Predictors of Later Psychopathology in Young Children with Disruptive Mood Dysregulation Disorder

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Abstract

Objective: This study aimed to identify childhood factors that predict later psychiatric problems in children with disruptive mood dysregulation disorder (DMDD).

Methods: The sample consisted of 36 6-year-old children who met criteria for DMDD who were followed up at 9 years of age. Child psychopathology was assessed at age 6 using the Preschool Age Psychiatric Assessment (PAPA) and at age 9 using the Kiddie-Schedule for Affective Disorders and Schizophrenia. We compared children with DMDD at age 6 who continued to have a psychiatric diagnosis at age 9 ($n = 17$) to children with DMDD at age 6 with no psychiatric diagnosis at age 9 ($n = 19$) across several age 6 predictors: child psychopathology, irritability and temperament, parenting, and maternal psychopathology. In addition, we examined whether children with DMDD at age 6 and no psychiatric diagnosis at age 9 continued to experience elevated psychiatric symptoms and impairment at age 9 compared to children with a non-DMDD diagnosis at age 6 and no psychiatric diagnosis at age 9 ($n = 44$) and children with no psychiatric diagnosis at age 6 or 9 ($n = 266$).

Results: The following variables predicted which children with DMDD at age 6 would have a psychiatric diagnosis at age 9: higher levels of externalizing symptoms, anger/frustration, headstrong/hurtful behaviors, functional impairment, and temperamental surgency and negative affect; lower levels of effortful control/executive functioning; and maternal depression. However, children with DMDD at age 6 and no psychiatric diagnosis at age 9 continued to demonstrate greater disruptive behavior disorder symptoms and impairment at age 9 compared to children with no psychiatric diagnosis at age 6 or 9.

Conclusions: These findings identify factors predicting later psychopathology in children with DMDD. In addition, we found that the subgroup of children with DMDD at age 6 but no psychiatric diagnosis at age 9 continued to evidence symptomatology and impairment 3 years later.

Keywords: course, disruptive mood dysregulation disorder, DMDD, predictors

Introduction

DISRUPTIVE MOOD DYSREGULATION DISORDER (DMDD), characterized by severe temper tantrums and persistently angry/irritable mood across contexts for at least 12 months, was added as a new diagnosis for children and adolescents in the fifth edition of the *Diagnostic and Statistical Manual for Mental Disorders* (DSM-5; American Psychiatric Association, 2013). Nevertheless, this inclusion has not been without controversy given the limited data on DMDD and concerns that DMDD would provide little clinical utility over and above co-occurring conditions (Copeland et al. 2013). Research has demonstrated that DMDD is relatively common in clinical samples (26.0%–31.0%) (Axelson et al. 2012; Margulies et al. 2012; Freeman et al. 2016) and less common in community samples (0.8%–8.2%) with rates decreasing across

childhood and adolescence (Copeland et al. 2013; Dougherty et al. 2014, 2016). Community-based studies have demonstrated that DMDD frequently co-occurs with another disorder; rates of co-occurrence ranged from 60.5% to 92.0%, with the highest rates of co-occurrence with depression and oppositional defiant disorder (ODD) (Copeland et al. 2013; Dougherty et al. 2014). Recent findings demonstrate that children with DMDD are at increased risk for psychopathology and functional impairment across childhood and into adulthood, poorer peer functioning and service use in childhood, and greater health, legal, and financial problems in adulthood (Copeland et al. 2014; Dougherty et al. 2016). However, no studies have examined which childhood factors predict persistent psychiatric problems in children with DMDD.

Using data from the Stony Brook Temperament Study (SBTS), a large longitudinal, community-based study, Dougherty et al. (2016)

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investigated associations of a DMDD diagnosis at age 6 years with psychiatric disorders, functional impairment, peer functioning, and service use at age 9 years. Although rates of DMDD decreased from age 6 (7.6%) to age 9 (1.3%), DMDD at age 6 was a significant predictor of a DMDD diagnosis at age 9 years. Moreover, children with DMDD at age 6 were at high risk for other forms of psychopathology and impairment 3 years later. Specifically, a diagnosis of DMDD at age 6 predicted current and lifetime depressive disorder and attention-deficit/hyperactivity disorder (ADHD), and poorer psychosocial functioning at age 9, even after accounting for comorbid disorders at age 6. Nevertheless, a subset of children with DMDD at age 6 did not continue to meet criteria for any psychiatric disorder at age 9.

