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Research paper

Adult outcomes of childhood disruptive disorders in offspring of depressed and healthy parents

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ABSTRACT

Background: Longitudinal studies of children with disruptive disorders (DDs) have shown high rates of antisocial personality disorder (ASPD) and substance use in adulthood, but few have examined the contribution of parental disorders. We examine child-/adulthood outcomes of DDs in offspring, whose biological parents did not have a history of ASPD, bipolar disorder, or substance use disorders.

Method: Offspring (N = 267) of parents with or without major depression (MDD), but no ASPD or bipolar disorders were followed longitudinally over 33 years, and associations between DDs and psychiatric and functional outcomes were tested.

Results: Eighty-nine (33%) offspring had a DD. Those with, compared to without DDs, had higher rates of MDD (adjusted odds ratio, AOR = 3.42, $p < 0.0001$), bipolar disorder (AOR = 3.10, $p = 0.03$), and substance use disorders (AOR = 5.69, $p < 0.0001$) by age 18, as well as poorer school performance and global functioning. DDs continued to predict MDD and substance use outcomes in adulthood, even after accounting for presence of the corresponding disorder in childhood (MDD: hazards ratio, HR = 3.25, $p < 0.0001$; SUD, HR = 2.52, $p < 0.0001$). Associations were similar among the offspring of parents with and without major depression. DDs did not predict adulthood ASPD in either group.

Limitations: Associations are largely accounted for by conduct disorder (CD), as there were few offspring with ADHD, and oppositional defiant disorder (ODD) was not diagnosed at the time this study began.

Conclusion: If there is no familial risk for ASPD, bipolar disorder or substance use, childhood DDs do not lead to ASPD in adulthood; however, the children still have poorer prognosis into midlife. Early treatment of children with DD, particularly CD, while carefully considering familial risk for these disorders, may help mitigate later adversity.

1. Introduction

Disruptive disorders (DD) in childhood are associated with poor mental health and social outcomes in later life (Erskine et al., 2016; Sayal et al., 2015). The most common DDs are attention deficit hyperactivity disorder (ADHD), conduct disorder (CD), and oppositional defiant disorder (ODD). Although unique diagnoses (American Psychiatric Association, 2013), they share traits such as irritability and distractibility (Krieger et al., 2013), have quite high comorbidity (Moffitt et al., 2015), and commonly predict adulthood outcomes such as depression (Meinzer et al., 2013; Stringaris et al., 2014) and substance use (Copeland et al., 2009; Ottosen et al., 2016). Since Robins' classic 1966 study (Robins, 1966) of deviant children grown up, there has been interest in the long-term outcomes of children with DDs. A recent meta-analysis of studies comprising at least two years of follow-up found that both CD and ADHD were associated with

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a broad range of outcomes from depression and substance use disorder (SUD) to problems in school and the judicial system (Erskine et al., 2016). Fewer studies have followed participants into mid-adulthood, but those that have also reported increased adult antisocial personality disorder, overall poor physical and mental health functioning, and increased rates of substance use and abuse, as well as occupational and social impairment (Breaux et al., 2014; DeKlyen, 1996; Klein et al., 2012; Moffitt et al., 2015; Wertz et al., 2018).

Adult psychiatric disorders linked to childhood DDs (e.g., antisocial personality disorder [ASPD] and substance use), as well as related behavioral traits such as impulsivity and aggression, run in families and may be present at higher rates among parents of children with DDs (Bornovalova et al., 2010; Haberstick et al., 2008; Heiser et al., 2006; Young et al., 2009). Similarly, childhood DDs are associated with higher parental aggression and poorer parental attachment (Flouri and Midouhas, 2017; Tremblay et al., 2018), suggesting non-normative behaviors in the parental generation. This raises the question of whether persistent adversity associated with childhood DDs is a direct consequence of having the disorder in childhood, or is better explained by parental psychopathology. This distinction can have significant implications for understanding disease trajectories and for treatment approaches. Yet, most of the aforementioned literature has not assessed the conributing role of parental psychopathology.

