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Longitudinal Associations Between Preschool Disruptive Mood Dysregulation Disorder Symptoms and Neural Reactivity to Monetary Reward During Preadolescence

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Abstract

Objective: Reward-processing abnormalities are thought to be a key feature of various psychiatric disorders and may also play a role in disruptive mood dysregulation disorder (DMDD), a new diagnosis in DSM-5. In the current study, we used event-related potentials (ERP) sensitive to monetary gains (i.e., the reward positivity [RewP]) and losses (i.e., the N200) to examine associations between symptoms of DMDD during early childhood and later reward processing during preadolescence.

Methods: To assess early emerging DMDD symptoms in a large longitudinal community sample ($n = 373$) of 3-year old children, we administered a diagnostic interview, Preschool Age Psychiatric Assessment (PAPA) with parents. At a later assessment, ~6 years later, children completed a monetary reward task while an electroencephalogram (EEG) was recorded. Children's lifetime history of psychopathology was also assessed at that time using Kiddie-Schedule of Affective Disorders and Schizophrenia (K-SADS) with the child and parent.

Results: Multiple regression analyses revealed that age 3 DMDD symptoms predicted an enhanced RewP to monetary rewards in preadolescence. This association is independent of demographics and lifetime history of symptoms of depression, any anxiety disorder, attention-deficit disorder, oppositional defiant disorder, or conduct disorder

Conclusions: Early manifestations of DMDD in children as young as 3 years old predicted enhanced reward processing later in development. These findings add to the growing corpus of literature on the pathophysiology of DMDD, and underscore the predictive validity of preschool DMDD on a neural level.

Introduction

Disruptive mood dysregulation disorder (DMDD), recently introduced in the *Diagnostic and Statistical Manual of Mental Disorders,* 5th ed.'s (DSM-5) section on childhood and adolescent disorders, is characterized by a pervasive sad, irritable, or angry mood, occurring nearly every day, and punctuated by developmentally inappropriate temper outbursts that are grossly out of proportion to the immediate situation (American Psychiatric Association 2013). Its inclusion is intended to identify youth who show impaired mood and temper regulation across development, and distinguish them from youth who exhibit early manifestations of bipolar spectrum disorders (Copeland et al, 2013, 2014). This addition to the DSM-5 has preliminary support from both clinical and large longitudinal community samples suggesting that school-age DMDD and chronic irritability predict higher levels of anxiety and depression, but not bipolar disorder, during later points in development (Copeland et al. 2014; Deveney et al. 2014). Even though it is a distinct condition from pediatric bipolar disorder, DMDD is nonetheless a severe childhood disorder associated with impaired functioning, and is predictive of poor outcomes later in life. These outcomes include higher incidence of suicide, more adverse health outcomes, lower educational attainment, and poorer social functioning in adulthood (Copeland et al. 2014). Despite the prevalence and clinical importance of chronic irritability and severe temper outbursts in children, research on the pathophysiology of DMDD is very limited.

Most relevant work has focused on severe mood dysregulation (SMD), a diagnostic construct that preceded DMDD; in addition to its chronic irritability symptoms, SMD also includes symptoms of hyperarousal (e.g., insomnia, agitation, distractibility). A small body of research shows that SMD is associated with aberrant emotion–attention interactions, particularly in the context of threat (e.g., Hommer et al. 2013). Other studies have shown that SMD is

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associated with abnormal patterns of neural activation to angry, fearful, and neutral faces compared with that of healthy controls, although findings are contradictory, supporting both hypo- and hyperactivation of the amygdala (Thomas et al 2013, 2014).

