Archival Report

The Relationship Between Depression Symptoms and Adolescent Neural Response During Reward Anticipation and Outcome Depends on Developmental Timing: Evidence From a Longitudinal Study

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ABSTRACT

BACKGROUND: Blunted neural reward responsiveness (RR) is observed in youth depression. However, it is unclear whether symptoms of depression experienced early in development relate to adolescent RR beyond current symptoms and, further, whether such relationships with RR differ during two key components of reward processing: anticipation and outcome.

METHODS: Within a prospective longitudinal study oversampled for early depression, children and caregivers completed semiannual diagnostic assessments beginning in preschool. In later adolescence, mean age = 16.49 years (SD = 0.94), youths' (N = 100) neurophysiological responses to cues signaling likely win and loss and these outcomes were assessed. Longitudinally assessed dimensional depression and externalizing symptoms (often comorbid with depression as well as associated with RR) experienced at different developmental periods (preschool [age 3–5.11 years], school age [6–9.11 years], early adolescence [10–14.11 years], current) were used as simultaneous predictors of event-related potentials indexing anticipatory cue processing (cue-P3) and outcome processing (reward positivity/feedback negativity and feedback-P3).

RESULTS: Blunted motivated attention to cues signaling likely win (cue-P3) was specifically predicted by early-adolescent depression symptoms. Blunted initial response to win (reward positivity) and loss (feedback negativity) outcomes was specifically predicted by preschool depression symptoms. Blunted motivational salience of win and loss outcomes (feedback-P3) was predicted by cumulative depression, not specific to any developmental stage.

CONCLUSIONS: Although blunted anticipation and outcome RR is a common finding in depression, specific deficits related to motivated attention to cues and initial outcome processing may map onto the developmental course of these symptoms.

Appropriate response to reward is critical for motivated behavior and learning. Although reward responsiveness (RR) increases normatively through adolescence (1), blunted RR is consistently implicated in adolescent depression and may play a role in its pathogenesis (2,3). For example, blunted RR is observed in remitted depression (4), nondepressed but high-risk groups, including first-degree relatives of depressed persons (5), offspring of depressed parents (6,7), and adolescents known to develop later depression (8). Because of this, blunted RR has been conceptualized as a trait vulnerability and potential biomarker of depression risk. In a separate line of inquiry, early experiences, particularly of trauma or deprivation, but also of depression, have been linked to blunted RR later in life (9–13) as well as concurrently during preschool (14). These studies suggest that early life may be a sensitive period, wherein negative experiences known to blunt RR alter the hedonic set point (10). Conversely, negative experiences, such as experiencing depression, at later points in development may relate to other types of reward dysfunction; for example, there is particularly strong evidence for blunted responding to cues signaling potential reward in adolescent depression (10,12,15,16). Another related view is that blunted RR reflects a scar of earlier experience of depression symptoms and plays a role in heightened risk for reoccurrence, supported by findings of blunted RR in remitted depression (4). However, there has been no prospective investigation of whether early experience of depression symptoms affects neural RR later in adolescence, the developmental period most commonly examined in

studies of reward processing and depression risk in youth (3). Understanding how past early depression versus recent depression in adolescence might affect RR is critical for understanding not only the pathophysiology of depression and its maintenance over the course of development, but also how blunted RR evolves over the course of development and may function as a depression biomarker in the high-risk period of adolescence.

RR is a multifaceted construct and in the functional magnetic resonance imaging (fMRI) literature it is common to index both reward anticipation (i.e., response to cues signaling that either a win or loss is likely to occur) and response to outcomes (i.e., receipt of win or loss outcomes). Using electroencephalography (EEG), which has much higher temporal resolution than fMRI, anticipation and outcome processing can be further broken down into subprocesses indexed by specific event-related potentials (ERPs) (17). For example, motivated attention to anticipatory cues is indexed by the cue-P3, a centroparietal positivity that is increased following cues indicating likely reward (18). Initial responsiveness to win outcomes is indexed by the reward positivity (RewP), a frontocentral positivity associated with good outcomes. The loss-related equivalent of this component, the feedback negativity (FN), is a negativity for bad outcomes. The difference between win and loss, the ΔRewP, is frequently blunted in depression and depression risk (19). Motivational salience of win and loss outcomes is indexed by the feedback-P3 (fb-P3), a centroparietal positivity that is greater for good or more salient feedback (20,21).

To date, the literature on depression and reward using ERPs has most often employed the doors task (22), which, although ideally suited for evaluating responsiveness to win versus loss feedback via the ΔRewP, does not assess the anticipation-related components of RR. Recently, there has been a growing call to examine other reward-related components in addition to the RewP/FN (17). Here, for the first time, we have modified an fMRI reward task, the cards task, which is commonly used in the adolescent depression literature (15), for use with EEG. This task isolates responses not only to win and loss outcomes, but also to cues predictive of those outcomes. Only a handful of EEG studies have investigated both anticipation and outcome reward-related ERPs in relation to depression (23–25). Although those studies implicate both phases of RR in depression, the exact ERPs implicated often differ across studies. The common depression-related findings are blunted amplitude or latency for the fb-P3 as well as null effects of current depression on the RewP and cue-P3.