We have a unique opportunity to address the clinical course of childhood DDs while holding parental psychopathology stable, using a 30-year family study of offspring, whose parental generation was screened out for lifetime history of antisocial personality disorder, primary substance use disorders, and bipolar disorder (Goldstein et al., 2017). Offspring have been now longitudinally interviewed up to 6 times over an average of 33 years (Weissman et al., 2016a; Weissman et al., 1987, 2016b, 2006). This has allowed us to test both child- and adulthood onset outcomes of DD in the absence of parental ASPD, bipolar disorder and substance use. Additionally, the parents were recruited into the study based on the lifetime presence or absence of major depressive disorder (MDD) with impairment. This allows us to further explore the moderating role of parental depression on child trajectories. Finally, the study included children with both conduct disorder and ADHD (oppositional defiant disorders, ODD, was not commonly diagnosed when the study began in 1982). We can thus explore patterns across the different DDs.

2. Methods

In the original study, two sets of generation 1 (G1) parents were recruited; parents with moderate to severely impairing major depressive disorder (MDD) were outpatients receiving medication for depression as part of research. Non-depressed parents were selected from an epidemiologic sample in the same community and had no lifetime history of psychiatric illness, as determined by several interviews. The depressed probands were extensively interviewed to exclude histories of schizophrenia, antisocial personality disorder, primary substance use disorder and bipolar disorder (Weissman et al., 1987; Weissman et al., 2016b). In addition, to enter the study, generation 1 had to have at least one biological child age 6 years of age. Data on how many who were eligible by the above criteria agreed to enter the study were not available.

The children and adolescents in the present study were the offspring of either depressed or not depressed parents (i.e., generation 2; G2). Offspring of depressed parents were defined as those having one or more parents with MDD; those of non-depressed parents were defined as having no parents with MDD (lifetime). Thus, as defined by family history, all offspring were at low familial risk for disruptive, bipolar, and substance use disorders; but one group, at high- risk, the other, low-risk, for mood disorders. Procedures and training remained similar across all waves to avoid variance in the methods and have been described in detail elsewhere (Weissman et al., 1987; Weissman et al., 2016b). Across all waves, the proband, spouse, and offspring were interviewed by independent interviewers who were blind to the clinical status of the first generation. All interviews were approved by the institutional review board at New York State Psychiatric Institute/Columbia University. Written informed consent was obtained from adults for themselves and minors; verbal assent was obtained from minors.

Table 1
Demographic and Study Characteristics of offspring with and without disruptive disorders.

	Disruptive disorder			
	Yes N = 89 N (%)	No N = 178 N (%)	X^2 (df 1)	*p*
Sex, Male	53 (59.6)	70 (39.3)	9.77	0.002
Parental Depression, Yes	70 (78.7)	115 (64.6)	5.50	0.02
Interviews	Mean (SD)	Mean (SD)	F (df 265)	*p*
Age at first interview	19.8 (6.8)	18.3 (6.7)	0.71	0.07
Age at last interview	41.6 (10.9)	39.4 (12.6)	1.95	0.17
Yrs between first and last interview	21.8 (10)	21.2 (10.1)	0.044	0.65
Number of interviews	4.2 (1.4)	4.1 (1.3)	0.92	0.56

There were six waves of interviews: wave/year 1, 2, 10, 20, 25, and 30 years. We considered any biological offspring (G2) who entered the study at Wave 1 or 2. Two hundred and sixty-seven offspring from 91 families were interviewed. Of these, 221 (83%) were interviewed at wave 3, 10 years later; 186 (69%) at wave 4, 20 years later; and 148 (55%) at waves 5/6, 25–30 years later. We have previously documented that offspring who participated at waves 3 (Weissman et al., 1997), 4 (Weissman et al., 2006), 5 (Peterson et al., 2009), and 6 (Weissman et al., 2016a) did not differ from those who did not on age, sex, familial risk status, or major depression at the last interview. We also document (Table 1) that the average age at first or last interview, and the number of interviews, did not vary by if the offspring had disruptive disorder diagnosis.