Less is known about neural responses to reward in DMDD. Leibenluft and Stoddard (2013) propose that children with DMDD may be vulnerable to high levels of frustration because they have difficulty adjusting their behavior to changing reward contingencies. To date, only one functional MRI (fMRI) study has examined this empirically, using a response reversal task in a sample of youth meeting criteria for SMD (Adleman et al. 2011). In this task, two stimuli, A and B, are presented. Through trial and error, participants learn that selecting A but not B results in a reward. Without warning, the stimulus-reinforcement relationship reverses, such that B but not A is the choice that results in a reward. While completing this task, children with SMD made more errors and showed reduced caudate and inferior frontal gyrus activity – brain regions associated with representation of context, contingency, and goals—during incorrect compared with correct trials (Adleman et al. 2011). The inability to learn from shifting reward contingency cues may be one mechanism through which reward-processing abnormalities result in an increased likelihood of blocked goal attainment and feelings of frustration.

Other studies have examined neural responses to reward within the context of frustration using a rigged affective Posner task. These studies found that SMD was associated with aberrant patterns of neural activation in response to negative feedback (Rich et al., 2011; Deveney et al. 2013). For example, Deveney and colleagues (2013) found that SMD was associated with reduced striatal activation to negative relative to positive feedback, suggesting that children with SMD experience frustrating negative feedback as more unexpected and aversive. However, in all of the aforementioned studies, it is unclear the degree to which symptoms of hyperarousal, which are characteristic of SMD, but not DMDD, influence these patterns of findings. Additional research is, therefore, needed to better understand the pathophysiology of DMDD and reward processing. Altered reward functioning is apparent in multiple psychiatric disorders, including depressive (Russo and Nestler 2013), bipolar (Nusslock et al. 2012), substance use (Koob and Volkow 2010), and, possibly, anxiety (Guyer et al. 2012) disorders, and may contribute to multiple behavioral, social, and emotional outcomes (Forbes and Goodman 2014). Identifying longitudinal associations between DMDD symptoms in early childhood and reward-processing disruptions in preadolescence may shed light on the processes linking DMDD to the development of other forms of psychopathology and adverse functional outcomes in adolescence and adulthood.

Event-related potentials (ERPs) derived from electroencephalography (EEG) can assess brain processes related to reward sensitivity across development in a reliable and cost-efficient manner (Nelson and McCleery 2008). The feedback negativity (FN) is an ERP component peaking $\sim$300 ms after feedback and observable over frontocentral recording sites, which is elicited by monetary gain compared with loss. Recent evidence conceptualizes the FN as two separate but temporally comparable components: the reward positivity or RewP, a positivity in response to rewards; and the N200, a negativity in response to losses (Holroyd et al. 2008; Proudfit 2015). Whereas the N200 has been linked to activation in the anterior cingulate cortex, the RewP has been associated with increased activation in the ventral striatum and medial prefrontal cortex, key reward-related brain regions (Carlson et al. 2011). Furthermore, the RewP has been used to reliably measure reward sensitivity and approach-related affect in children (Bress et al. 2012; Kujawa et al. 2015) and adults (Foti et al. 2014; Liu et al. 2014).

In the current study, our primary goal was to evaluate the relationship between preschool DMDD symptoms and later reward processing. DMDD cannot be diagnosed according to the DSM-5 until age 6. However, we previously reported data supporting the clinical significance and predictive validity of chronic irritability characteristic of DMDD in children as young as 3 years old (Dougherty et al. 2013, 2015). In this report, we aimed further to elucidate the predictive validity of very early manifestations of DMDD on a neural level. Although our initial assessment predated the definition of DMDD, we retrospectively applied DSM-5 DMDD criteria to a structured psychiatric interview to assess DMDD in a large sample of 3-year-old children. Approximately 6 years later, children completed a monetary reward task while ERPs were recorded. Given evidence that categorical diagnoses of DMDD do not capture the full range of youth whose irritability is significant and impairing (Deveney et al. 2014) and paralleling the National Institute of Mental Health (NIMH) Research Domain Criteria position that dimensional approaches to psychopathology are better suited for detecting brain–behavior relationships (Bebko et al., 2014), we used a dimensional measure of DMDD. Finally, to demonstrate that the longitudinal relationship between preschool DMDD symptoms and preadolescent reward processing was not better accounted for by other psychopathology, we controlled for lifetime symptoms of anxiety, depression, attention-deficit/ hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), and conduct disorder (CD) assessed in preadolescence.

