Disruptive mood dysregulation disorder in offspring of parents with depression and bipolar disorder

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Background
It has been suggested that offspring of parents with bipolar disorder are at increased risk for disruptive mood dysregulation disorder (DMDD), but the specificity of this association has not been established.

Aims
We examined the specificity of DMDD to family history by comparing offspring of parents with (a) bipolar disorder, (b) major depressive disorder and (c) a control group with no mood disorders.

Method
We established lifetime diagnosis of DMDD using the Schedule for Affective Disorders and Schizophrenia for School Aged Children for DSM-5 in 180 youth aged 6–18 years, including 58 offspring of parents with bipolar disorder, 82 offspring of parents with major depressive disorder and 40 control offspring.

Results
Diagnostic criteria for DMDD were met in none of the offspring of parents with bipolar disorder, 6 of the offspring of parents with major depressive disorder and none of the control offspring. DMDD diagnosis was significantly associated with family history of major depressive disorder.

Conclusions
Our results suggest that DMDD is not specifically associated with a family history of bipolar disorder and may be associated with parental depression.

Declaration of interest
None.

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Disruptive mood dysregulation disorder and family history

Participants

The participants were youth aged 6–18 years who were assessed for DMDD while taking part in the Families Overcoming Risks Building Opportunities for Wellbeing (FORBOW) project.24 Offspring of parents with bipolar disorder and offspring of parents with major depressive disorder were enrolled through affected parents receiving in-patient and out-patient psychiatric services in Nova Scotia, Canada, where clinicians systematically enquire whether patients with major mood and psychotic disorders have biological children in the eligible age range. Participants were enrolled irrespective of whether any psychopathology was present in the offspring. Comparison offspring of parents without major mood disorders were enrolled through schools serving the geographic areas from which high-risk offspring were recruited. Inclusion criteria were availability of at least one biological parent for assessment and age 6–18 years, the recommended age range for DMDD diagnosis. Exclusion criteria were brain injury or severe intellectual disability of a degree that would preclude valid assessment. The study protocol was approved by the Nova Scotia Health Authority Research Ethics Board. All participants with capacity provided written informed consent. For children who did not have the capacity to make a fully informed decision about participating, a parent or guardian provided a written informed consent and the child gave an assent.

Parent assessments

Parents and children were assessed by separate teams of assessors. We established parent DSM-IV and DSM-5 diagnoses with the Schedule for Affective Disorders and Schizophrenia (SADS)25 and the Structured Clinical Interview for DSM Disorders (SCID),26 followed by clinical consensus with a psychiatrist masked to the referral source and parent diagnosis. Youth assessors masked to the referral source and parent diagnosis interviewed the youth participants and their parents or other caregivers with the Schedule for Affective Disorders and Schizophrenia for School Aged Children for DSM-5, Present and Lifetime version (K-SADS-PL).28 The DMDD module of the K-SADS-PL was administered to all participants in full. This module establishes the presence of each symptom of DMDD, including frequent (three or more times per week) severe temper outbursts inconsistent with developmental level, persistent irritability and onset before the age of 10 years. Each symptom is rated as 1, absent; 2, present at subthreshold level; or 3, present at threshold level. Lifetime diagnosis of DMDD and other mental and behavioural disorders was then established in consensus meetings with licensed child and adolescent psychiatrists presented with all available information on offspring but masked to information on parents. The diagnoses were recorded without hierarchy, so that if a participant met diagnostic criteria for DMDD and for oppositional defiant disorder (ODD), both diagnoses were recorded. We measured socioeconomic class as a sum of five binary indicators: mother’s education greater than high school, father’s education greater than high school, family income $40 000 or more, ownership of family residence, ratio of bedrooms to household member one or higher.

Data analysis

After data quality control, we examined the relationship between parent diagnosis (bipolar disorder, major depressive disorder, no mood disorder) and three dichotomous outcomes in offspring: frequent temper outbursts, persistent irritability and lifetime DMDD diagnosis. Because of zero prevalence rates in one or more groups, logistic regression was not applicable. Therefore, we examined the relationship between parent diagnosis and offspring outcomes using a bootstrap version of the chi-squared test ($\chi^2$), which has been shown to be more accurate than standard $\chi^2$ or Fisher’s exact test and provide adequate type I error rates across the full range of outcome frequency.29 For each test, the contingency table is resampled (with replacement) 10 000 times to obtain a distribution of $\chi^2$ estimates and a corresponding non-parametric $P$-value. Results with $P = 0.05$, two tailed, are reported as significant. Analyses were carried out in Stata 14.

Results

Participants

Between October 2013 and May 2016, we completed the K-SADS and the DMDD module with 180 participants (85 males and 95 females) aged 6–18 years (mean age 11.6 years, s.d. = 3.5), including 82 offspring of parents with major depressive disorder, 58 offspring of parents with bipolar disorder and 40 comparison offspring of parents with no mood disorder. The youth included in this sample had high rates of psychopathology, including consensus-confirmed lifetime diagnoses of multiple externalising and internalising disorders (Table 1).

