Preschool Irritability: Longitudinal Associations With Psychiatric Disorders at Age 6 and Parental Psychopathology

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Objective: There is increasing scientific and clinical attention to chronic irritability in youth. However, little is known about the predictive validity and clinical significance of chronic irritability during early childhood. This prospective, longitudinal study examined associations of chronic irritability with psychiatric disorders and parental psychopathology in a large community sample of preschoolers. **Method:** Four hundred sixty-two preschool-age children were assessed at 3 and 6 years of age. Child psychopathology was assessed at baseline (3 years) and follow-up (6 years) using a diagnostic interview, the Preschool Age Psychiatric Assessment, with parents. Items from the Preschool Age Psychiatric Assessment were used to create a dimensional measurement of chronic irritability. Parental psychopathology was assessed with a diagnostic interview at baseline. **Results:** Chronic irritability was concurrently associated with a wide range of psychiatric disorders and functional impairment at 3 and 6 years of age. Irritability at 3 years predicted depression, oppositional defiant disorder, and functional impairment at 6 years after controlling for baseline disorders. Irritability also was associated with parental depression and anxiety. **Conclusions:** Findings underscore the central role of irritability in early-emerging mental health problems. They are consistent with longitudinal studies in older youth indicating that chronic irritability predicts later depression and anxiety and support the importance of early detection and interventions targeting preschool irritability. J. Am. Acad. Child Adolesc. Psychiatry, 2013;52(12):1304–1313. **Key Words:** irritability, longitudinal, mood dysregulation, preschool

In recent years, there has been growing clinical and scientific interest in youth irritability.[1] The importance of irritability in child psychiatry has long been reflected in the psychiatric nosology, where it is a criterion for several emotional and behavioral disorders, including major depressive disorder, generalized anxiety disorder, and oppositional defiant disorder (ODD; *DSM-5*).[2] In addition, disruptive mood dysregulation disorder, a condition characterized by recurrent temper outbursts and severe and chronic irritability, has recently been added to the *DSM-5* for childhood and adolescent disorders.[2] Despite its inclusion as a symptom of multiple disorders and the cornerstone of disruptive mood dysregulation disorder, youth irritability remains largely understudied.[3] Surprisingly, little is known about the phenomenology of irritability across the lifespan or its associations with psychopathology and family history, which could inform the understanding of genetics and pathophysiology.[1,3]

Irritability has been defined as a mood of easy annoyance and touchiness characterized by anger and temper outbursts.[1] Recent investigations of youth irritability have indicated that chronic irritability, characterized by increased reactivity to negative emotional stimuli and irritability, anger, and/or sadness that is noticeable to others and present most of the time, is a common and impairing symptom in children and adolescents[1,3]; prevalence estimates have ranged from 3.3% to 5.0% in epidemiologic samples.[4,5] In addition, a few recent studies have documented associations between irritability and risk for later psychopathology. Studies using prospective, community-based designs have found that school-age children and adolescents evidencing chronic irritability are at increased risk for emotional

disorders, specifically depressive and anxiety disorders, in early[4,6] and later[7] adulthood. Moreover, youth irritability has been associated with significant impairment even in the absence of psychiatric disorders[5] and has predicted lower income and less educational attainment in a 20-year follow-up.[7]

Longitudinal data showing that chronic irritability predicts depression and anxiety are consistent with findings that the irritability dimension of ODD differentially predicts depressive and anxiety disorders, whereas the headstrong/hurtful dimension is more strongly associated with behavioral disorders and delinquency.[8-10] Facets of irritability also have been associated with externalizing behaviors.[4,6,7,11] Thus, examining predictive associations between irritability and psychopathology may shed light on the comorbidity between internalizing and externalizing disorders and possibly the developmental link between ODD in youth and depression in adulthood.[12]

Although these studies provide compelling evidence linking irritability to a poor long-term course, significant gaps in the literature persist. Existing studies have focused on school-age children through adolescence and adulthood; little work has examined chronic irritability during early childhood. Irritability is a key facet of temperamental negative affect (e.g., anger, frustration), which emerges early in life[13,14] and is linked to later psychopathology.[11,15] Studying irritability as children progress through the preschool years may provide a clearer picture of the developmental course, continuity, and predictive validity of chronic irritability and help determine whether the pattern of irritability-psychopathology associations is similar to studies of older youths and adults. In addition, although periods of irritability are common in early childhood, more frequent bouts of irritability appear to hold clinical utility in identifying high-risk children.[16] Thus, there is a pressing need to explore irritability-psychopathology associations at this stage of development to improve early identification and intervention efforts.