Methods

Participants

Participants were part of a larger prospective study of the role of temperament in risk for psychopathology (see Olino et al. 2010). A total of 559 families with 3-year-old children were recruited through a commercial mailing list. Families with children with no significant medical condition or developmental disability living with at least one biological parent were eligible. Only one child per family was included. Of those families, 541 provided diagnostic information about the child. When the child was 9 years of age, 425 families returned for a laboratory visit, at which time the reward task was administered. There were no significant differences between families who did and did not participate on demographic variables. Fifty-one participants were excluded because of poor EEG quality, and data from one participant was lost through a technical error. Therefore, this report's final sample included 373 children (166 females): 94.9% white, 2.7% black or African American, and 2.4% Asian. With regard to ethnicity, 7.5% were of Hispanic or Latino origin. In 30.6% of families, one parent, and in 35.9% of families, two parents had a college degree. The Institutional Review Board approved all study procedures. Families were compensated for their time. After written informed consent from parents and oral assent from children were obtained, children began the EEG portion of the visit, including a 10 minute monetary reward task. Children and parents also completed a semistructured diagnostic interview to assess lifetime child psychopathology.

Measures

Preschool DMDD. At the age 3 assessment, parents (typically the mother) were assessed for their children's symptoms using the Preschool Age Psychiatric Assessment (PAPA) (Egger and Angold 2004). A 3-month primary period was used to enhance recall, but symptom onset dates were obtained for all criteria.

DMDD symptoms were defined based on DSM-5 criteria (American Psychiatric Association 2013) Although the PAPA was not designed to assess DMDD, it contained information needed to rate all DMDD criteria (see Copeland et al. 2013). Six items from the PAPA were used to assess DMDD: 1) Irritable mood (depression section), 2) feelings of anger/bad temper under minor provocation (depression section), 3) displays of anger under minor provocation (depression section), 4) feelings of frustration under minor provocation (depression section), 5) discrete episodes of temper without violence (ODD section), and 6) discrete episodes of excessive temper, manifested by shouting, crying, or stamping, and/or involving violence/damage (ODD section). Items were rated for intensity, frequency, and duration. If the child was prone to feelings of anger, irritability, or low frustration tolerance more days than not (i.e., >45 times in the past 3 months), those items were coded as present. Items querying temper outbursts were coded as present if they occurred at least three times per week (i.e., >36 times in the past 3 months). The total DMDD scale consisted of the sum of symptoms coded as present according to the frequency criteria described. The Cronbach α coefficient of internal consistency for the DMDD scale was 0.75.

Lifetime child psychopathology. At the age 9 assessment, one parent (generally the mother) and the child were interviewed using the *Diagnostic and Statistical Manual of Mental Disorders,* 4th ed. (DSM-IV) version of the Schedule of Affective Disorders and Schizophrenia for School-Age Children - Present and Lifetime (K-SADS-PL) (American Psychiatric Association 1994; Birmaher et al. 2009). Advanced doctoral students in clinical psychology and a masters-level clinician administered the K-SADS first to the parent and then to the child. Further information was then obtained to reconcile discrepancies. Summary ratings for each symptom during the worst lifetime episode of the corresponding form of psychopathology were derived based on the combination of parent and child reports. Lifetime symptoms of depressive disorders ($\alpha = 0.91$), anxiety disorders ($\alpha = 0.82$), ADHD ($\alpha = 0.86$), ODD ($\alpha = 0.89$), and CD ($\alpha = 0.65$) were rated on a three point scale (0 = Not present, 1 = Subthreshold, 2 = Threshold) and these items were summed to create dimensional scores that were used as covariates in the current analyses. Administration of the K-SADS was supervised in a group format by an experienced child psychiatrist and licensed clinical psychologist. To assess interrater reliability, a second rater independently derived ratings from videotapes for 74 participants. Intraclass correlations for dimensional lifetime psychopathology symptom scores ranged from 0.86 to 0.97.