DMDD symptoms

DMDD symptoms including frequent temper outbursts and persistent irritability were most common among offspring of parents with major depressive disorder (Fig. 1). Frequent temper outbursts were present in 2 (3.4%) of the 58 offspring of parents with bipolar disorder, 11 (13.4%) of the 82 offspring of parents with depression and 1 (2.5%) of the 40 comparison offspring. Frequent temper outbursts were significantly associated with family history across the three groups ($\chi^2_{\text{bootstrapped}} = 6.70, P = 0.035$) and were more common in offspring of parents with major depressive disorder than in offspring of parents with bipolar disorder at any time.27 However, given the age of the parents, depressive disorder is never final since it can convert to bipolar disorder at any time.27 However, given the age of the parents, depressive disorder is never final since it can convert to bipolar disorder at any time.27

Youth assessments

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disorder (χ² bootstrap(1) = 4.01, P = 0.045). Persistent irritability was present in 2 (3.4%) of the 58 offspring of parents with bipolar disorder, 8 (9.8%) of the 82 offspring of parents with depression and 1 (2.5%) of the 40 comparison offspring. Persistent irritability did not significantly vary with family history (χ² bootstrap(2) = 3.52, P = 0.172). Only seven participants, all sons and daughters of parents with major depressive disorder, had both frequent temper outbursts and persistent irritability (Fig. 1).

**DMDD diagnosis**

Of the 180 participants only 6 (3.3%) met the diagnostic criteria for DMDD. All six participants with DMDD were offspring of parents with major depressive disorder (Table 2). In all six, the mother was affected with major depressive disorder. In one, both mother and father were affected with major depressive disorder. In one, the youth also fulfilled criteria for other externalising and/or internalising disorders, including attention-deficit hyperactivity disorder (ADHD), ODD, conduct disorders, major depressive disorder and anxiety disorders (Table 2). One additional participant, also the offspring of a mother with major depressive disorder, fulfilled the symptomatic criteria A–E, but did not receive the diagnosis of DMDD because symptoms were not consistently present in multiple settings and, therefore, criterion F was not met. The diagnosis of DMDD varied significantly by family history (χ² bootstrap(2) = 7.42, P = 0.025) and was significantly more common in offspring of parents with major depressive disorder than in offspring of parents with bipolar disorder (χ² bootstrap(1) = 4.43, P = 0.035). None of the 58 offspring of parents with bipolar disorder fulfilled criteria for DMDD and none had a combination of frequent anger outbursts and persistent irritability (Fig. 1).

**Main findings**

This is the first study to apply a dedicated diagnostic instrument to study DMDD in youth at high risk for mood disorders and it suggests that DMDD diagnosis is uncommon. Although there were high rates of psychopathology in the present sample, only 6 of 180 participants (3.3%) met DSM-5 diagnostic criteria for DMDD. With all six occurring among offspring of parents with major depressive disorder and none in offspring of parents with bipolar disorder, our results do not support a specific association between DMDD and family history of bipolar disorder.

The diagnosis DMDD has only recently been introduced¹ and estimates of its prevalence in the general population⁹,¹⁰ or in high-risk youth¹² depend on proxies extrapolated from diagnostic questions that were designed to diagnose other disorders. We present the results of the first study that used a diagnostic instrument that was designed to assess DMDD. Our finding that the DMDD diagnosis is uncommon even in a sample of youth at high risk for psychopathology is consistent with the more conservative proxy estimates of DMDD prevalence rates.⁹,¹⁰ In addition, the finding that all individuals with DMDD also met diagnostic criteria for one or more other mental disorders suggests that the introduction of DMDD will not lead to more youth being diagnosed.