Given the importance of prospective, community-based designs to study irritability,[4,6,7] data from a large, community sample of preschoolers followed longitudinally from 3 to 6 years of age were used to extend previous studies by examining the predictive validity and clinical significance of chronic irritability in early childhood.

The first aim was to examine whether chronic irritability at 3 years predicts *DSM-IV* disorders and functional impairment at 6 years in unadjusted models and in models adjusting for disorders at baseline. The adjusted models tested whether irritability at 3 years predicts the emergence of new psychiatric diagnoses at 6 years over and above homotypic and heterotypic continuity.[17] In addition, cross-sectional associations between irritability and *DSM-IV* disorders and functional impairment at 3 and 6 years of age were examined. Based on prior work in older youth, the authors hypothesized that although symptoms of chronic irritability would demonstrate wide-ranging cross-sectional associations, irritability at 3 years of age would prospectively predict depression and anxiety at 6 years, given research demonstrating that chronic youth irritability shows strong associations with emotional disorders.[7-10] The authors also hypothesized that irritability would prospectively predict ODD, because evidence suggests that irritability has pronounced associations with emotional *and* behavioral problems in youths.[4,6,7,10] Moreover, the authors hypothesized that chronic irritability at 3 years of age would predict greater functional impairment at 6 years, even after accounting for psychiatric disorders at baseline and follow-up.

Because associations between irritability and psychopathology may be due to the inclusion of irritability as a criterion for several disorders or the stability of irritability over time, a series of parallel analyses was conducted using irritability at 3 years to predict nonoverlapping dimensional symptom scales of depression, anxiety, attention-deficit/hyperactivity disorder (ADHD), and ODD at 6 years. The scales were created by excluding irritability items from the symptom scales to confirm the authors' findings on the unique predictive associations of irritability with psychiatric disorders at 6 years of age.

The second aim was to examine the relation between children's irritability and parental history of depressive, anxiety, and substance use disorders. In light of research documenting longitudinal associations between irritability and risk for future depression and anxiety[4,6,7] and a twin study supporting a genetic association between irritability and depression,[10] the authors hypothesized that chronic irritability would be linked with a family history of depression and anxiety.

METHOD

Participants

The authors recruited families with a 3-year-old child living within 20 contiguous miles of Stony Brook University for a study of temperament and psychopathology.[18] Potential participants were identified by a commercial mailing list; eligible families had a child 3 to 4 years of age with no significant medical conditions or developmental disabilities and at least 1 English-speaking biological parent. Of the 815 families who were identified as eligible, 66.4% (n = 541) entered the study and provided diagnostic information about the child. There were no significant differences between families who did and did not participate on demographic variables. Table 1 presents demographic information on the study sample (see Bufferd *et al.*[17,19] and Dougherty *et al.*[18] for details about the recruitment procedures and sample characteristics). Census data suggested the sample was reasonably representative of the surrounding county, where 79.0% of individuals were Caucasian/non-Hispanic and 48.1% of adults 25 to 54 years old graduated from college. The study was approved by the Stony Brook University human subjects review committee. Informed consent was obtained from parents, and families were compensated for participating.