Assessments were described previously (Weissman et al., 1987; Weissman et al., 2016b) and are summarized briefly. The diagnostic interview across all waves was the Schedule for Affective Disorders and Schizophrenia–Lifetime Version (SADS-L) for adults (Mannuzza et al., 1986) and the Kiddie-SADS child version modified for DSM-IV for individuals between 6 and 17 years of age (Kaufman et al., 1997; Orvaschel et al., 1982). The Kiddie-SADS-E (Orvaschel et al., 1982) was used in Wave 3, and the Kiddie-SADS–PL version (Kaufman et al., 1997) was used subsequently in Waves 4 through 6. Final diagnoses were made by an experienced M.D. or Ph.D. level clinician using the best estimate procedure, which integrates sources of information for direct interview, records and family history data across current and past waves of the study (Leckman et al., 1982). Individuals were rated at each wave on the Global Assessment Scale (GAS) (Endicott et al., 1976) or the child version of the scale (Children's Global Assessment Scale) if they were younger than 18 years. The GAS, scored from 0 to 100 points, provides an overall estimate of current functioning, with higher scores denoting better functioning. School performance was obtained using the Social Adjustment Inventory for Children and Adolescents (John et al., 1987). For this study, ADHD and/or CD diagnosis, classified together in the Behavioral (overt) group in the Disorders Usually First Evident in Infancy, Childhood, or Adolescence section of DSM-III at the time the study began, were considered together as a diagnosis of a disruptive disorder (DD). Oppositional defiant disorder (ODD) was not a routinely assessed disorder when the study began.

2.1. Statistical analysis

Preliminary analyses of group differences in mean values for continuous outcomes by presence or absence of childhood DDs were tested using a *t* test; ordinal outcomes were tested with the Kruskal–Wallis chi-

square test, and categorical outcomes were compared with the chi-square test. Sex and parental depression were considered a priori to be confounding variables and were retained in every model. For analyzing the association between DD and childhood or adolescent onset of a psychiatric disorder, we applied a generalized estimating equation approach using the GENMOD procedure in the SAS software package (SAS Software 9.3, 2010) to estimate parameters and to adjust for potential non-independence of outcomes for offspring from the same family. Survival analysis techniques adjusting for correlated survival times were used to estimate cumulative lifetime rates in adulthood of psychiatric disorders (SPSS Inc, 2008). Cox proportional hazards regression models modified to adjust for clustered data were used, following the approach described by Lin and Wei (Lin and Wei, 1989). Adjusting for clustered data was necessary to account for potential non-independence of outcomes for related offspring. Sex and parental depression were the covariates for this analysis. To determine whether DD was associated with a new onset or the recurrence of a psychiatric disorder in adulthood, regardless of childhood/adolescence diagnoses, analyses controlled for the onset of the correspondent psychiatric disorder before age 18. Finally, we stratified participants by MDD or SUD onset in childhood/adolescence to test if DD was associated with incidence of MDD or SUD, respectively, in adulthood.

3. Results

Two hundred and sixty-seven participants were interviewed at study inclusion (Wave 1 and/or 2). Of them, 89 (33.3%) offspring were diagnosed with DD. This included 70 offspring of depressed parents, and 19 offspring of non-depressed parents. Offspring with DDs, as compared to without, were more likely to be male (59.6 vs. 39.3%), but did not otherwise differ on age at first or most recent interview, the number of years between interviews, or the number of interviews (Table 1**)**. Of the 89 offspring, 65 (73%) had conduct disorder (CD) only, 11 (12.4%) had ADHD only, and 13 (14.6%) had both. Average age of onset for DD was 10.6 ± 5.2 (mean, std) years [when examined separately, for ADHD: 4.0 ± 4.2 years; CD: 12.7 ± 3.1 years].