**Discussion**

*Table 1* Demographic and clinical characteristics by parent diagnosis

<table>
<thead>
<tr>
<th>Parent diagnosis</th>
<th>No mood disorder (n = 40)</th>
<th>Bipolar disorder (n = 58)</th>
<th>Major depressive disorder (n = 82)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at assessment, mean (s.d.)</td>
<td>11.35 (3.02)</td>
<td>12.25 (3.60)</td>
<td>11.29 (3.69)</td>
</tr>
<tr>
<td>Socioeconomic status (range 0–5), mean (s.d.)</td>
<td>3.10 (1.28)</td>
<td>3.02 (1.26)</td>
<td>2.76 (1.46)</td>
</tr>
<tr>
<td>Gender, female: n (%)</td>
<td>17 (42.5)</td>
<td>44 (53.7)</td>
<td>34 (40.5)</td>
</tr>
<tr>
<td>Ethnicity, White: n (%)</td>
<td>35 (87.5)</td>
<td>54 (91.1)</td>
<td>71 (86.6)</td>
</tr>
<tr>
<td>Living with both biological parents, n (%)</td>
<td>23 (57.5)</td>
<td>36 (62.1)</td>
<td>47 (57.3)</td>
</tr>
<tr>
<td>Lifetime diagnoses, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attention-deficit hyperactivity disorder</td>
<td>3 (7.5)</td>
<td>19 (32.8)</td>
<td>22 (26.8)</td>
</tr>
<tr>
<td>Oppositional defiant disorder⁹</td>
<td>2 (5.0)</td>
<td>7 (12.1)</td>
<td>8 (9.5)</td>
</tr>
<tr>
<td>Conduct disorder</td>
<td>0 (0)</td>
<td>2 (3.4)</td>
<td>2 (2.4)</td>
</tr>
<tr>
<td>Depression</td>
<td>1 (2.5)</td>
<td>15 (25.9)</td>
<td>13 (15.9)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>13 (32.5)</td>
<td>33 (56.9)</td>
<td>28 (34.1)</td>
</tr>
<tr>
<td>Disruptive mood dysregulation disorder</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>6 (7.3)</td>
</tr>
<tr>
<td>Any diagnosis</td>
<td>14 (35.0)</td>
<td>34 (58.6)</td>
<td>40 (48.8)</td>
</tr>
</tbody>
</table>

Depression, includes lifetime diagnosis of major depressive disorder or persistent depressive disorder, anxiety, includes lifetime diagnosis of generalised anxiety disorder, panic disorder, social anxiety disorder, agoraphobia or other anxiety disorder.

a. All diagnoses were lifetime and established without hierarchies. Therefore, diagnosis of oppositional defiant disorder is recorded if symptomatic criteria were met at any time, even if the disruptive mood dysregulation disorder diagnosis is present.

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**Fig. 1** Prevalence of symptoms of disruptive mood dysregulation disorder (DMDD) in offspring of parents with bipolar disorder, parents with depression and a control group of parents with no mood disorders.

The height of each bar indicates the number of participants with symptoms above the clinical threshold level. Error bars indicate a standard error of the proportion.
Comparison with findings from other studies

One of the major issues of debate has been the relationship between DMDD and bipolar disorder. Longitudinal studies have reported developmental continuity between DMDD proxies and depression, but not bipolar disorder. In contrast, a family high-risk study reported high rates of DMDD among offspring of parents with bipolar disorder, established based on an extrapolation of questions designed to assess ODD. Since the existing studies used varying proxy concepts of DMDD diagnosis and no previous study used an instrument designed to assess DMDD, the discrepancies may be a result of either different study design or different concepts and assessments.

The present study has sought to resolve the discrepant findings by applying a diagnostic instrument designed to assess DMDD in offspring of parents with bipolar disorder and adding a comparison with offspring of parents with major depressive disorder. Our result that DMDD is associated with family history of major depressive disorder but not bipolar disorder is consistent with prior population-based studies. Our findings are in disagreement with a prior familial high-risk study. In spite of high rates of both externalising and internalising psychopathology, the symptoms of frequent temper outbursts and chronic irritability were not particularly elevated and there was no diagnosis of DMDD among the offspring of parents with bipolar disorder. The difference between the present findings and those of Sparks and colleagues suggests that the divergence of results is unlikely to be the result of chance alone. One plausible explanation for the difference is the use of questions designed to diagnose ODD. The definition of symptoms and the frequency and persistency requirements differ substantially between DMDD and ODD. We found an elevated rate of ODD and more morbidity overall but not DMDD among offspring of parents with bipolar disorder. This finding is consistent with evidence for the association between severe irritability in youth and familial liability to depression reported in the literature. We conclude that DMDD is a manifestation of familial disposition that overlaps with liability for major depressive disorder.

Implications

Our results have implications for clinical practice and future research. Clinicians who use DSM-5 criteria may be relieved to know that the newly introduced DMDD diagnosis only captures a few patients who are severely affected, does not contribute to overdiagnosis of mental illness in children and does not carry the overdiagnosis of mental illness in children and does not carry implications regarding liability to bipolar disorder. Given the current state of knowledge, clinicians should avoid raising parallels with bipolar disorder when discussing temper outbursts and persistent irritability with patients and families. Regarding implications for future research, the present work emphasises the need for a dedicated diagnostic instrument and cautions against extrapolating symptom indicators from other diagnostic concepts to DMDD. Longitudinal follow-up of individuals diagnosed with appropriate instruments is needed to establish the predictive value of the DMDD diagnosis. In conclusion, the first familial high-risk study with directly established diagnosis of DMDD does not support a specific association between DMDD and familial liability to bipolar disorder. The results suggest that the DMDD and its symptoms may be more prevalent among offspring of parents with clinical depression.
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References