Of the 541 parents who were interviewed regarding their 3-year-old child (m = 3.6, SD = 0.3 years) at baseline, 462 parents (85.4%) were interviewed again when their child turned 6 years old (m = 6.1, SD = 0.4 years). Children who completed the 2 assessments were compared with children who completed only the

TABLE 1 Demographic and Clinical Characteristics of the Study Sample

	Assessment at 3 y	Assessment at 6 y
Demographic characteristics		
Child age, y, m (SD)	3.6 (0.3)	6.1 (0.4)
Child sex, female, n (%)	212 (45.9)	
Child race/ethnicity, n (%)		
White/non-Hispanic	401 (86.8)	
Hispanic	39 (8.4)	
Black/African American	7 (1.5)	
Asian	9 (2.0)	
Other	6 (1.3)	
Biological parents' marital status, n (%)		
Married	435 (94.2)	413 (89.4)
Divorced, separated, or widowed	9 (1.9)	32 (6.9)
Never married	18 (3.9)	17 (3.7)
Parents' education, graduated college, n (%)		
Mother	258 (56.7)	245 (59.3)
Father	209 (46.7)	195 (47.8)
Child irritability (0–7), m (SD); range	0.69 (1.27); 0–7	0.80 (1.35); 0–6
Child psychopathology, n (%)		
Depressive disorder	6 (1.3)	25 (5.4)
Anxiety disorder	89 (19.3)	72 (15.6)
ADHD	11 (2.4)	25 (5.4)
ODD	47 (10.2)	41 (8.9)
Child functioning		
Child GAF (1–100), m (SD); range	84.5 (13.76); 45–100	75.31 (11.18); 42–100
Child impairment ratings, m (SD); range	0.84 (1.45); 0–8	5.40 (3.87); 0–18
Received referrals for treatment, n (%)	12 (2.6)	
Parental lifetime psychopathology, n (%)		
Depressive disorder	194 (42.5)	
Anxiety disorder	210 (45.7)	
Substance use disorder	235 (51.5)	
Maternal lifetime depressive disorder	152 (33.0)	
Maternal lifetime anxiety disorder	154 (33.3)	
Maternal lifetime substance use disorder	106 (23.0)	
Paternal lifetime depressive disorder	79 (17.4)	
Paternal lifetime anxiety disorder	95 (20.9)	
Paternal lifetime substance use disorder	179 (39.3)	

Note: ADHD = attention-deficit/hyperactivity disorder; GAF = Global Assessment of Functioning; ODD = oppositional defiant disorder; y = years.

first assessment on demographic variables and diagnoses at 3 years. There was only 1 significant difference: 85.9% of children without depression at 3 years participated at 6 years (456 of 531), whereas only 60.0% of children with depression at 3 years (6 of 10) participated at 6 years ($n = 541$, $\chi^2_1 = 5.27$, $p < .05$).

Measurements

Child Irritability and Psychiatric Disorders. The Preschool Age Psychiatric Assessment (PAPA)[20] is a parent-based structured diagnostic interview designed to assess a range of *DSM-IV* psychiatric disorders in preschoolers 2 to 6 years old. As described elsewhere,[17,19] *DSM-IV* diagnoses were derived using algorithms created by the instrument's developers. PAPA interviews were conducted with parents when the children were 3 and 6 years old. Emotional disorders included depressive (major depressive disorder, dysthymic disorder, or depression not otherwise specified) and anxiety (specific phobia, separation anxiety disorder, social phobia, generalized anxiety disorder, agoraphobia, selective mutism) disorders; behavioral disorders included ADHD and ODD. Symptoms occurring 3 months before the interview were rated to maximize recall. For information on the interview's psychometric properties, see Egger *et al.*[20]

At 3 years of age, interviews were conducted by advanced graduate students in clinical psychology who received training from an experienced interviewer from the group that developed the interview. Interviews usually lasted 1 to 2 hours and were conducted by telephone. Based on 21 randomly selected audiotaped interviews that oversampled participants with psychopathology, κ values were 1.00 for all diagnostic categories at 3 years of age. At 6 years of age, interviews were conducted by a master's-level clinician with training in the PAPA. This interviewer was not aware of the results of the interview at 3 years. At 6 years, interviews were conducted face to face. Diagnostic interviews with parents regarding their children have yielded equivalent results when administered by telephone and face to face.[21] Based on 35 audiotapes, κ values for diagnoses at 6 years of age were 0.64 for depression, 0.89 for any anxiety disorder, 0.64 for ADHD, and 0.87 for ODD. See Bufferd *et al.*[17] for a complete description of the rates of psychiatric disorders at 3 and 6 years of age.