Another concern is that depression is often comorbid with other forms of psychopathology that may also show disruptions in RR, such as externalizing disorders (26). Furthermore, recent work in adults highlights the importance of considering both depression and externalizing dimensions when investigating RR (23). Thus, including externalizing symptoms as a covariate will be critical for evaluating the specificity of relationships between depression and RR in adolescence.

The present study capitalizes on rich longitudinally assessed diagnostic information spanning ~13 years, beginning when children were 3 to 5 years of age, combined with EEG assessed later in adolescence, to examine relationships between ERP responses to both anticipation and receipt of wins and losses and depression/externalizing symptom severity at different phases of

development (preschool, school age, early adolescence, and current). We addressed 3 main goals with this approach. First, we examined relationships between anticipation and outcome ERPs during adolescence using a modified version of the cards task, originally designed for and commonly used with fMRI, to probe reward anticipation/outcome responses in depression. Second, we examined effects of depression on RR above and beyond externalizing symptoms. We hypothesized that depression symptoms specifically would be related to blunted ERP responses to both winning and losing. Third, we examined how symptoms during distinct developmental stages might differentially affect reward responsiveness later in adolescence. We hypothesized that preschool and current depression symptoms would show unique relationships with RR.

METHODS AND MATERIALS

Participants

Adolescents from the Preschool Depression Study (27) who completed the final follow-up session participated. The Preschool Depression Study is a longitudinal study at Washington University School of Medicine in St. Louis, Missouri, that initially recruited children aged 3.0–5.11 years from primary caregivers, day care centers, and preschools, oversampling for depression using the Preschool Feelings Checklist (28). The Preschool Feelings Checklist is sensitive for preschool depressive symptoms but also identifies children with other disorders, including disruptive disorders (29). Children with elevated Preschool Feelings Checklist scores (≥3) and scores of 0 (presumed healthy) were contacted for participation. Exclusion criteria included autism spectrum disorder (no other psychiatric disorders); chronic illness; speech, language or cognitive delays; and neurological disorders. Children then underwent approximately annual diagnostic assessments over 12–15 years that were used to create dimensional symptom scores. Caregivers completed informed consent and child verbal/written assent was obtained before study participation. The Washington University School of Medicine Institutional Review Board approved all procedures. The current protocol was completed at the ninth follow-up assessment, and of the 170 participants who completed the follow-up session, 158 consented to participate in the EEG, 152 of which completed the EEG (dropouts: 2 no longer interested, 1 due to hairstyle, 3 due to scheduling). After data processing and cleaning to ensure enough usable segments (discussed below), 6 participants were excluded and 3 had technical malfunctions. Of the 144 participants with usable data, 38 were enrolled in the study at later waves and thus symptom counts could not be calculated for preschool age, and 6 had missing demographic covariate information from early sessions. This resulted in a sample of 100 participants (see Table 1 for demographic and clinical information and Table S6 for demographic and symptom comparisons between participants in the EEG assessment and the remaining study participants).

Measures

Depression and Externalizing Severity Scores. Dimensional depression and externalizing severity scores were created using diagnostic interviews of the caregiver-administered Preschool-Age Psychiatric Assessment (PAPA) (30) through age 7,

Table 1. Demographic and Clinical Characteristics of the Study Participants (N = 100)

Characteristic	Mean	SD	Minimum	Maximum
Age at EEG Assessment, Years	16.49	0.94	14.35	18.32
Sex, Female, n (%)	48 (48%)			
Race, White, n (%)	55 (55%)			
Baseline Income-to-Needs	2.09	1.16	0	3.93
Historical Depression Symptoms, Average of PAPA/CAPA Depression Core Symptoms				
Preschool (3.0–5.11 years)	2.38	1.61	0	7
School age (6.0–9.11 years)	2.19	1.44	0	6
Early adolescence (10.0–14.11 years)	2.23	1.53	0	7
Historical Externalizing Symptoms—Average of PAPA/CAPA Externalizing Dimensional Scores				
Preschool (3.0–5.11 years)	6.60	6.10	0	31
School age (6.0–9.11 years)	5.67	5.65	0	24
Early adolescence (10.0–14.11 years)	4.31	5.55	0	25
Current Symptoms, Sum of K-SADS Items				
Depression (core symptoms)	1.73	2.45	0	9
Externalizing (ADHD/ODD/CD screen items)	0.23	0.53	0	3
Depression Diagnosis, n	Yes	No		
Preschool	35	65		
School age/early adolescence	45	55		
Current	15	85		
Ever	57	43		