The current report examined which factors at age 6 predict subsequent psychiatric disorders in children with DMDD. In our initial investigation examining DMDD in this sample of 6-year-old children (Dougherty et al. 2014), we found that several early childhood factors predicted a diagnosis of DMDD at age 6, including age 3 child psychopathology and functioning, child temperament, parenting, and maternal psychopathology. Thus, in this study, we examined whether these child- and/or parent-level factors at age 6 predicted which 6-year-olds would meet criteria for a psychiatric diagnosis at age 9 ($n=17$), and which would no longer meet criteria for any diagnosis at age 9 ($n=19$). In addition, we examined whether children with DMDD at age 6 and no psychiatric diagnosis at age 9 demonstrate greater psychiatric symptoms and impairment at age 9 than children with a non-DMDD diagnosis at age 6 and no psychiatric diagnosis at age 9 ($n=44$), and children with no psychiatric diagnosis at age 6 or 9 ($n=266$). We hypothesized that greater psychopathology, irritability, and impairment, temperamental emotional lability/reactivity, and environments characterized by problematic parenting and maternal psychopathology would predict later psychiatric problems in children with DMDD. We also hypothesized that children with DMDD at age 6 who were free of any psychiatric diagnosis at age 9 would continue to evidence subthreshold symptoms and impairment compared to children with no psychiatric diagnosis at ages 6 or 9, but would not differ from children with a non-DMDD diagnosis at age 6 and no psychiatric diagnosis at age 9.

Methods

Participants

The SBTS is a longitudinal study investigating early temperament and risk for psychopathology (Olino et al. 2010). We recruited 559 families with a 3-year-old child living within 20 miles of Stony Brook University. Eligible families, identified via a commercial mailing list, had a 3-year-old child with no significant medical or developmental disabilities, and at least one English-speaking biological parent. The sample has been described previously (Bufferd et al. 2011; Dougherty et al. 2016). The study was approved by the Stony Brook University Institutional Review Board. Informed consent was obtained from parents, and child assent was obtained at age 9.

Participants were assessed at ages 3, 6, and 9 years. At age 6, an additional 50 non-White minority children were recruited to increase the diversity of the sample. Advertisement flyers were placed throughout Stony Brook University's campus and in surrounding Long Island, NY communities with a high proportion of racial and ethnic minorities to recruit these additional children and families. As seen in Tables 1 and 2, the groups for this study did not significantly differ on child race (White vs. non-White). Findings on the age 3 predictors and concurrent correlates of DMDD at age 6

(Dougherty et al. 2014) and the age 9 outcomes of DMDD at age 6 (Dougherty et al. 2016) have been previously reported. At age 6, 516 parents were interviewed regarding their 6-year-old child ($M=6.10$, standard deviation [SD]=0.43 years), and 488 parents and children completed another diagnostic clinical interview at age 9 ($M=9.23$, $SD=0.42$ years). As detailed in Dougherty et al. (2016), 36 children met criteria for DMDD at age 6 and were reassessed at age 9. Of the 36 children, 17 (47.2%) children continued to meet criteria for at least one current psychiatric diagnosis at age 9 (DMDD $n=5$; any depressive disorder $n=1$; any anxiety disorder $n=6$; any ADHD $n=12$; ODD $n=7$), and 19 (52.8%) children did not meet criteria for a psychiatric diagnosis at age 9.

Age 6 assessment

Disruptive mood dysregulation disorder. Parents were interviewed regarding their child's psychopathology using the Preschool Age Psychiatric Assessment (PAPA) (Egger et al. 1999). Although the PAPA was not designed to assess DMDD, it contains information on the frequency and duration of children's irritability and temper tantrums during the past 3 months, which was used to derive a diagnosis of DMDD based on DSM-5 criteria (for a description of the PAPA items, see Copeland et al. 2013; Dougherty et al. 2014).

Child psychopathology and functioning. As described elsewhere (Bufferd et al. 2012), DSM-IV-TR disorders in the previous 3 months were assessed with the PAPA, including the following: any depressive disorder (major depressive disorder [MDD] using modified criteria for preschoolers [Luby et al. 2003], dysthymia, or depression-not otherwise specified [NOS]); any anxiety disorder (specific phobia, separation anxiety, social phobia, generalized anxiety disorder [GAD], agoraphobia, and selective mutism); ADHD; and ODD. Dimensional symptom scales for depression ($\alpha=0.74$), anxiety ($\alpha=0.85$), ADHD ($\alpha=0.88$), and ODD ($\alpha=0.79$) were created by summing items in each diagnostic category. We created total internalizing ($\alpha=0.86$) and externalizing ($\alpha=0.89$) symptom scales by summing the depression and anxiety symptom scales, and the ADHD and ODD symptom scales, respectively. Interrater reliability for all diagnoses (kappas=0.64–0.89) and symptom scales (intraclass correlation coefficient [ICC]=0.71–0.97) was good.