Reward task. At the age 9 assessment, the reward task was conducted. The task was administered using Presentation software (Neurobehavioral Systems) similar to the version used in previous studies (Foti and Hajcak 2009). Participants were instructed to click either the left or right mouse button when presented with images of two doors, to guess which hid a monetary prize. They were told they could win $0.50 or lose $0.25 on each trial and win up to $5.00 total, which would be given to them upon task completion. Given that losses are weighted more heavily than gains (Tversky and Kahneman, 1992), these values were selected to equalize the subjective value of outcomes. At the beginning of each trial, participants were presented with images of two doors, which remained on the screen until the participant responded. Next, a fixation mark (+) appeared for 1000 ms, and feedback was presented for 2000 ms. A win was indicated by a green ''↑,'' and a loss, by a red ''↓.'' A fixation mark appeared for 1500 ms, followed by the message ''Click for the next round'' which remained on the screen until the participant responded and the next trial began. Across the task, 30 win and 30 loss trials were presented in a random order.

EEG data acquisition and processing. EEG was recorded using a 34 channel Biosemi system based on the 10/20 system (32 channel cap with Iz and FCz added). Electrooculogram and mastoid activity were also recorded. During acquisition, the common-mode sense and the driven right leg electrodes formed the ground electrode. The data were digitized at 24 bit resolution with a least significant bit value of 31.25 nV and a sampling rate of 1024 Hz, using a low-pass fifth-order sinc filter with −3 dB cutoff points at 208 Hz. Off-line analysis was performed using Brain Vision Analyzer (Version 2.0.4; GmbH; Munich, Germany; Brain Products). Data were converted to an average mastoid reference, band-pass filtered from 0.1 to 30 Hz, segmented for each trial 200 ms before feedback onset and continuing for 1000 ms after onset. The EEG was corrected for eye blinks (Gratton et al. 1983). Artifact rejection was completed using semiautomated procedures and the following criteria: A voltage step >50 μV between sample points, a voltage difference of 300 μV within a trial, and a voltage difference of <0.50μV within 100 ms intervals. Visual inspection was used to remove residual artifacts due to eye movement, muscle activity, linear drift, and artifacts related to electronics. After artifact rejection, participants, on average, were left with 29 trials for each condition. Participants with fewer than 20 valid trials in either condition were excluded from analyses. Data were baseline corrected using the average activity in the 200 ms interval prior to feedback.

ERPs were separately averaged across win and loss trials. The RewP and the N200 were quantified as the mean amplitude from 275 to 375 ms following win and loss feedback, respectively, and were pooled across FCz and Cz, which is consistent with previous research (Bress et al. 2012, 2013) and where the difference between gains and losses were maximal (see Fig. 1). In order to isolate the variance unique to ERPs in response to win trials and loss trials, we used residuals that reflected the difference between an individual's observed response to the outcome of interest and what would be predicted from an individual's response to the alternate outcome. These residuals were independent from the average response to the alternate outcome, but correlated with the average response to the outcome of interest. In the present study, we conducted two regressions to calculate residuals – one with the N200 as the independent variable and the RewP as the dependent variable (i.e., the RewP residual), and the other with the RewP as the dependent variable and the N200 as the dependent variable (i.e., the N200 residual).[1] A more positive RewP and a more negative N200 indicate greater sensitivity or an enhanced response to monetary rewards and losses, respectively.

Data Analysis

To evaluate the relationship between preschool symptoms of DMDD and later neural response to monetary gains and losses, we conducted multiple regression analyses. Separate models were run for the RewP residual and the N200 residual. All models included child demographics (gender and age at the time of the ERP assessment); age 3 DMDD symptoms; and lifetime symptoms of depression, anxiety, ADHD, ODD, and CD as covariates.