ADHD, attention-deficit/hyperactivity disorder; CAPA, Childhood and Adolescent Psychiatric Assessment; CD, conduct disorder; EEG, electroencephalography; K-SADS, Kiddie Schedule for Affective Disorders and Schizophrenia; ODD, oppositional defiant disorder; PAPA, Preschool-Age Psychiatric Assessment.

the caregiver- and child-administered Childhood and Adolescent Psychiatric Assessment (CAPA) (31) for ages 8 and older, and the caregiver- and child-administered Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) (32) at the final assessment. As is standard for the PAPA and CAPA, raters were first trained to reliability, all diagnostic assessments were audiotaped, and 20% of tapes were reviewed by a master coder for reliability with discrepancies resolved in consultation with a senior child psychiatrist (JLL). For the K-SADS, interrater reliability for depression diagnoses was $\kappa = 0.81$ and agreement was 93.2%.

Depression severity scores were calculated by summing the number of 9 core depression symptoms endorsed by the caregiver and/or child at each assessment. Externalizing severity scores were the combined sum scores of symptoms from the attention-deficit/hyperactivity disorder, oppositional defiant disorder, and conduct disorder modules. Symptoms were considered to be present if either the parent or child endorsed them. For PAPA/CAPA, this included subthreshold, but for K-SADS, symptoms were counted when endorsed at threshold. To create mutually exclusive symptom scores for each symptom domain from each developmental period, means of symptoms were calculated for each participant from diagnostic interviews conducted when participants were within each of the following age ranges: preschool age, <6.0 years; school age, 6.0–9 years 11 months; and early adolescence, 10–14 years 11 months. Early-adolescence symptoms did not include symptoms from the current EEG assessment wave. Means of symptoms from preschool up to, but not including, the current wave were used for past cumulative symptoms. Internal consistency scores for depression and externalizing severity scores during the preschool period were $\alpha = .62$ and .92, respectively. Internal

consistency scores for depression and externalizing severity scores across longitudinal assessments were $\alpha = .63$ and .90, respectively. See Figure S2 for histograms depicting the distribution of all symptom measures and Table S5 for bivariate relationships between symptom measures.

Income-to-Needs Ratio. At baseline, caregivers reported on family income, and the income-to-needs ratio was calculated as total family income divided by the federal poverty level based on family size at time of collection (33).

Cards Anticipation and Outcome ERP Reward Task. Participants completed an EEG card-guessing task (Figure 1) modeled from a neuroimaging paradigm (34) that assessed responses during anticipation and receipt of reward feedback. Participants completed 72 trials across 2 blocks, with 24 likely win trials, 24 likely loss trials, 12 either win or lose trials, and 12 neither win nor lose trials. In total there were 22 possible instances of win feedback, 22 of loss feedback, and 28 of neutral feedback. Participants were told that their performance would determine a monetary reward after the scan; however, feedback outcomes were presented in a fixed order and were unrelated to the participants' high/low value choice. Participants were told that they had won $17 following the task, but specific values were not assigned to win and loss events. Participants with 10 or fewer usable trials for any of the cue/outcome types of interest were excluded from analyses (n = 6) (35,36). Descriptive statistics for usable segments and Cronbach's α (internal consistency) for all ERPs are presented in Table S1.
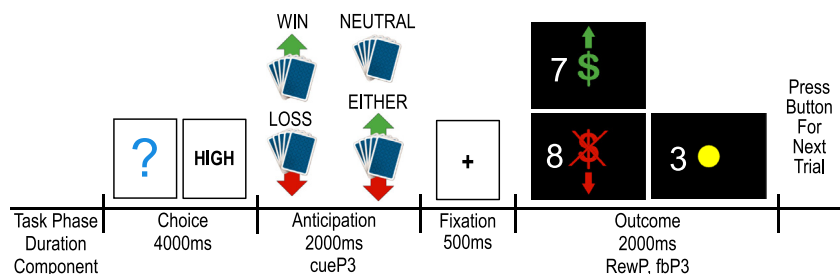
Figure 1. Trial structure for the card-guessing task. On each trial, a mystery card was presented during which the participant guessed whether the card's value was high or low via button press (high or low guess was displayed following choice, for a total of 4000 ms). Next, 1 of 4 possible cue types was displayed for 2000 ms. Cues indicated the type and probability of possible outcomes: likely win (followed by win 67% or neutral 33% of the time), likely loss (followed by loss 67% or neutral 33% of the time), either win or loss (each outcome 50%), or neutral (100% neutral). Cues were followed by 500 ms of fixation. Next, win, loss, or neutral outcome was presented for 2000 ms. Finally, participants were instructed to press a button to initiate the next trial. If participants did not make a high/low choice, they were told that they didn't respond and saw fixation and dashes for the remainder of the trial. Following completion of the task, participants were told that they won $17. fb, feedback; RewP, reward positivity.