3.1. Associations between DDs and psychiatric diagnoses and functioning in childhood

Rates of psychiatric disorders by age 18 are shown in Table 2 for offspring with and without DDs. Odds ratios, adjusted for offspring sex and parental depression, are shown in the right columns. Offspring with DDs had more than 3-fold higher rates of major depressive disorder (MDD, Adjusted Odds Ratio, AOR = 3.42, p < 0.001) and bipolar disorder (AOR = 3.1, p = 0.01), and a five-fold increase in substance use disorders (SUD, AOR = 5.69, < 0.0001).

To further explore whether these associations varied by presence of depression in the parental generation, we examined the associations separately in offspring of depressed and non-depressed parents. As shown in Table S1, similar patterns emerged. DDs were associated with MDD and SUD regardless of whether offspring were from families with or without a parental history of depression. Formal tests of interaction indicated that the observed associations between DDs and MDD (p = 0.41), and between DD and SUDs (p = 0.19), did not significantly differ by parental depression (see limitations regarding interpretation of interaction effects).

We also examined associations with schooling and global functioning. Offspring with DDs were more likely to have been suspended, expelled, or held back a grade, and had worse scores on academic performance, relationships with teachers, and general behavior (Table 2, bottom). Global functioning scores, determined by independent clinical evaluation, were also significantly lower (indicative of greater functional impairment) among offspring with, as compared to without, DDs (57.3 vs 72.2, p < 0.0001).

Table 2
Association between Disruptive disorder and childhood and Adolescent-onset (< 18 years) Psychiatric Disorders, School performance and overall functioning.

	Disruptive disorder Yes N = 89	No N = 178		
Psychiatric disorders, < 18 years[a]	*N (%)*	*N (%)*	*AOR (95% CI)*	*p*
Any mood Disorder	55 (61.8)	63 (35.4)	3.71 (2.09–6.58)	< 0.0001
Major Depressive Disorder	41 (46.1)	40 (22.5)	3.42 (1.94–6.02)	< 0.0001
Bipolar I or II disorder	12 (13.5)	8 (4.5)	3.10 (1.24–7.75)	0.01
Any substance use disorder[g]	33 (37.1)	16 (9)	5.69 (2.78–11.65)	< 0.0001
Any Anxiety Disorder[h]	32 (36)	51 (28.7)	1.43 (0.81–2.53)	0.21
Suicide ideation or attempts[b,c]	13 (14.8)	17 (9.6)	2.50 (0.72–8.70)	0.15
School functioning	*N (%)*	*N (%)*	*X^2 (df 1)*	*p*
Suspended or expelled[d,e]	16 (20.5)	2 (1.3)	26.147	< 0.0001
Held back in school[e]	16 (20.3)	16 (10.7)	3.956	0.047
Worse, compared to other children				
Academic performance[f]	12 (15.2)	9 (6)	5.325	0.02
Academic ability[f]	7 (8.9)	7 (4.6)	1.620	0.20
Relationships with teachers[d,f]	7 (8.9)	3 (2)	5.893	0.03
Relationships with kids[f]	7 (8.9)	9 (6)	0.674	0.41
Athletic ability[e]	9 (11.4)	18 (12)	0.018	0.89
General behavior[d,e]	9 (11.5)	2 (1.3)	11.734	0.001
Global Functioning	*Mean (SD)*	*Mean (SD)*	*F (df)*	*p*
Global Assessment Scale score	57.3 (11.3)	72.2 (14.3)	6.672 (265)	< 0.0001

AOR: Adjusted Odds Ratio; **SD:** Standard Deviation

[a] Generalized estimating equations controlling for sex and parental depression

[b] Generalized estimating equations controlling for sex, parental depression and major depressive disorder onset before 18 years old;

[c] Information missing for one participant

[d] Fisher Exact Test;

[e] Information missing for 38 participants;

[f] Information missing for 37 participants;

[g] Includes drug or alcohol use disorder (findings were significant for each when examined separately)

[h] Includes specific phobia, social anxiety disorder, generalized anxiety disorder and panic disorder