[1]Analyses using the ΔFN, which reflects the difference in mean amplitude on loss relative to gain trials, yielded virtually identical results as those using the RewP.

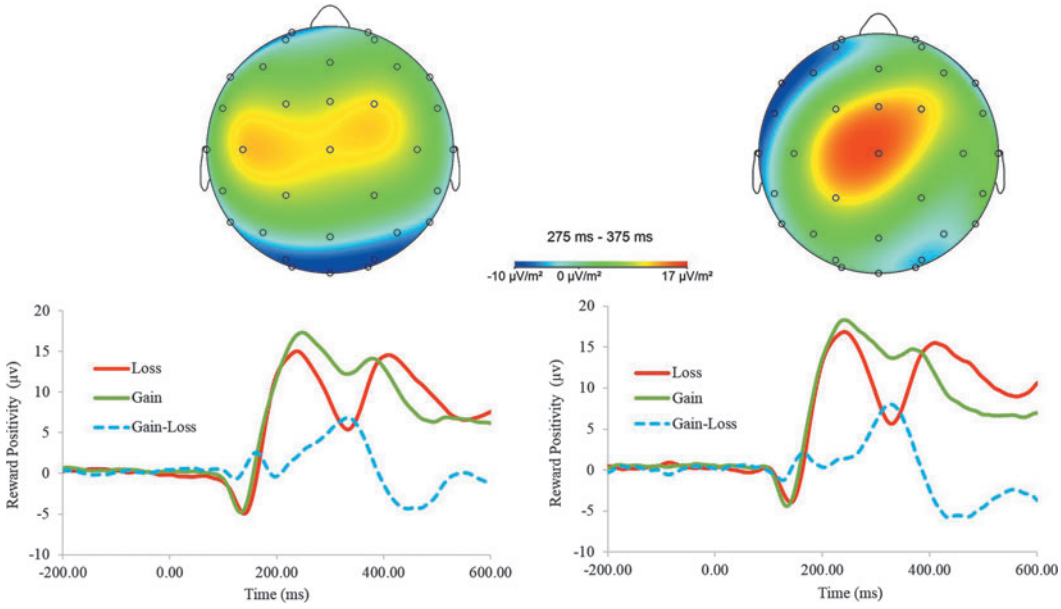

FIG. 1. Event-related potentials (ERPs) at FCz/Cz following feedback (bottom) and the scalp distribution (top) depicting the gain–loss difference 275–375 ms after feedback for children with low levels of disruptive mood dysregulation disorder (DMDD) symptoms (left) and high levels of DMDD symptoms (right) based on a median split. No children in the low group had any clinically significant symptoms of DMDD, whereas all children in the high group had at least one symptom. A color version of this figure is available in the online article at www.liebertpub.com/jcap

Results

Table 1 presents the descriptive statistics and bivariate correlations of the study variables. As expected, lifetime symptoms of psychopathology exhibited low-moderate intercorrelations, with the exception of CD and ODD with anxiety, and CD with depression. Greater DMDD symptoms at age 3 were associated with male gender and a higher number of lifetime symptoms of anxiety, ADHD, and ODD, which is consistent with previous work examining associations between preschool persistent irritability and later psychopathology in middle-late childhood (Dougherty et al. 2015). An enhanced, or more positive, RewP was associated with male gender and increased age 3 DMDD symptoms (see Fig. 1). There was no association between age 3 DMDD symptoms and the N200 to loss. An enhanced (i.e., more negative) N200 to monetary loss was related to male gender and greater lifetime depression symptoms.