The PAPA interviewer also completed the Children's Global Assessment Scale (CGAS) (Shaffer et al. 1983), a measure of children's overall functioning with scores ranging from 0 (worst) to 100 (superior) (ICC=0.86). Impairment was also rated across several domains (parental, sibling, and peer relationships, household and recreational activities, school life) on 5-point scales ranging from 0 (none) to 4 (severe) and summed for a total impairment score (ICC=0.84).

Child executive functioning. Children participated in three tasks designed to assess facets of executive functioning: working memory, cognitive inhibitory control, and attention shifting. To assess working memory, children completed a Color Span task in which they were shown a series of colored triangles with each trial increasing in the number of colored triangles presented. Participants were asked in Part A to name the color of each triangle in the order they were presented and in Part B to name the color of each triangle in the reverse order in which they were presented. Children had to recall all items in at least one out of every two trials to move onto the next level. Separate scores were calculated for Parts A and

TABLE 1. COMPARISONS BETWEEN CHILDREN WHO MET CRITERIA FOR DISRUPTIVE MOOD DYSREGULATION DISORDER AT AGE 6 AND ANY PSYCHIATRIC DIAGNOSIS AT AGE 9 AND CHILDREN WHO MET CRITERIA FOR DISRUPTIVE MOOD DYSREGULATION DISORDER AT AGE 6 AND NO PSYCHIATRIC DIAGNOSIS AT AGE 9

Age 6 variable	Any diagnosis at age 9 (n=17)	No diagnosis at age 9 (n=19)	Odds ratio	95% CI
Demographic characteristics				
Child mean age in years (SD)	6.14 (0.55)	6.25 (0.36)	0.55	0.12–2.52
Child female sex, <i>n</i> (%)	6 (35.3)	10 (52.6)	0.49	0.13–1.88
At least one parent with a 4-year college degree, <i>n</i> (%)	11 (64.7)	10 (52.6)	1.65	0.43–6.31
Race White, <i>n</i> (%)	16 (94.1)	17 (89.5)	1.89	0.16–22.83
Child psychiatric diagnoses, <i>n</i> (%)				
Current Depressive Disorder	4 (23.5)	1 (5.3)	5.54	0.55–55.49
Current Anxiety Disorder	2 (11.8)	2 (10.5)	1.13	0.14–9.07
Current ADHD	3 (17.36)	1 (5.3)	3.86	0.36–41.20
Current ODD	11 (64.7)	9 (47.4)	2.04	0.53–7.79
Mean total diagnoses at age 6 (SD)	1.18 (1.01)	0.68 (0.75)	1.90	0.87–4.16
Mean child psychopathology and functioning (SD)				
PAPA Internalizing Symptoms	22.35 (11.81)	15.53 (7.22)	1.07 ^a	1.00–1.18
PAPA Externalizing Symptoms	16.94 (12.16)	8.42 (5.27)	1.14 ^b	1.02–1.28
Children's Global Assessment Scale	59.24 (10.70)	68.47 (10.41)	0.92 ^b	0.86–0.99
Child Impairment Ratings	10.82 (3.38)	7.95 (3.37)	1.27 ^b	1.02–1.57
Mean child irritability (SD)				
Frequency of tantrums (per week)	7.47 (9.12)	2.43 (3.25)	1.14 ^a	1.00–1.30
PAPA Chronic Irritability Scale	3.65 (1.27)	3.26 (1.05)	1.35	0.75–2.44
Mother-reported CBCL Irritability	2.44 (1.26)	1.76 (1.71)	1.36	0.84–2.19
Mother-reported CBCL Headstrong/Hurtful	3.93 (2.17)	2.24 (1.29)	1.67 ^b	1.08–2.59
Mother-reported CBQ Anger/Frustration Subscale	5.28 (0.74)	4.59 (0.75)	3.98 ^b	1.19–13.37
Mean mother-reported child temperament (SD)				
CBQ surgency	5.36 (0.66)	4.84 (0.55)	4.54 ^b	1.16–17.85
CBQ negative affect	4.18 (0.60)	3.85 (0.61)	2.61	0.76–9.05
CBQ effortful control	4.58 (0.49)	5.00 (0.55)	0.21 ^b	0.05–0.93
Mean executive functioning (SD)				
Executive functioning	−0.15 (0.53)	0.19 (0.30)	0.21 ^b	0.05–0.99
Mean parent and child observed behavior (SD)				
Maternal hostility	1.22 (0.34)	1.18 (0.40)	1.40	0.21–9.19
Maternal support	3.91 (0.48)	4.13 (0.57)	0.43	0.11–1.69
Child negative affect	1.53 (0.40)	1.23 (0.38)	7.15 ^b	1.03–49.54
Child positive affect	2.51 (0.68)	3.00 (0.77)	0.39 ^a	0.14–1.07
Maternal psychopathology, <i>n</i> (%)				
Maternal lifetime depressive disorder	9 (52.9)	3 (15.8)	6.43 ^b	1.32–31.37
Maternal lifetime anxiety disorder	6 (35.3)	5 (26.3)	1.56	0.37–6.62
Maternal lifetime substance use disorder	2 (11.8)	5 (26.3)	0.37	0.06–2.26