Six items from the PAPA were used to assess irritability in children at 3 and 6 years. Items corresponded to items from the Affective Reactivity Index, a parent- and child-reported chronic irritability scale for older youth.[22] The following PAPA items were used.

1. Child experiences irritable mood, which is the ease of precipitation of externally directed feelings of anger, bad temper, short temper, resentment, or annoyance present in at least 2 activities (depression section).
2. Child is generally prone to feelings of anger, bad temper, short temper, resentment, sulking, or annoyance under minor provocation (depression section).
3. Child is generally prone to manifestations or displays of anger or resentment under minor provocation (depression section).
4. Child is generally prone to feelings of frustration under minor provocation (depression section).
5. Child experiences discrete episodes of temper manifested by shouting or name calling but without violence (ODD section).
6. Child experiences discrete episodes of excessive temper, frustration, or upset, manifested by shouting, crying, or stamping, and/or involving violence or attempts at damage directed against oneself, others, or property (ODD section).

The PAPA items were rated for intensity, frequency, and duration. The intensity rating indicates whether a symptom was absent or present and the extent to which it was intrusive, interfering, and generalizable across activities. A rating of at least 2 indicates that the symptom was present at a threshold level of intensity. Frequency items reflect the number of occurrences during the previous 3 months. According to the guidelines for chronic irritability by Brotman *et al.*[4] and Copeland *et al.*,[23] each item was coded as present if a child was prone to the behavior at least 45 times in the past 3 months. To assess whether the child experienced irritable mood states for a long time, this criterion was coded present if the child was rated as having an at least 30-minute duration of irritable mood, prone to frustration, annoyance, or anger, or difficulty recovering from temper tantrums. The total irritability scale consisted of the sum of symptoms coded as present according to the intensity, frequency, and duration criterion described earlier. If the 2 items selected from the ODD scale were screened and skipped out (see below), they were coded as absent. However, when analyses were conducted excluding the 2 ODD items from the irritability scale for all participants, results were similar. The Cronbach α coefficient of internal consistency for the measurement of irritability was 0.73 at the 2 assessments.

Given that the individual PAPA items used to derive the irritability scale also were used to derive diagnoses for any depressive disorder, any anxiety disorder, and ODD, the authors created "nonoverlapping" symptom scales for each diagnostic category to avoid item overlap. Symptom scales were created by summing items in each diagnostic category, excluding any irritability items. No adjustment was needed for ADHD because there were no overlapping items. Interrater reliability, as indexed by the intraclass correlation coefficient, for the symptom scales at 3 and 6 years of age, respectively, were 0.97 and 0.95 for depression, 0.99 and 0.70 for anxiety, 0.99 and 0.97 for ADHD, and 0.99 and 0.97 for ODD. Internal consistency (α) of

TABLE 2 Concurrent Associations of Parent-Rated Irritability and *DSM-IV* Diagnoses and Functioning at 3 and 6 Years of Age

Diagnosis	At 3 y old (n = 541) Irritability OR (95% CI)	At 6 y old (n = 482) Irritability OR (95% CI)
Depressive disorder	3.38*** (1.83–6.26)	2.17*** (1.59–2.96)
Anxiety disorder	1.47*** (1.20–1.81)	1.17 (0.92–1.48)
ADHD	1.53* (1.01–2.30)	1.46* (1.06–2.00)
ODD	4.30*** (3.10–5.97)	4.76*** (3.28–6.92)
Functional impairment		
GAF	$r = -0.52$***	$r = -0.53$***
Impairment rating	$r = 0.56$***	$r = 0.51$***

Note: All logistic regression models controlled for age, sex, and parental education. ADHD = attention-deficit/hyperactivity disorder; GAF = Global Assessment of Functioning; ODD = oppositional defiant disorder; OR = odds ratio; y = years.
*p < .05; **p < .01; ***p < .001.

the symptom scales at 3 and 6 years, respectively, were 0.54 and 0.69 for depression, 0.80 and 0.85 for anxiety, 0.89 and 0.88 for ADHD, and 0.83 and 0.72 for ODD.