Table 2 shows longitudinal associations between symptoms of DMDD at age 3 and the RewP and N200 at age 9, after controlling for child demographics and lifetime symptoms of depression, anxiety, ADHD, ODD, and CD. Symptoms of DMDD at age 3 and male gender significantly predicted an enhanced RewP in response to monetary gains at age 9. Additionally, whereas lifetime depression symptoms were positively associated with a greater RewP, greater lifetime symptoms of ODD were associated with reduced or more blunted reactivity in response to monetary gains.[2] Male gender and lifetime depression symptoms also predicted an enhanced or more negative N200 in response to monetary losses. Age 3 DMDD symptoms did not predict the N200, suggesting that the association between preschool DMDD and the RewP was specific to monetary gains.

Discussion

The current study examined whether preschool DMDD symptoms predicted children's ERP responses to monetary rewards (i.e., the RewP) and losses (i.e., the N200) in preadolescence. Results suggested that DMDD symptoms at age 3 predicted ERP responses to monetary gains 6 years later. Children who are reported by their parents to exhibit more clinically significant symptoms of preschool DMDD showed a more positive or enhanced RewP to monetary gains. Importantly, the DMDD–RewP relationship was independent of demographics or lifetime history of symptoms of depression, any anxiety disorder, ADHD, ODD, or CD. Moreover, preschool DMDD did not predict the N200 to losses.

Chronic irritability symptoms have previously been linked to abnormalities in reward processing on neuroimaging and behavioral measures (Adleman et al. 2011; Rich et al. 2011; Deveney et al. 2013). However, to our knowledge this is the first study to use a dimensional measure of DMDD, while controlling for other symptom dimensions, to examine its *unique* association with reward processing. Importantly, the current results demonstrate that early-emerging symptoms of DMDD predict *enhanced* neural sensitivity to reward in preadolescence, despite enormous developmental changes in both biological and socioemotional systems (Ernst et al. 2009; Giedd and Rapoport 2010)

The RewP and N200 are posited to reflect activity of a reinforcement learning system that is used to adjust subsequent behavior, such that a positive dopamine signal is elicited when an event is better than predicted (i.e., the RewP), and a negative dopamine signal is elicited when an event is worse than expected (i.e.,

[2]To demonstrate that the regression coefficients of lifetime ODD and age 3 DMDD significantly differ, we used the procedures outlined by Efron and Tibshirani (1998): We standardized all variables using Fisher Z transform and used a bias-corrected accelerated bootstrap procedure to test the significance of the effects. Unstandardized effects were then computed for each of 1000 bootstrapped samples, and the 95% confidence interval was computed by determining the effects at the 2.5th and 97.5th percentiles. The bootstrapped unstandardized effects of lifetime depression, lifetime ODD, and age 3 DMDD were 0.11, –0.12, and 0.15, and the 95% confidence intervals were from 0.04 to 0.22, from –0.21 to –0.02, and from 0.05 to 0.25.

TABLE 1. DESCRIPTIVE STATISTICS AND BIVARIATE ASSOCIATIONS BETWEEN VARIABLES

	1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*
1. Gender (female)	—	−0.02	−0.10*	−0.02	−0.04	−0.26**	−0.12*	−0.08	−0.20**	0.15**
2. Age		—	−0.02	−0.02	0.04	0.03	−0.03	−0.02	0.01	0.06
3. Age 3 DMDD			—	−0.03	0.21**	0.20**	0.44**	0.03	0.11*	−0.08
4. Age 9 lifetime depression				—	0.28**	0.12*	0.22**	0.01	0.08	−0.10*
5. Age 9 lifetime anxiety					—	0.17**	0.06	0.05	0.05	0.00
6. Age 9 lifetime ADHD						—	0.31**	0.18**	0.04	0.00
7. Age 9 lifetime ODD							—	0.13**	−0.01	−0.08
8. Age 9 lifetime CD								—	0.06	−0.01
9. RewP									—	−0.70**
10. N200										—
	Mean(SD)	9.20(0.40)	0.70(1.28)	0.94(3.10)	4.80(3.10)	4.78(3.10)	1.16(3.10)	0.04(3.10)	0.02(6.97)	−0.02(6.83)
	Range	8.75–10.92	0–6	0–34	0–45	0–34	0–15	0–3	−20.31–19.15	−19.86–18.46

*$p \leq 0.05$, **$p < 0.01$.
DMDD, disruptive mood dysregulation disorder; ADHD, attention-deficit/hyperactivity disorder; ODD, oppositional defiant disorder; CD, conduct disorder; RewP, reward positivity.