^a*p* < 0.10; ^b*p* < 0.05.

ADHD, attention-deficit/hyperactivity disorder; CBCL, Child Behavior Checklist; CBQ, Child Behavior Questionnaire; CI, confidence interval; DMDD, disruptive mood dysregulation disorder; ODD, oppositional defiant disorder; PAPA, Preschool Age Psychiatric Assessment; SD, standard deviation.

B by summing the number of correct trials. To assess cognitive inhibitory control, children completed the Sun-Moon Stroop Task, during which children were instructed to say “Sun” in response to the moon picture and “Moon” in response to the sun picture. The number of correct trials was summed to create a total score. To assess attention shifting, children completed the Trail Making task, during which they were asked to connect numbers followed by letters in the correct order as quickly as possible. The number of errors was summed to create a total score. All scores (Color Span A, Color Span B, Sun-Moon, and Trails total errors [reversed-scored]) were z-scored and averaged to create a composite measure of executive functioning. Higher scores indicate better executive functioning.

Child temperament. Mothers completed the Child Behavior Questionnaire (CBQ) (Rothbart et al. 2001), a 194-item parent-

report measure of temperament for 3- to 7-year-old children, which assesses three temperament dimensions: surgency (e.g., high-intensity pleasure, impulsivity; 52 items, $\alpha=0.79$); negative affectivity (e.g., anger/frustration, sadness; 49 items, $\alpha=0.76$); and effortful control (e.g., inhibitory control, attentional focusing; 40 items, $\alpha=0.89$).

Observed parent and child behavior. Parent-child dyads participated in a parent-child interaction task using a modified version of the Teaching Tasks battery (Egeland et al. 1995). Interactions were videotaped and coded for maternal hostility and support on separate 5-point scales and child positive and negative affect on separate 3-point scales; ratings were averaged across tasks. Interrater reliability and internal consistencies were good for all scales (ICC = 0.74–0.86; $\alpha=0.66$ –0.86).

TABLE 2. COMPARISONS BETWEEN CHILDREN WITH A DISRUPTIVE MOOD DYSREGULATION DISORDER DIAGNOSIS AT AGE 6 AND NO PSYCHIATRIC DIAGNOSIS AT AGE 9, CHILDREN WITH A NON-DISRUPTIVE MOOD DYSREGULATION DISORDER DIAGNOSIS AT AGE 6 AND NO PSYCHIATRIC AT AGE 9, AND CHILDREN WITH NO PSYCHIATRIC DIAGNOSES AT AGES 6 OR 9