Early Childhood Inventory–4. The Early Childhood Inventory–4 (ECI-4) is a parent rating scale used to screen *DSM-IV* emotional and behavioral disorders in 3- to 6-year-olds.[24] Parents completed the ADHD and ODD sections of the inventory when children were 3 years old. Sprafkin *et al.*[25] reported that the correct classification rates for ADHD and ODD with respect to chart diagnoses were 60% and 74%, respectively. In the present sample, coefficient α values for the ECI-4 were 0.79 (ADHD-inattention), 0.82 (ADHD-hyperactivity/impulsivity), and 0.85 (ODD).

Owing to concerns about administration time, in the first 53.2% of this sample (n = 246) at 3 years, the interviewer used the ECI-4 ADHD and ODD scales as a screen to help determine whether to complete the ADHD and ODD sections of the PAPA. All ECI-4 ODD and ADHD items were reviewed by the interviewers. When parent reports on the ECI-4 indicated a low likelihood of ODD or ADHD symptoms (i.e., most items were endorsed as "never" or "sometimes"), interviewers probed the broad domains of oppositionality, inattention, hyperactivity, and impulsivity to confirm the absence of symptoms before skipping out. When parent reports on the ECI-4 indicated a potential likelihood of ODD or ADHD symptoms (i.e., items endorsed as "often" or "very often"), the corresponding PAPA sections were administered in their entirety. In the remaining 46.8% of the sample (n = 216) and in the entire sample at 6 years, the PAPA ADHD and ODD sections were administered to all parents. Importantly, all results were similar for the subsamples that did and did not receive the full ADHD and ODD sections. ADHD and ODD dimensional scores were estimated for children for whom these sections were skipped using the ECI-4 ADHD and ODD items and maximum likelihood estimation procedures for missing values.[26] This is less biased than pairwise and list-wise deletion procedures, even with large amounts of missing data.[27]

Functional Impairment. The PAPA interviewer completed the Children's Global Assessment Scale and functional impairment ratings after administration of the PAPA. The Children's Global Assessment Scale is a global measurement of children's level of functioning.[28] Scores range from 0 to 100, with 0 indicating the worst functioning and 100 indicating superior functioning. The inter-rater reliabilities (intraclass correlation coefficients) for the Children's Global Assessment Scale ratings were 0.92 and 0.86 at 3 and 6 years old, respectively. At 3 years, impairment also was rated across several domains (parental relationship quality, household and recreational activities, sibling relationships, peer relationships, daycare/school life) on a 3-point impairment scale (0 = none, 1 = partial, 2 = severe). Ratings were summed across all domains for a total impairment rating. At 6 years, impairment was rated across similar domains on a 5-point scale ranging from 0 (very good functioning/no impairment) to 4 (very poor functioning/severe impairment) and summed across domains for a total impairment rating.

Parental Psychopathology. At the 3-year assessment, children's biological parents were interviewed using the Structured Clinical Interview for *DSM-IV*, Non-Patient Version.[29] Interviews were conducted by telephone, which yields similar results as face-to-face interviews,[30] by 2 master's-level raters. Structured Clinical Interview for *DSM-IV* sessions were obtained from 459 (99.4%) mothers and 385 (83.3%) fathers. When parents were unavailable, family history interviews were conducted with the co-parent (1 mother and 70 fathers). Based on audiotapes of 30 Structured Clinical Interview for *DSM-IV* interviews, κ values for inter-rater reliability of lifetime diagnoses were 0.93 for any depressive disorder, 0.91 for anxiety disorder, and 1.00 for substance abuse/dependence.

Of the children, 194 (42.5%) had at least 1 parent with a lifetime depressive disorder, including 152 (33.0%) mothers and 79 (17.4%) fathers; 210 children (45.7%) had a parent with a lifetime anxiety disorder, including 154 (33.5%) mothers and 95 (20.9%) fathers; and 235 children (51.5%) had a parent with a lifetime substance abuse or dependence disorder, including 106 (23.0%) mothers and 179 (39.3%) fathers.