TABLE 2. MULTIPLE REGRESSION ANALYSES REGRESSING PRESCHOOL DMDD AND LIFETIME SYMPTOMS OF PSYCHOPATHOLOGY ON THE REWP AND THE N200

	b(SE)	*β*
	RewP	
Gender (Female)	−1.37(0.37)	−0.20***
Age (Years)	0.24(0.89)	0.01
Age 3 DMDD	0.79(0.32)	0.14*
Age 9 lifetime depression	0.25(0.12)	0.11*
Age 9 lifetime anxiety	−0.01(0.06)	−0.01
Age 9 lifetime ADHD	−0.02(0.04)	−0.03
Age 9 lifetime ODD	−0.32(0.16)	−0.12*
Age 9 lifetime CD	1.38(1.29)	0.06
	$F(8,372) = 3.23$**, $R^2 = 0.07$	
	N200	
Gender (Female)	1.13(0.37)	0.17***
Age (Years)	0.87(0.87)	0.05
Age 3 DMDD	−0.37(0.31)	−0.07
Age 9 lifetime depression	−0.26(0.12)	−0.12*
Age 9 lifetime anxiety	0.04(0.06)	0.04
Age 9 lifetime ADHD	0.06(0.04)	0.08
Age 9 lifetime ODD	−0.07(0.16)	−0.03
Age 9 lifetime CD	−0.20(1.27)	−0.01
	$F(8,372) = 2.36$* $R^2 = 0.05$	

*$p \leq 0.05$, **$p < 0.01$, ***$p < 0.001$.
DMDD, disruptive mood dysregulation disorder; ADHD, attention-deficit/hyperactivity disorder; ODD, oppositional defiant disorder; CD, conduct disorder; RewP, reward positivity.

the N200) (e.g., Holroyd et al. 2008). From this perspective, our finding that symptoms of DMDD were prospectively associated with an enhanced RewP in response to monetary reward is inconsistent with evidence suggesting that chronic irritability is associated with impaired reward learning (Adleman et al., 2011). However, there is emerging evidence in both adults (Cavanagh 2015) and children (Hämmerer et al. 2010) to suggest that the RewP is specific to surprising rewarding events and may not be directly associated with behavioral adjustments. Rather, the RewP may encode and classify whether an outcome is beneficial to a predefined goal (Hämmerer et al. 2010). Speculatively, children with early emerging symptoms of DMDD may be hypersensitive to reward and that hypersensitivity may lead to exaggerated stimulus-response learning, such that they create strong associations between a particular pattern of responses or thinking and rewarding environmental cues. These strong associations may enhance punctate task-set-like decision making that leads to perseveration and difficulties modulating behavior in response to changing reward contingencies. Consequently, there is an increased likelihood of goal blockage that ultimately results in feelings of frustration and anger. However, further research is needed to explore this possibility.