3.2. Associations between DDs and psychiatric diagnoses and functioning in adulthood

We next examined whether DDs were also associated with psychiatric disorders after age 18 (Table 3**)**. Offspring with DDs were at more than a 3-fold increased risk for major depressive (hazard ratio, HR = 3.41, p < 0.0001) and substance use (HR = 3.23, p < 0.0001) disorders after age 18 (middle columns). Furthermore, these associations remained significant after accounting for the presence of the respective disorder in childhood (right columns), indicating an independent association between disruptive behaviors in childhood and depression and substance use in adulthood. There was also a trend where offspring with DDs reported higher rates of suicide attempts and ideations than those without (27.3% vs 11.2%, p = 0.07). Finally, global functioning remained lower in offspring with, as compared to without, a DD (76 vs 84, p = 0.001). Similar findings were observed across the offspring of depressed and non-depressed parents when examined separately (Table S2**)**, and formal tests of interaction indicated no significant differences by parental risk status (DD and MDD, p = 0.42; DD and SUD, p = 0.43). Finally, offspring with and without

Table 3
Association between Disruptive disorder and adult (≥18 years) Psychiatric Disorders.

	Disruptive disorder Yes (N = 89)	No (N = 178)	Unadjusted for childhood diagnosis		Adjusted for childhood diagnosis	
Psychiatric disorder	*N (%)*	*N (%)*	*HR[a] (CI 95%)*	*P*	*HR[b] (CI 95%)*	*p*
Any mood Disorder	75 (84.3)	95 (53.4)	2.19 (1.55–3.08)	< 0.0001	1.12 (0.78–1.62)	0.55
Major depressive disorder	67 (75.3)	70 (39.3)	3.41 (2.41–4.82)	< 0.0001	3.25 (2.28–4.65)	< 0.0001
Bipolar disorder	16 (18.0)	13 (7.3)	2.35 (1.09–5.10)	0.03	0.77 (0.32–1.83)	0.55
Any substance use disorder[c]	47 (52.8)	31 (17.4)	3.23 (2.10–4.97)	< 0.0001	2.52 (1.58–4.02)	0.0001
Any anxiety disorder[d]	38 (42.7)	58 (32.6)	1.38 (0.96–2.00)	0.08	1.34 (0.91–1.98)	0.14
Antisocial personality disorder	3 (3.4)	0	n/e		n/e	
Suicide ideation or attempts	24 (27.3)	20 (11.2)	1.92 (0.94–3.95)	0.07	-	
Global Functioning	*Median (IQR)*	*Median (IQR)*				
Global Assessment Scale score[e,f]	76 (61.5–85)	84 (75–89)	-	0.001	–	–

HR: Hazards Ratio. A h ratio > 1 indicates a greater risk for the psychiatric outcome in offspring with as compared to without DDs; a ratio < 1 indicates a lower risk of the psychiatric outcome in offspring with, compared to without DDs.
IQR: Inter-quartile Range.
n/e: Not estimable.
[a] cox regression analysis controlling for sex and parental depression status.
[b] cox regression controlling for sex, parental depression status, and the correspondent outcome in childhood and adolescence.
[c] Includes drug or alcohol use disorder (findings were significant for each when examined separately).
[d] Includes specific phobia, social anxiety disorder, generalized anxiety disorder and panic disorder.
[e] Kruskal-Wallis test.
[f] Last assessment.

DDs did not differ on socioeconomic outcomes, including marital status, education, employment, or household income **(**Table S3**).**

To further compare effects of childhood DDs on adulthood recurrence versus new onset (incidence), we examined the relationship between DDs and adult disorders separately in subgroups of offspring with and without the disorder in childhood (**Table 4**). DDs predicted adulthood MDD regardless of whether childhood MDD was present (that is, recurrence; HR = 2.70, p < 0.0001) or absent (incidence; HR = 3.31, p < 0.0001). However, for substance use, DDs only predicted adulthood onset of substance use disorders in offspring without substance use disorders in childhood (HR = 3.45 (2.00–5.92), p < 0.0001).

