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

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### Abstract

**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 ages 3 and 6. Child psychopathology was assessed at baseline (age 3) and follow-up (age 6) using a diagnostic interview, the Preschool Age Psychiatric Assessment (PAPA), with parents. Items from the PAPA were used to create a dimensional measure of chronic irritability. Parental psychopathology was assessed with a diagnostic interview at baseline.

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**Results**—Chronic irritability was concurrently associated with a wide range of psychiatric disorders and functional impairment at ages 3 and 6. Age 3 irritability predicted age 6 depression, oppositional defiant disorder, and functional impairment after controlling for baseline disorders. Irritability was also 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.

### Keywords

irritability; longitudinal; mood dysregulation; preschool

## Introduction

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

Irritability has been defined as a mood of easy annoyance and touchiness characterized by anger and temper outbursts.<sup>1</sup> Recent investigations of youth irritability<sup>1,3</sup> indicate 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; prevalence estimates range from 3.3% to 5.0% in epidemiological samples.<sup>4,5</sup> Additionally, a few recent studies have documented associations between irritability and risk for later psychopathology. Studies utilizing 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 both early<sup>4,6</sup> and later adulthood.<sup>7</sup> Moreover, youth irritability has been associated with significant impairment even in the absence of psychiatric disorders<sup>5</sup> and predicted lower income and less educational attainment in a 20-year follow-up.<sup>7</sup>

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.<sup>8,9,10</sup> Facets of irritability have also been associated with externalizing behaviors.<sup>4,6,7,11</sup> 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.<sup>12</sup>

Although these studies provide compelling evidence linking irritability to a poor longterm course, significant gaps in the literature persist. Existing studies have focused on schoolage

children through adolescence and adulthood; little work has examined chronic irritability during early childhood. Irritability comprises a key facet of temperamental negative affect (e.g. anger, frustration), which emerges early in life<sup>13,14</sup> and is linked to later psychopathology.<sup>11,15</sup> 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, even though periods of irritability are common in early childhood, more frequent bouts of irritability appear to hold clinical utility in identifying high-risk children.<sup>16</sup> 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,<sup>4,6,7</sup> we used data from a large, community sample of preschoolers followed longitudinally from age 3 to age 6 to extend previous studies by examining the predictive validity and clinical significance of chronic irritability in early childhood.

Our first aim was to examine whether chronic irritability at age 3 predicts *DSM-IV* disorders and functional impairment at age 6 in unadjusted models and in models adjusting for disorders at baseline. The adjusted models tested whether irritability at age 3 predicts the emergence of new psychiatric diagnoses at age 6 over and above homotypic and heterotypic continuity.<sup>8</sup> We also examined cross-sectional associations between irritability and *DSM-IV* disorders and functional impairment at age 3 and at age 6. Based on prior work in older youth, we hypothesized that although symptoms of chronic irritability would demonstrate wide-ranging cross-sectional associations, irritability at age three would prospectively predict depression and anxiety at age 6, given research demonstrating that chronic youth irritability shows strong associations with emotional disorders.<sup>7,9,10,18</sup> We also hypothesized that irritability would prospectively predict ODD, as evidence suggests that irritability has pronounced associations with emotional *and* behavioral problems in youths.<sup>4,6,7,18</sup> Lastly, we hypothesized that chronic irritability at age 3 would predict greater functional impairment at age 6, even after accounting for psychiatric disorders at baseline and follow-up.

As 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, we also conducted a series of parallel analyses using irritability at age 3 to predict non-overlapping dimensional symptom scales of depression, anxiety, attention-deficit/hyperactivity disorder (ADHD) and ODD at age 6. The scales were created by excluding irritability items from the symptom scales to confirm our findings on the unique predictive associations of irritability with psychiatric disorders at age 6.

Our 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<sup>4,6,7</sup> as well as a twin study supporting a genetic association between irritability and depression,<sup>11</sup> we hypothesized that chronic irritability would be linked with a family history of depression and anxiety.