EEG Data Collection and Processing

Continuous EEG was recorded using the actiCHamp 32-channel active channel amplifier system (Brain Vision, Morrisville, NC). Electrodes were mounted using a subset of the International 10/20 System using 32 sites with a ground electrode located at FPz. The electrooculogram generated from blinks and eye movements were recorded from 5 facial electrodes placed around the eyes. Brain Vision Analyzer 2 software (Brain Products, Gilching, Germany) was used for offline analysis. All data were re-referenced to the average of TP9 and TP10 and high-pass filtered using a 0.1-Hz half-power cutoff. The EEG was then segmented for each trial, from 200 ms before anticipation cue and continuing for 1000 ms. Segmentation for outcome events began 200 ms before feedback and continued for 1000 ms. The EEG was corrected for electrooculogram artifacts (37) and physiological artifacts removed using an automatic procedure with a maximum allowed voltage step of 50 μV within a 400-ms interval length, a maximum absolute difference between any 2 points of 175 μV, and a minimum allowed activity of 0.50 μV within a 100-ms interval length. Trials were then averaged and baseline corrected (−200 to 0 ms) and low-pass filtered from 30 Hz.

Anticipation ERPs were quantified separately for likely win and likely loss cues; outcome ERPs were quantified separately for win and loss feedback. Feedback ERPs include all win and loss outcomes regardless of cue type, because feedback valence effects (RewP/FN) did not significantly differ based on cue type ($F_{1,99} = 0.64$, $p = .43$). Time windows for ERPs were based on previous literature (35) and a visual inspection of grand average waveforms. The cue-P3 was quantified as mean activity at the Pz electrode site 350–450 ms after onset of anticipation cues. The RewP/FN was quantified as mean activity at Fz 250–350 ms after feedback. The fb-P3 was quantified as mean activity at Pz 350–450 ms after feedback. See Table S2 for descriptive statistics for each ERP.

Statistical Analysis

All analyses were conducted using SPSS version 26.0.0.0 (IBM Corp., Armonk, NY). Paired-sample *t* tests tested for effects of anticipatory cue (likely win vs. likely loss) and feedback type (win vs. loss) for the cue-P3 and the RewP/FN/fb-P3,

respectively. Bivariate correlations evaluated relationships between components for win or loss.

For each component, a repeated-measures analysis of variance (ANOVA) was conducted with mean amplitude as the dependent measure and cue/outcome valence (win or loss) as the within-subject factor. Symptoms at 4 mutually exclusive periods in development (preschool, school age, early adolescence, and current) for both depression and externalizing dimensions were included simultaneously. ANOVAs also controlled for sex (1 = male, 2 = female), baseline income-to-needs ratio, and age at EEG assessment. Both main effects of symptoms and interactions between symptoms and cue/outcome valence are of interest and reported. This repeated-measures ANOVA approach was chosen because it is the most conservative and parsimonious way to test whether specific symptom domains at specific developmental time points relate to ERPs in similar or different ways depending on cue/outcome valence, our main question of interest.

Significant interactions between cue/outcome valence and symptoms indicate that the relationship between symptoms and the ERP differs significantly depending on cue/outcome valence. Post hoc regressions (detailed below) are then necessary to identify direction of symptom relationships for each valence (win or loss), controlling for the alternative cue/outcome type. Interactions are particularly expected for the RewP/FN where the sign of this ERP differs for win and loss feedback (i.e., a greater response to win is reflected by a more positive RewP, whereas a greater response to loss is reflected by a more negative FN). Main effects of symptoms suggest that symptoms relate significantly to the ERP in question regardless of the cue/outcome valence—this would indicate greater responsiveness to feedback or cues generally. Post hoc regressions predicting the mean of win and loss are needed to identify the direction of this effect.

We conducted post hoc regressions for all significant symptom effects in the repeated-measure ANOVAs. All covariates and symptom measures were regressed on 1) win and loss separately (controlling for the other type of cue/outcome) to examine significant interactions with valence from the repeated-measures ANOVAs or 2) on the mean of win and loss to examine significant main effects of symptoms. Supplemental bivariate correlations between symptom measures and ERPs were conducted for descriptive purposes; with several correlated symptom measures in the ANOVA/regression

analyses, it was possible that individual symptom effects that might be masked or inflated.

False discovery rate (FDR) correction (Benjamini-Hochberg procedure) was applied across the 3 ANOVAs to determine whether nominally significant main effects of symptoms or interactions between symptoms and cue/outcome valence remained significant after correcting for multiple comparisons.