Data Analyses

Binary logistic regression analyses were conducted to examine concurrent and longitudinal associations between irritability and the 4 psychiatric diagnoses (any depressive disorder, any anxiety disorder, ADHD, and ODD). Odds ratios (ORs) provide the effect size estimate. Separate models were run for each of the 4 diagnoses. The irritability measurement was standardized (*z* score) and entered as the independent variable. All models included child age, gender, and parental education as covariates. Models predicting longitudinal outcomes at 6 years were adjusted for all 4 groups of baseline disorders at 3 years (any depression, any anxiety, ADHD, and ODD). To ensure that irritability symptom criteria did not account for the predictive associations between irritability and psychiatric disorders, the authors used nonoverlapping symptom scales of depression, anxiety, ADHD, and ODD with all irritability items removed as outcomes in the 4 additional linear regression models.

Functional impairment ratings at 6 years were used as dependent variables in linear regression models, including unadjusted models, models adjusted for psychiatric disorders at 3 years, and models adjusted for psychiatric disorders at 6 years. Logistic regression analyses were used to examine longitudinal associations between irritability and parental psychopathology.

RESULTS

Table 2 presents significant concurrent associations between irritability at 3 years with all diagnoses and functional impairment at 3 years. There were significant concurrent associations between irritability at 6 years and any depression, ADHD, and ODD and greater functional impairment at 6 years. Symptoms of chronic irritability demonstrated moderate stability (Spearman $\rho = 0.38$, $p < .001$).

Parent-Rated Irritability at 3 Years as Predictor of Psychiatric Disorders at 6 Years

Table 3 presents associations between irritability at 3 years and disorders at 6 years, unadjusted and adjusted for disorders at 3 years. In unadjusted models, irritability at 3 years significantly predicted any depression, any anxiety disorder, ADHD, and ODD at 6 years. After controlling for all 4 groups of psychiatric disorders at 3 years, irritability at 3 years remained a significant predictor of any depressive disorder and ODD at 6 years.

Irritability at 3 Years as Predictor of Nonoverlapping Symptom Scores at 6 Years

Controlling for the effect of item overlap, the authors examined whether irritability at 3 years predicted nonoverlapping symptom scales at 6 years (Table 4). In unadjusted models, irritability at 3 years predicted depression, anxiety, ADHD, and ODD symptom scores at 6 years. After adjusting for symptoms scales at baseline, irritability at 3 years continued to predict depression and ODD symptoms at 6 years.

Irritability at 3 Years as Predictor of Functional Impairment at 6 Years

Irritability at 3 years predicted significantly higher ratings of impairment and lower Global Assessment of Functioning scores at 6 years (Table 5). These associations remained significant after controlling for psychiatric disorders at 3 and 6 years of age.

TABLE 3 Parent-Rated Irritability at 3 Years of Age as Predictor of *DSM-IV* Disorders at 6 Years

	Not Adjusted		Adjustment for Emotional and Behavioral Disorders at 3 y	
Disorder at 6 y old	**Odds Ratio**	**95% CI**	**Odds Ratio**	**95% CI**
Depressive disorder	1.65**	1.23–2.22	1.96***	1.35–2.85
Anxiety disorder	1.32*	1.06–1.64	1.30†	0.97–1.76
ADHD	1.39*	1.02–1.91	0.90	0.52–1.56
ODD	1.90***	1.49–2.43	1.54*	1.09–2.16

Note: All logistic regression models controlled for age, sex, and parental education. Adjustment for disorders at 3 years of age included depression, anxiety, attention-deficit/hyperactivity disorder (ADHD), and oppositional defiant disorder (ODD). y = years.

†$p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$.

TABLE 4 Irritability at 3 Years of Age as Predictor of Nonoverlapping Symptom Scores at 6 Years

	Not Adjusted		Adjustment for Corresponding Scale at 3 y old	
Symptoms at 6 y old	**B (SE)**	**β**	**B (SE)**	**β**
Depressive symptom scale	0.22 (0.05)	0.22***	0.14 (0.05)	0.14**
Anxiety symptom scale	0.16 (0.05)	0.16**	0.02 (0.04)	0.02
ADHD symptom scale	0.17 (0.05)	0.17***	0.01 (0.04)	0.01
ODD symptom scale	0.36 (0.04)	0.36***	0.10 (0.05)	0.10*

Note: All linear regression models controlled for age, sex, and parental education. ADHD = attention-deficit/hyperactivity disorder; ODD = oppositional defiant disorder; y = years.
*p < .05; **p < .01; ***p < .001.