Finally, we explored whether the findings varied by type of DD by attempting to examining the associations among offspring with only CD or ADHD, but not the other. When examined independently, similar findings (increased associations with both childhood (Table S4) and adulthood (Tables S5) onset of mood and substance use disorders) were observed for children with CD. We were unable to model analogous associations for ADHD, as there were too few children with the disorder (see limitations).

Table 4
Association between childhood/adolescence DD, adult recurrence and adult incidence of psychiatric disorder.

		MDD in Adulthood Yes N (%)	No N (%)	*HR[a]* (CI 95%)	*p*
With Childhood MDD	DD	36 (87.8)	5 (12.2)	2.70 (1.70–4.28)	< 0.0001
	No DD	26 (65.0)	14 (35.0)		
Without Childhood MDD	DD	31 (64.6)	17 (35.4)	3.31 (1.97–5.56)	< 0.0001
	no DD	44 (31.9)	94 (68.1)		
		SUD in adulthood Yes N (%)	No N (%)	*HR* [a] (CI 95%)	*p*
With Childhood SUD	DD	21 (63.6)	12 (36.4)	1.08 (0.53–2.19)	0.78
	no DD	9 (56.3)	7 (43.7)		
Without Childhood SUD	DD	26 (46.4)	30 (53.6)	3.45 (2.00–5.92)	< 0.0001
	no DD	22 (13.6)	140 (86.4)		

HR: Hazards Ratio; **MDD**: Major depressive disorder; **SUD**: substance use disorder.
[a] Cox regression analysis controlling for sex and parental depression

4. Discussion

We followed offspring with and without disruptive behavior disorders (DDs) into mid-adulthood in one of the longest follow-ups of DD. We report that children and adolescents with DD have worse outcomes in both child- and adulthood. These include greater psychiatric disorders, more academic problems, and poorer clinician-rated global functioning. What is novel about this study is that the offspring represent a group at low familial risk for DDs, given that the parental generation was extensively screened out for lifetime history of substance use disorder, bipolar disorder, and ASPD; yet we find that *even in the absence of these parental risk factors,* children with DDs go on to have distinctly poorer outcome, and that these outcomes persist into adulthood. This suggests overall that the presence of DDs in childhood, and not only an underlying genetic or other familial vulnerability, predisposes offspring to poorer outcomes in later life**.** The presence or absence of depression in the parental generation does not appear to increase or decrease this risk appreciably. Interestingly, in this population, DDs did not predict adulthood ASPD, suggesting that parental antisocial personality disorder or traits may be necessary for this transition. The implications of the findings are summarized below.

4.1. DDs, psychiatric outcomes, and functioning

Numerous studies have shown childhood DDs to predict a longitudinal course of impairment (Brook et al., 2013; Klein et al., 2012; Moffitt et al., 2015). We found that offspring who had DD had higher rates of mood disorders (major depressive disorder, bipolar disorder, and dysthymia) and substance use (both drug and alcohol) disorders. Associations were significant in both childhood and adulthood and, importantly, the adult diagnoses could not be explained by the presence of the corresponding disorder in childhood (Tables 3 and 4). This suggests that DDs in childhood independently increase the risk for adult *incidence* of depressive and substance use disorders. Offspring with DDs had significantly worse school performance in several academic and behavioral domains. Not only were the global functioning (GAS) scores lower for those with, as compared to without, DD, average GAS scores for the DD group were only 57, reflecting a range of significant *clinical* impairment in multiple areas of functioning. As offspring entered adulthood, the magnitude of the difference in functioning between those with and without childhood DDs attenuated, but remained

significant. The offspring with and without DDs did not differ by marital status, income or employment in adulthood, suggesting that even though they seem to struggle in school as kids, near-term academics do not necessarily predict long-term achievement.