In addition to symptoms of early-emerging DMDD, we found that lifetime symptoms of both depression and ODD assessed at age 9 each predicted unique variance in the RewP. Whereas lifetime symptoms of depression showed the same pattern as symptoms of DMDD and were associated with an enhanced RewP, lifetime symptoms of ODD were associated with a blunted or less positive RewP. Despite the moderate correlation between symptoms of ODD at age 9 and DMDD symptoms at age 3 in the present study

and the high rates of their co-occurrence (Dougherty et al. 2013), their disparate patterns of neural reactivity in response to monetary gains is likely indicative of a suppression effect (Watson et al. 2013) and is consistent with evidence that ODD is composed of etiologically distinct dimensions (Stringaris and Goodman 2009). Specifically, the headstrong and/or hurtful behaviors, rather than irritability, that constitute ODD may be characterized by reward insensitivity. Although previous research has found that a reduced RewP is associated with depressive symptoms (Bress et al. 2012) and risk for depression (Kujawa et al. 2014), we found an opposite pattern of results. One possibility is that depressive symptoms in children may be associated with distinct patterns of reward reactivity compared with those seen later in development. Consistent with this, childhood depression has been associated with different neurobiological correlates than depression in adolescents (Kaufman et al. 2001). There is also evidence that a reduced RewP observed in depressive disorders may be more specific to anhedonia (Foti et al. 2014; Liu et al. 2014), which some have found to be less common in younger children (Ryan et al. 1987; Carlson and Kashani 1988). Our findings that both lifetime symptoms of depression and early-emerging DMDD are associated with an enhanced RewP raises the possibility that later-emerging symptoms of irritability characteristic of youth depression are also associated with enhanced reward sensitivity.

Although symptoms of lifetime depression were also associated with enhanced neural reactivity to negative feedback, we did not find an effect of DMDD on the N200. Previous fMRI and magnetoencephalography (MEG) research has found that SMD in 8–17-year-old youth is associated with aberrant neural responses that are specific to monetary loss during a frustration induction (Rich et al. 2011; Deveney et al. 2013). It is possible that discrepant findings are indicative of state versus trait influences as a result of task differences. Chronically irritable children may process rewards and losses differentially in the context of frustration. Given that prior studies included children meeting criteria for SMD, it is also possible that the ADHD symptoms of hyperarousal—which are also associated with reward abnormalities (von Rhein et al. 2015)— rather than irritability, may account for these differences. Alternatively, it is possible that these discrepancies are a result of developmental differences in irritability, such that abnormalities in reward processing associated with symptoms of irritability during late childhood and adolescence, compared with those in early childhood, are less specific to positive feedback. Future studies should examine associations between DMDD and reward-processing abnormalities across development, to explore these possibilities.

Despite its strengths, such as the large sample size and our dimensional construct of DMDD symptoms which, in comparison with a categorical approach, allowed us to capture a fuller range of youth whose irritability was significant and impairing, the current study is not without limitations. First, symptoms of DMDD were assessed using a parent-reported psychiatric interview that was not designed to assess DSM-5 DMDD. Secondly, our monetary reward task included only one class of reward and we did not collect ratings of the degree to which the children found the monetary incentives to be rewarding. It remains to be seen whether our findings generalize to nonmonetary stimuli or are indicative of neural processes associated with the subjective experience of reward receipt. Lastly, we did not examine the RewP in early childhood or current symptoms of DMDD; therefore, we are unable to establish the temporal sequence between these two variables.

Conclusions

The present study was the first to use a neural measure of reward to examine longitudinal associations between symptoms of DMDD during early childhood and reward sensitivity in preadolescence. Results suggest that symptoms of DMDD in preschoolers are prospectively associated with enhanced reward sensitivity later in development, independent of demographics or lifetime symptoms of depression, any anxiety disorder, ADHD, ODD, or CD. These findings underscore the predictive validity of preschool DMDD symptoms. They also point to the utility of using the RewP to identify reward-processing abnormalities in youth at risk for psychopathology and adverse functional outcomes in adolescence and adulthood.

Clinical Significance

The results of the current study indicate that early manifestations of DMDD in children as young as 3 years predict enhanced reward processing later in development. These results contribute to our understanding of the pathophysiology of DMDD and suggest the possible efficacy of interventions that seek to strengthen children's regulatory capacity to control reward reactivity or frustration due to non-reward for young children presenting with symptoms of DMDD.

Disclosures

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