RESULTS

Group Average Anticipatory ERPs

The cue-P3 was maximal at Pz with a significantly greater positivity observed for likely win than likely loss cues: $t_{99} = 6.55$, $p < .001$ (Figure 2A).

Group Average Consummatory ERPs

The RewP/FN was maximal at frontal midline sites with a significantly greater positivity to win than loss feedback: $t_{99} = 4.76$, $p < .001$ (Figure 2B). The fb-P3 was maximal at Pz with a significantly greater positivity observed for win than loss feedback: $t_{99} = 3.96$, $p < .001$ (Figure 2C).

The RewP/FN and fbP3 were significantly correlated for residual response to both win feedback ($r = .34$, $p < .001$) and loss feedback ($r = .31$, $p = .002$). All other relationships were nonsignificant (Table S3).

Depression Symptom Effects

The RewP/FN showed a significant interaction between depression symptoms and feedback valence. Preschool depression symptoms, specifically, significantly interacted with feedback valence (win vs. loss) for the RewP/FN (Table 2; Figure 3); this relationship was also observed in bivariate correlation (Table S4). Post hoc regressions to follow up on the significant interaction showed that preschool depression significantly predicted a less positive response to win feedback, indicating blunted response to win, and a less negative response to loss feedback, also indicating a blunted response to loss (Table 3; Figure S1).

Early-adolescence depression symptoms, specifically, interacted with cue valence (likely win vs. likely loss) for the cue-P3 (Table 2); this relationship approached significance only after correcting for multiple corrections. In post hoc regressions early-adolescence depression predicted blunted response to likely win cues, but not likely loss cues (Table 3).

No significant effects of symptoms at specific ages were observed for the fb-P3 in ANOVA/regression analyses with depression symptoms at different developmental time points as simultaneous predictors (Tables 2 and 3). However, in bivariate correlations, increased depression related to blunted fb-P3, with a similar effect size across developmental time points (Table S4). Furthermore, exploratory bivariate correlations showed that cumulative past depression predicted a blunted fb-P3 (Table S4). A further exploratory regression showed that this effect remained when controlling for past cumulative externalizing symptoms and demographic covariates ($\beta = -.35$, $p = .023$) (Table S7).
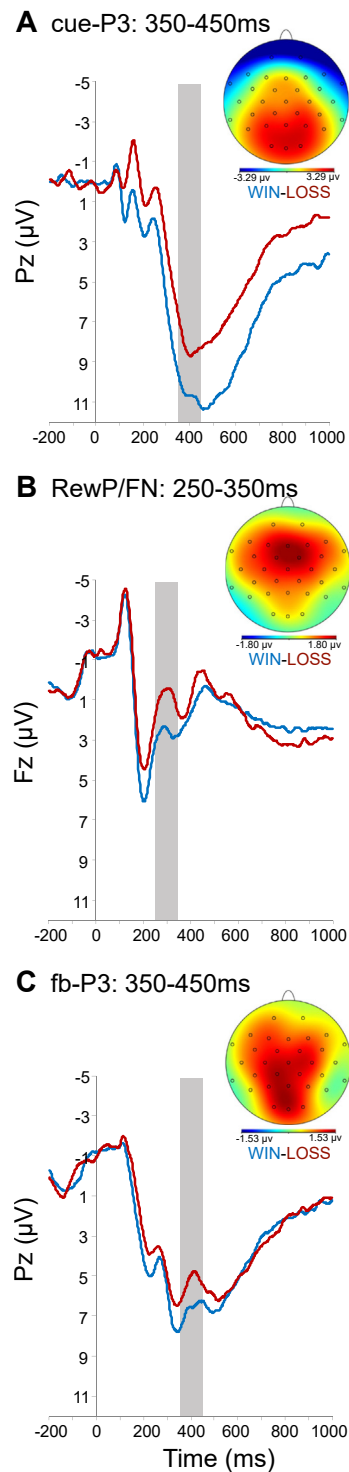
Figure 2. Anticipation **(A)** and outcome **(B, C)** event-related potentials (ERPs) and scalp topographies. ERP waveforms are at electrodes Fz **(B)** or Pz **(A, C)**. Cue or outcome onset was at 0 ms. Shaded regions indicate the time windows during which each ERP was scored. fb, feedback; FN, feedback negativity; RewP, reward positivity.

