. This represents another intriguing avenue for future research, as it suggests another potential pathway through which

poverty confers risk for psychopathology. Adolescents with fewer monetary resources may be more sensitive to loss. That is, adolescents with lower SES may seek to avoid potential losses. This shift towards avoidance of negative reinforcements may come at the expense of experiencing positive reinforcements. Moreover, an enhanced response to losses has been associated with depression risk (Luking et al., 2016a, 2015), and depression is associated with a focus on reducing negative reinforcement at the cost of potential positive reinforcements (for a review of how this is target in psychotherapy see Dimidjian et al., 2011). Thus, if lower SES is associated with greater sensitivity to loss and a blunted response to reward, this could confer risk for developing depression. If these findings are replicated, future studies should seek to examine the mechanisms responsible for and the outcomes of the link between poverty, blunted responses to social acceptance, and blunted reward bias and enhanced loss avoidance.

4.6 Strengths and Limitations

This study represents an important step in our understanding of the function of the brain's response to social feedback, and how that function is different in depression and social anxiety. The current study has a number of strengths, including a) the preregistration of hypotheses and analyses (osf.io/x8rdh), b) testing of reverse inference assumptions, c) use of dimensional measures of depression and social anxiety, and d) robust multiple regression and structural equation modeling analyses that include demographic covariates, including SES. Moreover, this study provides intriguing exploratory findings that could have implications for our understanding of how poverty affects processing of social acceptance feedback.

These strengths must also be considered in light of the current study's limitations. First, our study may have been under-powered to detect the hypothesized relationships. Post-hoc

power analyses suggested that the sample (\overline{N} = 113) has 95% power to detect moderate effects $(\sqrt{f^2} = 0.15)$, and 83% power to detect smaller effects $(\sqrt{f^2} = 0.10)$, at an alpha of 0.05 with two predictors of interest and six covariates in the multiple regression. However, we were underpowered to detect a correlation between the RewP to social acceptance and depression severity at the effect size found in three prior studies $(r = -0.11;$ Kujawa et al., 2017; Pegg et al., 2021, 2019). That being said, finding a similar effect size among *four* independent studies of adolescents—one of which was preregistered—suggests that this may represent a true population effect albeit of small magnitude. Second, one may take issue with our use of multiple regressions as overly conservative. To guard against potential Type II error, we also examined zero-order correlations between the variables of interest. These correlations largely converged with the results of the regression models. Third, convergence of the current findings with studies using other behavioral measures of reward and loss are needed to verify whether or not these ERP components truly represent engagement of reward and loss systems. Fourth, although boasting greater temporal resolution, subcortical processing of social feedback may be affected in depression and social anxiety. ERP measures would be able to detect downstream consequences in cortical regions (e.g., insula, cortical networks; Rappaport and Barch, 2020), however it may be limited in detecting subcortical origins of such individual differences (e.g., in the subgenual ACC or striatum; Silk et al., 2014). FMRI however carries its own limitations. The low temporal resolution of fMRI would limit the ability to distinguish between the different processes thought to underlie the response to social feedback. Further, fMRI risks reducing psychological phenomena to specific regions of interest. Future studies using both ERP and fMRI methods will be able to address this.

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4.6 Conclusions

Overall, the current findings replicate and extend prior studies. Given the current studies findings, further investigation is warranted to support the assumption that brain responses to social acceptance and rejection reflect functioning of reward- and loss-related systems. Although non-significant in the current study, the finding of a preregistered and consistent, albeit small, relationship between depression and brain response to social acceptance across now four independent studies is notable. Finally, the exploratory findings that lower socioeconomic status is related to greater blunting of the brain response to social acceptance, enhanced loss avoidance and,—to a lesser extent—reduced behavioral reward bias, offers evidence of a potential novel mechanism linking poverty with psychopathology. Together these findings represent an important step in alleviating problems in interpersonal relationships.

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