Age 9 variable	Age 6 DMDD and no age 9 diagnosis (n = 19)	Age 6 non-DMDD diagnosis and no age 9 diagnosis (n = 44)	No age 6 diagnosis and no age 9 diagnosis (n = 266)	Group comparison statistic
Demographic characteristics				
Child mean age in years (SD)	9.33 (0.49)	9.18 (0.42)	9.18 (0.36)	$F(2, 326) = 1.36$
Child female sex, <i>n</i> (%)	10 (52.6)	22 (50.0)	130 (48.9)	$\chi^2(2) = 0.112$
At least one parent with a 4-year college degree, <i>n</i> (%)	10 (52.6)	26 (59.1)	188 (70.7)	$\chi^2(2) = 4.92^a$
Race White, <i>n</i> (%)	17 (89.5)	40 (90.9)	240 (90.2)	$\chi^2(2) = 0.035$
Mean child psychopathology and functioning (SD)				
K-SADS DMDD Symptoms	1.05 (1.65) ^e	0.52 (1.15) ^e	0.23 (0.88) ^e	$F(2, 36.51)^d = 3.37^b$
K-SADS Depression Symptoms	0.74 (1.73)	0.43 (1.22)	0.74 (1.73)	$F(2, 37.28)^d = 0.85$
K-SADS Anxiety Symptoms	3.32 (3.46) ^{e,f}	3.45 (4.03) ^e	1.82 (2.79) ^f	$F(2, 37.45)^d = 4.71^b$
K-SADS ADHD Symptoms	3.26 (4.79)	2.86 (5.82)	1.70 (4.16)	$F(2, 37.88)^d = 1.63$
K-SADS DBD Symptoms	2.21 (2.72) ^e	0.98 (1.56) ^{e,f}	0.49 (1.66) ^f	$F(2, 38.15)^d = 5.08^b$
Children's Global Assessment Scale	75.79 (7.86) ^e	80.18 (8.83) ^{e,f}	83.16 (8.64) ^f	$F(2, 325) = 8.06^c$

Non-DMDD diagnoses include any depressive disorder, any anxiety disorder, ADHD, or ODD.

^a $p < 0.10$; ^b $p < 0.05$; ^c $p < 0.001$.

^dWelch's adjusted *F* value reported.

^{e,f}Means with differing superscript letters ^{e,f} within rows are significantly different at the $p < 0.05$ based on Games-Howell *post hoc* comparisons for Welch's adjusted *F*-test or Tukey *post hoc* comparisons for ANOVA *F*-test.

ADHD, attention-deficit/hyperactivity disorder; ANOVA, analysis of variance; DBDs, disruptive behavior disorders; DMDD, disruptive mood dysregulation disorder; K-SADS, Kiddie-Schedule for Affective Disorders and Schizophrenia; ODD, oppositional defiant disorder; SD, standard deviation.

Child irritability. Several characteristics of child irritability were assessed using an interview-based measure and maternal report. First, as described elsewhere (Dougherty et al. 2013), a 7-item scale derived from the PAPA was used to assess chronic irritability ($\alpha = 0.73$). In addition, the PAPA interviewer assessed the average number of temper tantrums per week over the past 3 months. Third, mother reports on the Child Behavior Checklist/6–18 (CBCL) (Achenbach and Rescorla 2001) were used to score the child irritable mood (3 items, $\alpha = 0.69$) and headstrong/hurtful behavior (6 items, $\alpha = 0.71$) scales (for a description, see Roberson-Nay et al. 2015). Finally, we also examined the CBQ anger/frustration subscale (13 items, $\alpha = 0.82$).

Lifetime maternal psychopathology. Children's biological mothers were interviewed using the nonpatient Structured Clinical Interview for DSM-IV (SCID) (First et al. 1996). Kappas for inter-rater reliability of lifetime diagnoses were 0.93 for any depressive disorder, 0.91 for anxiety disorder, and 1.00 for substance use disorder.

Age 9 assessment

Child psychiatric disorders. Parents and their children were interviewed using the Kiddie-Schedule for Affective Disorders and Schizophrenia—Present and Lifetime (K-SADS-PL; Axelson et al. 2009). As described elsewhere (Dougherty et al. 2016), current and lifetime diagnoses were derived for the following DSM-IV-TR psychiatric disorders: any depressive disorder (MDD, dysthymia, and depressive disorder-NOS); any anxiety disorder (specific phobia, social phobia, separation anxiety, GAD, panic, agoraphobia, obsessive compulsive, post-traumatic stress, acute stress, and anxiety disorder-NOS); any ADHD (ADHD-inattentive, hyperactivity or combined type, ADHD-NOS); and any disruptive behavior

disorder (DBD; ODD, conduct disorder, and DBD-NOS). DMDD diagnoses were derived using the Axelson et al. (2012) operationalization for the K-SADS (Dougherty et al. 2016). Current symptoms were rated on 3-point scale (0 = not present; 1 = sub-threshold; 2 = threshold) and were summed to create dimensional scores for each diagnostic category ($\alpha = 0.73$ – 0.86). Inter-rater reliability for diagnoses (kappas = 0.58 – 0.85) and symptom scales (ICCs = 0.77 – 0.97) was acceptable. K-SADS interviewers also rated child CGAS scores (ICC = 0.56).