Associations With Parental Psychopathology

Irritability at 3 years was significantly associated with parental lifetime depressive (OR 1.32, 95% confidence interval [CI] 1.09–1.60, $p = .01$) and anxiety (OR 1.35, 95% CI 1.11–1.64, $p < .01$) disorders. No significant association was observed for parental lifetime substance use disorder (OR 1.14, 95% CI 0.94–1.38, $p = .18$). Child irritability at 6 years was significantly associated with a parental lifetime depressive disorder (OR 1.23, 95% CI 1.02–1.48, $p = .03$). No significant associations were observed for parental lifetime anxiety (OR 1.13, 95% CI 0.93–1.36, $p = .22$) or substance use disorder (OR 1.16, 95% CI 0.96–1.41, $p = .12$).

DISCUSSION

Although there has been growing clinical and scientific interest in chronic irritability in youth, many key questions remain regarding the course and clinical significance of irritability, particularly during early childhood, a period with important implications for early prevention and intervention.[1,3] Using data from a large, community sample of preschoolers, the authors examined symptoms of chronic irritability from 3 to 6 years of age, including concurrent and longitudinal associations between preschool irritability and psychopathology, functional impairment, and family history of psychopathology.

The authors found that chronic irritability during early childhood was associated with a wide range of psychiatric disorders and functional impairment concurrently and prospectively. However, after controlling for baseline disorders, irritability at 3 years predicted only depression and ODD at 6 years. Moreover, in parallel longitudinal analyses using dimensional scales that excluded any overlapping items between irritability and psychiatric diagnoses, the authors found that irritability continued to predict only symptoms of depression and ODD, suggesting that the present findings were not due to content overlap. The authors also found that irritability at baseline predicted children's functional impairment 3 years later; this association remained after controlling for diagnoses at baseline and concurrent diagnoses at follow-up. Moreover, child irritability was associated with a family history of depression and anxiety.

Using this sample, the authors previously reported that rates of disorders and patterns of homotypic and heterotypic continuity are similar to those observed in samples of older children.[17,19] The present study extends those findings by showing that chronic irritability in preschool predicted the emergence of new cases of depressive disorders and ODD at 6 years over and above continuity in psychiatric diagnoses over time.

Few studies of the course and outcome of youth irritability have focused on early childhood. Consistent with the present findings, studies of older youth have reported that irritability is concurrently[7] and longitudinally[6] associated with emotional and behavioral disorders in adolescence. In contrast, long-term follow-up studies of irritability in older youth have found that it predicts only emotional disorders in adulthood.[4,7] Taken together, these findings suggest developmental differences in the trajectories of irritability-psychopathology associations across the lifespan. Nevertheless, it is also possible that this pattern reflects the fact that there is no diagnostic equivalent of ODD in adulthood. The present finding that preschool irritability predicted ODD even after controlling for diagnoses at 3 years of age is particularly striking because ODD predicts depression in adulthood over and above depression in childhood.[12] Thus, irritability also likely plays a role

TABLE 5 Irritability at 3 Years of Age as Predictor of Functional Impairment at 6 Years

	Impairment Ratings at 6 y old		GAF at 6 y old	
Adjustment for disorders	**B (SE)**	**β**	**B (SE)**	**β**
Not adjusted	1.20 (0.17)	0.31***	−3.38 (0.49)	−0.30***
Adjusted for disorders at 3 y old	0.95 (0.21)	0.25***	−2.95 (0.62)	−0.26**
Adjusted for disorders at 6 y old	0.51 (0.14)	0.13***	−1.35 (0.41)	−0.12**

Note: All linear regression models controlled for age, sex, and parental education. Adjustment for disorders at 3 and 6 years of age included depression, anxiety, attention-deficit/hyperactivity disorder, and oppositional defiant disorder. GAF = Global Assessment of Functioning; y = years.
**p < .01; ***p < .001.

in concurrent and longitudinal associations between ODD and depression.[8,9]

These findings also suggest that irritability is a risk factor shared by internalizing and externalizing disorders in early childhood, perhaps increasing the risk for each and for their co-occurrence. Similarly, neuroticism in adults, which includes aspects of irritability, demonstrates strong and consistent associations with internalizing and externalizing disorders and might serve as a common underlying risk factor in psychopathology.[31,32] Thus, irritability may be an important phenotype that crosses diagnostic categories and may help identify unique and overlapping mechanisms in youth psychopathology.