Table 2. Repeated-Measures Analysis of Variance Outputs

Effect	Cue-P3			RewP/FN			fb-P3		
	F	p (p_{corr})	η_p^2	F	p (p_{corr})	η_p^2	F	p (p_{corr})	η_p^2
Valence	0.75	.387	.01	1.08	.302	.01	0.12	.727	<.01
Valence×PS DEP	0.23	.631 (.631)	<.01	6.72	.011 (.033)[a]	.07	1.35	.249 (.373)	.02
Valence×SA DEP	0.15	.696	<.01	0.12	.732	<.01	0.50	.484	.01
Valence×AD DEP	4.68	.033 (.099)	.05	0.38	.540 (.540)	<.01	1.31	.256 (.384)	.02
Valence×Current DEP	0.31	.578	<.01	0.14	.705	<.01	0.11	.746	<.01
Valence×PS EXTL	0.37	.544	<.01	0.01	.915	<.01	<0.01	.961	<.01
Valence×SA EXTL	0.82	.369	.01	0.92	.341	.01	0.05	.831	<.01
Valence×AD EXTL	3.76	.056	.04	0.98	.325	.01	1.88	.174	.02
Valence×Current EXTL	1.30	.257	.02	0.26	.609	<.01	0.54	.463	.01
Valence×Sex	0.14	.711	<.01	0.07	.796	<.01	2.75	.101	.03
Valence×Age	1.78	.186	.02	2.88	.093	.03	0.45	.506	.01
Valence×Income/Need	0.26	.613	<.01	2.10	.151	.02	1.90	.172	.02
PS DEP	0.40	.529	.01	0.42	.518	.01	0.18	.670	.00
SA DEP	1.51	.223	.02	0.03	.870	<.01	1.45	.232	.02
AD DEP	0.29	.592	<.01	1.52	.221	.02	1.31	.255	.02
Current DEP	<0.01	.956	<.01	0.08	.780	<.01	0.01	.946	<.01
PS EXTL	0.63	.428	.01	3.39	.069	.04	1.83	.179	.02
SA EXTL	2.74	.102	.03	1.09	.300	.01	3.59	.062	.04
AD EXTL	0.79	.378	.01	0.17	.678	<.01	0.31	.581	<.01
Current EXTL	0.84	.362 (.362)	.01	7.79	.006 (.018)[a]	.08	3.73	.057 (.085)	.04
Sex	0.62	.435	.01	0.51	.475	.01	0.06	.801	<.01
Age at EEG	0.58	.449	.01	0.56	.456	.01	1.08	.303	.01
Income/Need	0.22	.640	<.01	0.03	.854	<.01	0.04	.851	<.01

AD, early adolescence; DEP, depression; EEG, electroencephalogram; EXTL, externalizing; fb, feedback; p_{corr}, false discovery rate-corrected p value; PS, preschool; RewP/FN, reward positivity/feedback negativity; SA, school age.
[a]$p < .05$.

Externalizing Symptom Effects

The cue-P3 and RewP/FN also showed significant effects of externalizing symptoms; no significant effects were observed for the fb-P3. Early-adolescence externalizing symptoms, specifically, significantly interacted with cue valence for the cue-P3 (Table 2). Post hoc regressions showed that early-adolescence externalizing symptoms significantly predicted blunted response to likely loss cues but not response to likely win cues (Table 3). These effects were not observed in the bivariate correlations (Table S4; Figure 3B).

A significant main effect of current externalizing symptoms was observed for the RewP/FN (Table 2). Post hoc regressions showed that current externalizing symptoms positively predicted the RewP/FN across feedback types, indicating potentiated response to win and blunted response to loss outcomes (Table 3).

DISCUSSION

We modified a well-known reward processing paradigm, the cards task, which has been used extensively with fMRI in the adolescent depression literature (12,34), for use with EEG. Similar to work in adults, we identified a cue-P3 that was larger for anticipatory cues, indicating likely wins versus likely losses, as well as the RewP/FN and fb-P3 as ERPs sensitive to feedback about wins versus losses (17,23,35).
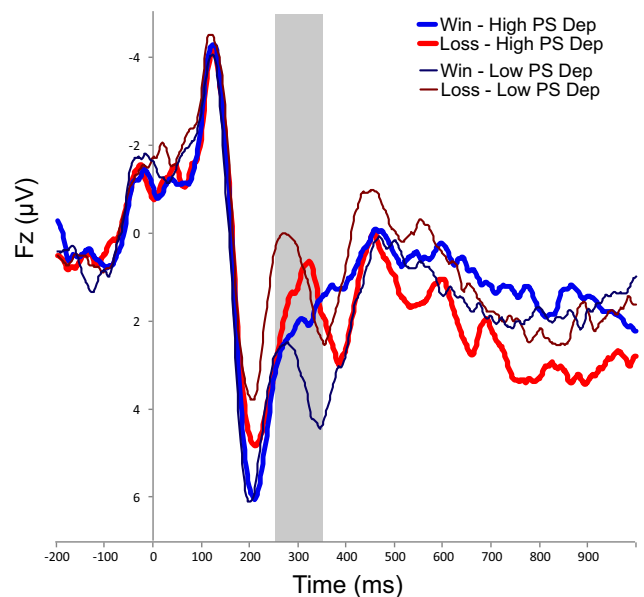
Figure 3. Outcome locked event-related potential waveforms at Fz for individuals with upper-tertile (thick lines) vs. lower-tertile (thin lines) preschool (PS) depression (Dep) symptoms. Time window for the reward positivity/feedback negativity (250–350 ms) is highlighted in gray.