Data analyses

Binary logistic regression analyses were conducted to identify which factors at age 6 distinguished children who met criteria for DMDD at age 6 and any diagnosis at age 9 ($n = 17$) from children who met criteria for DMDD at age 6 but no diagnosis at age 9 ($n = 19$). Odds ratios (ORs) provide the effect size estimate. Separate models were run for each of the age 6 predictors. Next, a one-way between-subjects analysis of variance (ANOVA; for continuous variables) or a Pearson's chi-square test (for categorical variables) was used to compare children with DMDD at age 6 and no psychiatric diagnosis at age 9 ($n = 19$), children with a non-DMDD psychiatric diagnosis at age 6 (any depressive disorder, any anxiety disorder, any ADHD, and/or ODD) and no psychiatric diagnosis at age 9 ($n = 44$), and children with no psychiatric diagnosis at age 6 or 9 ($n = 266$) on age 9 demographic variables, psychiatric symptoms, and impairment. Welch's ANOVA test was conducted for all models for which the assumption of homogeneity of variance was violated (Levene's Test $p < 0.05$). For statistically significant ANOVA results, *post hoc* comparisons were conducted with the Tukey test (if Levene's Test $p > 0.05$) or the Games-Howell test (if Levene's Test $p < 0.05$).

Results

Age 6 predictors

Table 1 shows comparisons among children who met criteria for DMDD at age 6 and any psychiatric diagnosis at age 9 and children who met criteria for DMDD at age 6 but no psychiatric diagnosis at age 9. The two groups did not differ on child gender, age, race, or parental education. There were no significant differences on psychiatric diagnoses or number of psychiatric diagnoses at age 6. The following age 6 variables predicted which children with DMDD at age 6 would have a psychiatric diagnosis at age 9: greater PAPA externalizing symptoms and functional impairment, and lower CGAS scores; higher levels of CBCL headstrong/hurtful behavior, CBQ surgency and anger/frustration, and observed negative affect; lower levels of CBQ effortful and laboratory-based executive functioning; and a greater proportion of mothers with a lifetime history of depression.^{*,†}

To examine whether comorbidity at age 6 explained the greater likelihood of having a psychiatric diagnosis at age 9 among children with DMDD at age 6, we reran all age 6 predictors controlling for total number of psychiatric diagnoses at age 6. Significant differences persisted for CBQ anger/frustration (OR = 3.61, 95% confidence interval [CI] = 1.04–12.53, $p = 0.04$), CBCL headstrong/hurtful (OR = 1.60, 95% CI = 1.60–2.53, $p = 0.04$), observed negative affect (OR = 16.18, 95% CI = 1.27–105.97, $p = 0.03$), laboratory-based executive functioning (OR = 0.17, 95% CI = 0.03–0.92, $p = 0.04$), and maternal lifetime depression (OR = 7.29, 95% CI = 1.33–39.88, $p = 0.02$). The following predictors became trend level associations ($p < 0.10$): PAPA externalizing symptoms, CGAS scores, impairment, frequency of tantrums, CBQ surgency, and CBQ effortful control.

Finally, we examined whether children with DMDD at age 6 and no psychiatric diagnosis at age 9 continued to demonstrate psychiatric symptoms and impairment 3 years later. We compared children with DMDD at age 6 and no psychiatric diagnosis at age 9 ($n = 19$), children with a non-DMDD diagnosis at age 6 and no psychiatric diagnosis at age 9 ($n = 44$), and children with no psychiatric diagnosis at age 6 or 9 ($n = 266$) on age 9 demographic variables and psychiatric symptoms and functioning. As seen in Table 2, children with an age 6 DMDD diagnosis and no age 9 diagnosis had significantly greater age 9 DBD symptoms and lower CGAS scores compared to children with no age 6 or 9 psychiatric diagnosis (Games-Howell test $p = 0.035$ and Tukey test $p = 0.001$, respectively). In addition, children with an age 6 non-DMDD diagnosis and no age 9 diagnosis had significantly greater age 9 anxiety symptoms compared to children with no age 6 or 9 psychiatric diagnosis (Games-Howell test $p = 0.033$). Although the one-way Welch's ANOVA indicated significant differences between groups on age 9 DMDD symptoms, the Games-Howell *post*

hoc tests were not significant. Finally, no significant differences were observed between children with an age 6 DMDD diagnosis and no psychiatric diagnosis at age 9 and children with an age 6 non-DMDD diagnosis and no psychiatric diagnosis at age 9.