Preschool irritability also was associated with concurrent and predictive ratings of children's functional impairment. Perhaps surprisingly, chronic irritability demonstrated unique predictive power over and above baseline diagnoses and concurrent diagnoses at 6 years of age. These findings strongly argue for the early identification of irritability in young children and the importance of intervening as soon as possible. Furthermore, understanding the processes by which irritability in young children leads to impairment is critical for developing effective interventions for this high-risk group. For instance, child irritability is likely to evoke negative reactions from parents, siblings, and peers that then may promote additional maladaptive child behaviors.

The authors also examined whether early chronic irritability is associated with parental psychopathology. They found that irritability was specifically linked to family histories of depression and anxiety. Similarly, Krieger *et al.*[33] recently reported that the irritability dimension of oppositional symptoms was associated with family history of depression in a large Brazilian sample of 6- to 12-year-old children. These findings also are consistent with evidence linking youth irritability to subsequent depressive and anxiety disorders[4,7] and supports conceptualizing irritability as closely related to mood and anxiety disorders. Based on a twin study, Stringaris *et al.*[10] found that the association between irritability and depression was largely explained by common genes. It will be important to investigate the mechanisms by which parental depression and anxiety are related to offspring's irritability in early childhood, including genetic and environmental mechanisms (e.g., parenting), either or both of which may influence affective processing and the associated neural circuitry in parents and offspring.

This study has several strengths. First, child psychopathology and irritability were assessed using a comprehensive interview, which allowed the authors to take into account the intensity, frequency, and duration of irritability. Second, a dimensional construct of youth irritability was used, as the boundaries between clinically significant irritability and normative irritability, particularly in preschoolers, continue to be investigated.[16] This approach is consistent with the National Institute of Mental Health Research Domain Criteria project, which aims to identify new ways to classify behavior based on dimensional measurements of behavior and neurobiological processes.[34] Third, a community sample of preschoolers was used, which is important because irritability is common in the course of typical development.

The study has several limitations. First, assessments of irritability and psychiatric diagnoses were based on parent report. It would be preferable to incorporate data from multiple sources to minimize shared method variance. Second, there is currently no validated measurement of chronic irritability for preschoolers; the authors derived a measurement of chronic irritability based on responses in a diagnostic interview. Third, the children who participated in the assessment at 6 years of age were less likely to

have a depressive disorder at baseline. The implications of this attrition are unknown but raise the possibility that the present findings underestimate the association between irritability and depression. Fourth, conduct disorder was not examined; including it may have yielded a different pattern of associations. Data suggest that youth oppositionality is comprised of at least 2 dimensions with different outcomes: an irritability dimension associated with depression and a headstrong/hurtful dimension associated with antisocial behaviors.[8,9]

Fifth, a screener for ADHD and ODD was used to shorten administration time for a portion of the sample at baseline. However, given the interviewers' confirmation of negative screen results, the false negative rate was probably low. In addition, results were comparable for the 2 portions of the sample. Nonetheless, the use of the screener might have resulted in some additional error variance. Sixth, the sample was largely white and middle class. Future research should extend this research to more ethnically and socioeconomically diverse samples.

In closing, the present findings underscore the clinical implications of irritability in early childhood. Preschool irritability was associated with parental depression and anxiety and predicted depression, ODD, and functional impairment 3 years later even after controlling for baseline disorders. Further work on irritability in preschoolers may help refine how preschool mental health problems are classified and treated. Specifically, more longitudinal work is needed to delineate the processes through which preschool irritability develops into adolescent and adult phenotypes. Future research also needs to examine the mechanisms involved in early chronic irritability, including genetic and environmental influences, and the associated affective and cognitive processes and neural circuitry. &

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