Table 3. Post Hoc Regressions Investigating Significant Effects From Repeated-Measure Analyses of Variance

Dependent Variable	Predictor	Cue-P3					RewP/FN				
		B	SE	Std. β	t	p	B	SE	Std. β	t	p
Win	(Constant)	−5.80	7.56		−0.77	.445	−7.32	6.99		−1.05	.298
	PS DEP	−0.17	0.39	−.04	−0.43	.671	−0.81	0.38	−.25	−2.14	.035[a]
	SA DEP	0.15	0.52	.03	0.30	.767	0.13	0.48	.04	0.27	.791
	AD DEP	−1.00	0.47	−.22	−2.15	.035[a]	0.09	0.46	.03	0.20	.839
	Current DEP	0.11	0.20	.04	0.55	.585	−0.08	0.19	−.04	−0.43	.671
	PS EXTL	0.06	0.12	.06	0.54	.592	−0.07	0.11	−.08	−0.62	.539
	SA EXTL	−0.13	0.17	−.11	−0.75	.454	−0.09	0.16	−.10	−0.57	.573
	AD EXTL	0.30	0.17	.24	1.81	.074[a]	0.12	0.16	.13	0.78	.439
	Current EXTL	−1.03	0.99	−.08	−1.04	.301	1.17	0.95	.12	1.23	.223
	Age	0.56	0.45	.08	1.24	.219	0.75	0.43	.14	1.76	.082
	Income/Need	0.21	0.40	.04	0.53	.6	−0.53	0.39	−.12	−1.37	.173
	Sex	0.27	0.87	.02	0.31	.758	0.03	0.83	.00	0.03	.976
	Loss ERP	0.96	0.07	.84	13.66	<.001	0.76	0.09	.69	8.57	<.001
	Model Statistics	$R^2 = .71$, adj. $R^2 = .67$, $F = 17.26$, $p < .001$					$R^2 = .53$, adj. $R^2 = .47$, $F = 8.19$, $p < .001$				
Loss	(Constant)	11.70	6.42		1.82	.072	5.52	6.29		0.88	.383
	PS DEP	0.27	0.33	.07	0.81	.422	0.92	0.34	.32	2.74	.007[a]
	SA DEP	−0.46	0.44	−.11	−1.03	.308	−0.18	0.43	−.05	−0.40	.687
	AD DEP	0.75	0.41	.19	1.85	.068	−0.49	0.41	−.16	−1.20	.234
	Current DEP	−0.09	0.17	−.04	−0.52	.602	0.04	0.17	.02	0.21	.835
	PS EXTL	−0.11	0.10	−.11	−1.02	.312	−0.09	0.10	−.11	−0.83	.409
	SA EXTL	0.26	0.15	.24	1.74	.085	0.20	0.14	.25	1.42	.159
	AD EXTL	−0.34	0.14	−.31	−2.38	.019[a]	−0.16	0.14	−.19	−1.13	.26
	Current EXTL	1.36	0.84	.12	1.61	.112	0.79	0.86	.09	0.92	.363
	Age	−0.67	0.39	−.11	−1.72	.09	−0.46	0.39	−.09	−1.18	.24
	Income/Need	−0.09	0.35	−.02	−0.26	.798	0.44	0.35	.11	1.25	.215
	Sex	−0.58	0.75	−.05	−0.78	.439	−0.45	0.74	−.05	−0.61	.545
	Win ERP	0.71	0.05	.81	13.66	<.001	0.61	0.07	.67	8.57	<.001
	Model Statistics	$R^2 = .71$, adj. $R^2 = .67$, $F = 18.05$; $p < .001$					$R^2 = .54$, adj. $R^2 = .48$, $F = 8.49$; $p < .001$				
Mean Win and Loss	(Constant)						−1.94	8.23		−0.24	.815
	PS DEP						0.29	0.44	.10	0.65	.518
	SA DEP						−0.09	0.57	−.03	−0.16	.87
	AD DEP						−0.65	0.53	−.22	−1.23	.221
	Current DEP						−0.06	0.22	−.03	−0.28	.78
	PS EXTL						−0.24	0.13	−.33	−1.84	.069
	SA EXTL						0.20	0.19	.25	1.04	.3
	AD EXTL						−0.08	0.18	−.09	−0.42	.678
	Current EXTL						3.03	1.09	.36	2.79	.006
	Age						0.38	0.50	.08	0.75	.456
	Income/Need						−0.08	0.46	−.02	−0.19	.854
	Sex						−0.70	0.97	−.08	−0.72	.475
	Model Statistics						$R^2 = .14$, adj. $R^2 = .04$, $F = 1.32$, $p = .228$				

AD, early adolescence; adj., adjusted; DEP, depression; ERP, event-related potential; EXTL, externalizing; PS, preschool; RewP/FN, reward positivity/feedback negativity; SA, school age; Std., standardized.