Discussion

This study provides the first data to identify early predictors of a poorer course for young children with DMDD. Compared to children with DMDD who no longer met criteria for a psychiatric disorder at age 9, children with DMDD at age 6 who continued to have a psychiatric diagnosis at age 9 evidenced higher levels of interviewer-rated externalizing symptoms and functional impairment, maternal-reported headstrong/hurtful behaviors, anger/frustration, and surgency, and observed negative affect; lower levels of maternal-reported effortful control and laboratory-based executive functioning; and were more likely to have a mother with a history of depression. These results largely persisted, at least at a trend level, after controlling for psychiatric comorbidity at age 6. Identifying early parent and child factors that predict a poorer course for children with DMDD can inform therapeutic interventions designed to improve long-term outcomes for these children.

In this study, 47.2% of children with DMDD at age 6 met criteria for a psychiatric disorder at age 9. Similarly, data from the Great Smoky Mountains Study demonstrated that 56.6% of children with DMDD met criteria for any psychiatric disorder in early adulthood (Copeland et al. 2014). These findings show that a significant proportion of youth with DMDD are at high risk for continued psychopathology, and we observed several notable deficits in emotional and behavioral regulation that predicted continued psychopathology. Specifically, higher levels of externalizing symptoms, functional impairment, surgency and negative affect, and lower levels of effortful control and executive functioning predicted continued psychopathology. These findings suggest that this high-risk group is characterized by significant emotional and behavioral lability/reactivity, along with deficits in cognitive and behavioral facets of executive functioning.

We also found that children with DMDD at age 6 and a psychiatric disorder 3 years later were rated higher by their mothers on the CBQ anger/frustration and the CBCL headstrong/hurtful scales, but no differences were observed on the interviewer-rated chronic irritability or the maternal-reported CBCL irritability scales. This may be due to the heterogeneity of the construct of irritability. For example, the high-risk group may be relatively elevated in anger/frustration but similar in other features of irritability (e.g., temper tantrums, irritable mood) at the time of the initial DMDD diagnosis, compared to youth with DMDD who were free of psychopathology 3 years later. It is also possible that existing measures do not adequately differentiate the features of irritability that distinguish problematic from typical behavior, especially in young children (Wakschlag et al. 2012; 2015). Alternatively, our analyses may have had insufficient power to detect more subtle differences in irritability between the two groups, particularly as a trend-level difference was observed for the frequency of tantrums. Furthermore, previous research has demonstrated that the headstrong and hurtful dimensions of ODD, which are distinct constructs from irritability but highly correlated, uniquely predict externalizing behavior problems and delinquency (Stringaris and Goodman 2009; Burke et al. 2010; Stringaris et al. 2012). Thus, the combination of high levels of anger/frustration and headstrong/hurtful behaviors may capture features of a more severe subgroup of children with DMDD. These features may evoke more negative or

^{*}In order to test whether children who met criteria for DMDD at age 6 and again at age 9 ("persistent/recurrent DMDD"; $n = 5$) demonstrated poorer functioning at age 6 compared to children with DMDD at age 6 and another psychiatric diagnosis at age 9 ("remitted DMDD"; $n = 12$), we compared the two groups on age 6 study variables, and no significant differences were observed.

[†]We found that age 6 ADHD symptoms (OR = 1.23, 95% CI = 1.03–1.48, $p = 0.02$) significantly predicted which children with DMDD at age 6 would have a psychiatric diagnosis at age 9. Age 6 anxiety symptoms (OR = 1.10, 95% CI = 0.99–1.22, $p = 0.08$) and age 6 depressive symptoms (OR = 1.28, 95% CI = 0.98–1.66, $p = 0.07$) were trend level predictors and age 6 ODD symptoms (OR = 1.20, 95% CI = 0.96–1.50, $p = 0.11$) were not significant. Nevertheless, these analyses may be limited by the potential restriction of range of symptoms and low power.

punitive responses from parents, teachers, and peers, which may, in turn, maintain continued psychiatric problems.