4.2. DDs did not predict ASPD in adulthood

A number of studies have found childhood DDs to predict ASPD in adulthood (Helgeland et al., 2005; Kjelsberg, 2006; Ramklint et al., 2003). The association is particularly strong for CD, where some studies report as high as 30–50% of all children with the disorder going on to develop ASPD (Moffitt et al., 2015; Moore et al., 2017; Olino et al., 2010). We did not detect increased rates of adult antisocial personality disorder (ASPD): only 3 (3.4%) of offspring with DD ever developed ASPD, while none of those without DD developed ASPD. The 3% rate is well below the rates of ASPD expected in offspring with DDs and is unlikely to be explained by insufficient length of follow-up as our offspring were followed-up until mean age 40 (Weissman et al., 2006; Welch et al., 2014).

The lower rates of ASPD may be due to the absence of ASPD in the parent generation. Antisocial traits and disorders are known to have a familial component, with first-degree relatives of individuals with ASPD being at increased risk for the disorder relative to the general population, and offspring with two parents more likely to have the disorder than those with one or none (Hay et al., 2010). In our study, the disorder was carefully screened out in the parental generation. All first generation probands (parents of the participants), were required to have no lifetime history of antisocial personality disorder (as documented through several interviews), as well as no history of bipolar disorder or primary substance use disorder, which are frequently comorbid with ASPD. Thus, offspring may have varied in their risk for depression (based on their parents' depression status), but would be expected to be at uniformly low risk for antisocial personality. The transition from childhood conduct disorder to adult ASPD may partly be a function of familial history of antisocial personality and, in the absence of that history, childhood DDs may still have other long-term sequel, but not ASPD. However, other mechanisms are possible, and further studies with comparable offspring groups with parents with and without ASPD would be required to further investigate this question empirically.

4.3. Limitations

Given the design of the study, all participants were offspring of either depressed or non-depressed parents. Thus, the overall rates of DD, as well as associations between DD and other clinical outcomes, may not reflect those in the general population. Although we found no formal differences in the associations between DD and outcomes between children of depressed and non-depressed parents, it is possible that the study lacked power to detect statistical interactions. Still, overall patterns are very similar. Finally, although the study examined DDs together, most diagnoses (75%) were of conduct disorder (CD) only. Findings were retained if we restricted the analyses to CD, but there were insufficient cases to examine ADHD alone. Thus, findings may be more applicable to offspring with conduct rather than other disruptive behavior problems. Related, the study does not assess ODD, which was not routinely diagnosed when the study began. Finally, even though we did not observe any differences in adulthood sociodemographic outcomes, this could be because of missing demographic data. Despite these limitations, there are also several strengths in this study, including the reliable diagnostic interviews with parents and offspring with multiple informants, the use of best estimate procedure for diagnosis, and the long-term and independent follow-up that allowed us to examine risks for clinical outcomes that do not emerge until late adolescence and adulthood.

5. Conclusions

The study demonstrates that clinical and functional problems in children with DD, and particularly conduct disorder, persist into mid-adulthood even among children with no parental history of externalizing-type psychopathology. The findings suggest that long-term course may vary as a function of familial diagnostic make up. If a parent does not have ASPD, primary substance use or bipolar disorder, adult ASPD in offspring with DDs may not be inevitable. However, adult depression and substance abuse still occurs in children with DD who do not have any family history of either externalizing or internalizing pathology. Early and tailored treatment of children with DD (particularly CD) while carefully considering familial risk for these disorders, may help mitigate adversity in later life.

Contributions

All authors contributed significantly to the work. APD prepared the primary draft of the manuscript. MMW, AT, CS, and PJW directed the study and the preparation of the manuscript; JS recruited the participants on which the analyses are based; MJG and VW provided data management and generation of the datasets; APD, BD and RZ conducted the statistical analyses, under the supervision of PJW; JP provided expert advice on clinical interpretation of the findings; MMW and JAG were involved in obtaining funding for this work; all authors provided critical feedback on the manuscript.

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Conflict of interest

None of the authors present a conflict of interest.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2018.10.086.

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