[a]$p < .05$.

Next, drawing on the strength of prospective longitudinal clinician ratings of depression and externalizing symptoms, we investigated how these ERPs, assessed in later adolescence, related to depression and externalizing symptoms experienced at specific periods earlier in development. We found that depression symptoms predicted blunted response to wins during both anticipation (at trend level) and outcome processing, as well as blunted response to loss outcomes; this general pattern is consistent with the extant fMRI and ERP literatures (38,39). However, there were both general and age-

specific effects of depression on RR that depended on the ERP in question.

Depression symptoms experienced during the preschool period were associated with blunted responsiveness during initial responding to both loss and win outcomes (FN and RewP). This relates to fMRI findings from our laboratory using the same sample that preschool depression specifically predicted adolescent blunted response to reward cues within a distributed network of reward-sensitive regions including the striatum and anterior cingulate cortex (12). Both of these regions are likely neural generators for the outcome-related RewP/FN (40,41). Blunted RewP/FN is one of the most frequently reported findings in the depression literature; however, it has been suggested that this component may function more as an underlying depression risk factor than a reflection of current symptoms (2). Blunted RewP/FN may also be more evident during simple gambling tasks rather than anticipation/outcome paradigms (42). Furthermore, studies using similar anticipation/outcome tasks have reported null direct effects of current depression on the RewP/FN (23–25). However, our results do add to a growing literature suggesting that early experiences linked to depression liability also affect RR observed later in life (9,12,13,43). Collectively, findings across studies suggest that early life, including the preschool period, may be a particular window of vulnerability where depression may negatively affect reward system function and development. This interpretation, as well as others (e.g., depression symptoms in preschool may reflect a more heritable form of depression with stronger links to adolescent anhedonia, with this underlying genetic risk driving both preschool depression and blunted adolescent RewP/FN) should be investigated in future work assessing both symptoms and RR in concert across development.

Early-adolescence depression, above and beyond symptoms at other ages, predicted blunted cue-P3, possibly reflecting reduced motivated attention specifically to cues signaling likely reward. The few studies investigating the cue-P3 in depression have reported null results for amplitude (23,24); there is evidence for prolonged latency in adolescent depression (25). However, a blunted P3 to salient stimuli in other task contexts, particularly oddball tasks, is a common finding with a number of types of psychopathology, including depression and externalizing disorders (44,45). In the present study, we show some interesting specificity to depression versus externalizing symptoms: The latter predicted blunted P3 response to cues signaling a likely loss. Given that depression and externalizing are often comorbid, considering both types of symptoms simultaneously may be particularly important for future studies.

Blunted fb-P3, thought to index motivated attention to win/loss outcomes, also was related to depression, but not at a specific developmental stage. Instead we observed a general effect where depression at each developmental period, as well as cumulative past depression, predicted a blunted fb-P3 for both win and loss feedback. Previous fMRI work from our laboratory demonstrated that cumulative depression, versus current depression, predicted blunted response to reward in a distributed network of reward-sensitive regions (12). This is particularly interesting given that the fb-P3 likely reflects activation within a large and distributed set of neural generators, including the lateral frontal cortex, parietal cortex, and medial temporal lobe (46).

Although the present study has many strengths, it also has limitations. Neural RR was assessed only once in late adolescence, precluding analysis of symptom effects on the trajectory of RR over development. Furthermore, diagnostic assessments shifted to the K-SADS at the time point when ERPs were assessed and depression symptoms were more skewed at this time point than at earlier ages, which could have influenced historical versus current symptom findings. It is also important to consider that our analytical approach focused on unique effects of symptoms experienced at different ages on RR; this residualizing of effects is useful analytically and conceptually but may not map onto lived experience of these disorders, which typically covary across domains and continue throughout development. Finally, there were not increases in depression symptoms from childhood to adolescence, as is typically observed in community samples; this is likely because the sample was enriched for depressive symptoms during preschool and as such experienced some regression to the mean of symptoms as the children developed. However, this atypical distribution of symptoms over the course development should be noted and further underscores the need for replication of these findings in other community-based samples.

Blunted RR during both anticipation and outcome phases of reward processing have been implicated in depression and depression risk (19,38). However, this is the first ERP evidence that depression symptoms experienced during different developmental periods show unique relationships with blunted RR during different phases of reward processing. More work is needed to investigate how these ERPs may act, either alone or in concert, when predicting trajectories of future depression and externalizing symptoms across the high-risk adolescent years.

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