Although anger/frustration and headstrong/hurtful behaviors are both features of ODD, the ODD symptom scale at age 6 did not predict which children with DMDD would meet criteria for a psychiatric diagnosis 3 years later. These findings suggest that these distinct features of ODD provide unique information. Interestingly, there has been debate about whether irritability is sufficiently distinct from oppositional behavior to support the diagnosis of DMDD, and some findings suggest that irritability may be better conceptualized as a dimension within ODD that can be related to other forms of psychopathology (Burke et al. 2014; Lochman et al. 2015). Although our findings cannot resolve this debate, previous findings from our sample indicate that a DMDD diagnosis provides unique incremental validity over and above a diagnosis of ODD (and other DSM diagnoses) in predicting youths' functional impairment across a number of domains (Dougherty et al. 2014, 2016). Further research is needed to determine how best to conceptualize irritability in developmental psychopathology to inform our diagnostic nosology and better understand its phenomenology, course, and pathophysiology.

We also found that maternal depression history predicted poorer outcomes in children with DMDD. This finding is consistent with data demonstrating that maternal depression predicts a more severe course of irritability across childhood (Wiggins et al. 2014) and is a potent predictor of later psychopathology and functional impairment across childhood and into adulthood (e.g., Klein et al. 2005; Weissman et al. 2006, 2016; Matijasevich et al. 2015). Given evidence supporting links between offspring irritability and maternal depression (Dougherty et al. 2013) and genetic links between irritability and depression (Stringaris et al. 2012), it is plausible that familial, possibly genetic, factors are driving this increased risk in youth with DMDD, particularly as observed parenting did not differentiate the groups. Nevertheless, these findings do not rule on the effects of gene-environment correlations or interactions, which warrant further investigation.

Lastly, despite not meeting threshold for any psychiatric diagnosis at age 9, children with DMDD at age 6 demonstrated greater DBD symptoms and functional impairment at age 9 compared to children without any psychiatric diagnosis at age 6 or 9. In contrast, children with a non-DMDD diagnosis at age 6 and no diagnoses at age 9 exhibited greater anxiety symptoms at age 9 compared to children without any psychiatric diagnosis at age 6 or 9. No significant differences were observed between children with an age 6 DMDD diagnosis and no psychiatric diagnosis at age 9 and children with an age 6 non-DMDD diagnosis and no psychiatric diagnosis at age 9. Notably, however, only the children with an age 6 DMDD diagnosis had significantly greater impairment at age 9 compared to children with no psychiatric diagnosis at age 6 or 9. Consistent with our findings, Deveney et al. (2015) reported that youth with severe mood dysregulation (SMD), the condition from which the construct of DMDD was developed, continued to show clinically significant impairment at 2- and 4-year follow-ups despite not meeting criteria for SMD at follow-up. These data suggest that even when youth with DMDD no longer meet criteria for a psychiatric diagnosis, they are at greater risk for exhibiting subthreshold symptoms and impairment that may warrant clinical attention.

This study had notable strengths, including providing the first data on predictors of course of DMDD and a multi-method design. The study also had limitations. First, we had a small number of participants with DMDD, which may have led to range restriction and large CIs, and affected the power to detect significant longi-

tudinal effects. It is also important to acknowledge that even though the ORs are significant, the estimates are based on a small number of cases, and thus should be interpreted with caution and must be replicated in larger samples of children with DMDD. Second, we assessed child psychopathology at ages 6 and 9 using different measures, and their concordance is unknown. Third, DMDD diagnosis relied on psychiatric interviews that were not designed to assess DSM-5 DMDD. Fourth, the sample was largely white and middle class. Future research should extend this research to more diverse samples. Lastly, we examined a large number of predictors and did not correct for multiple testing. Given the paucity of research on predictors of the course of DMDD, we chose to take an exploratory approach and investigate a broad range of variables/measures that are commonly used in the literature examining chronic irritability and DMDD. We believe that our findings provide valuable preliminary data and hypotheses to be replicated in larger studies.

Conclusions

In summary, our findings provide insight into factors predicting later psychopathology in children with DMDD, including early indicators of emotional and behavioral lability/dysregulation and a maternal history of depression. These predictors may be useful in identifying children with DMDD who are at greater risk for poor long-term outcomes, and may provide targets for intervention. Moreover, even though some children with DMDD no longer met diagnostic threshold at follow-up, they may be experiencing symptoms and impairment that warrant clinical attention.

Clinical Significance

This study is the first to identify specific parent and child factors that predicted a poorer course for children with DMDD in childhood. Identifying parent and child factors that predict later psychopathology and impairment in children with DMDD can help inform the development of intervention programs designed to improve long-term outcomes for children with DMDD. Future work is needed to replicate and extend our findings with larger longitudinal samples of children with DMDD.

Disclosures

No competing financial interests exist.

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