## Method

### Participants

We recruited families with a three-year-old child living within 20 contiguous miles of Stony Brook University (SBU) for a study of temperament and psychopathology.<sup>19</sup> Potential

participants were identified via a commercial mailing list; eligible families had a child between 3 and 4 years of age with no significant medical conditions or developmental disabilities, and at least one 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 <sup>8,19,20</sup> for details about the recruitment procedures and sample characteristics). Census data suggest the sample is reasonably representative of the surrounding county, where 79.0% of individuals were Caucasian/non-Hispanic; and 48.1% of adults aged 25–54 graduated from college. The study was approved by the SBU human subjects review committee. Informed consent was obtained from parents, and families were compensated for participating.

Of the 541 families, 531 parents (in almost all cases the primary caretaker) were interviewed regarding their 3-year-old child ( $M=3.6$  years,  $SD=0.3$ ); a parent of 462 children (85.4%) was interviewed again when the child was six-years old ( $M=6.1$  years,  $SD=0.4$ ). Children who completed both assessments were compared to children who completed only the first assessment on age 3 demographic variables and diagnoses. There was only one significant difference: 85.9% of children without depression at age 3 participated at age 6 (456/531) whereas only 60.0% of children with depression at age three (6/10) participated at age 6,  $\chi^2(1, N=541)=5.27, p<.05$ .

## Measures

**Child Irritability and Psychiatric Disorders**—The Preschool Age Psychiatric Assessment (PAPA)<sup>21</sup> is a parent-based structured diagnostic interview designed to assess a range of *DSM-IV* psychiatric disorders in preschoolers ages 2 to 6. As described elsewhere,<sup>8,20</sup> *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. 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 prior to the interview are rated to maximize recall. For information on the interview's psychometric properties, see Egger *et al.*<sup>21</sup>

At age 3, 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 1–2 hours and were conducted by telephone. Based on 21 randomly selected audiotaped interviews that oversampled participants with psychopathology, kappas were 1.00 for all diagnostic categories at age 3. At age 6, interviews were conducted by an M.A.-level clinician with training on the PAPA. This interviewer was not aware of the results of the age 3 interview. At age 6, 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.<sup>22</sup> Based on 35 audiotapes, kappas for age 6 diagnoses were: depression (.64), any anxiety disorder (.89), ADHD (.64) and ODD (.87). See Bufferd *et al.*<sup>21</sup> for a complete description of the rates of psychiatric disorders at ages 3 and 6 years.

Six items from the PAPA were used to assess irritability in children at ages 3 and 6. Items corresponded to items from the Affective Reactivity Index, a parent-and child-reported chronic irritability scale for older youth.<sup>18</sup> The PAPA items used were:

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 or more 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).

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 2 or higher indicates that the symptom was present at a threshold level of intensity. Frequency items reflect the number of occurrences during the last three months. Following Brotman *et al.*<sup>4</sup> and Copeland *et al.*<sup>23</sup>'s guidelines for chronic irritability, 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 at least a 30-minute duration on irritable mood, prone to frustration, annoyance or anger, or difficulty to recover 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 above. 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 alpha coefficient of internal consistency for the measure of irritability was .73 at both assessments.

Given that the individual PAPA items used to derive the irritability scale were also used to derive diagnoses for any depressive disorder, any anxiety disorder, and ODD, we created “non-overlapping” 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 as there were no overlapping items. Inter-rater reliability, as indexed by the intraclass correlation coefficient (ICC), for the symptom scales at ages 3 and 6, respectively, were: depression (.97 and .95), anxiety (.99 and .70), ADHD (.99 and .97), and ODD (.99 and .97). Internal consistency ( $\alpha$ ) of the symptom scales at ages 3 and 6, respectively, were: depression (.54 and .69), anxiety (.80 and .85), ADHD (.89 and .88) and ODD (.83 and .72).

**Early Childhood Inventory–4 (ECI-4)**—The ECI-4 is a parent rating scale used to screen *DSM-IV* emotional and behavioral disorders in 3- to 6-year-olds.<sup>24</sup> Parents completed the ADHD and ODD sections of the inventory when children were 3 years. Sprafkin *et al.* reported that the correct classification rates for ADHD and ODD with respect to chart diagnoses were 60% and 74%, respectively.<sup>25</sup> In the present sample, coefficient alphas for the ECI-4 were .79 (ADHD-Inattention), .82 (ADHD-Hyperactivity/Impulsivity), and .85 (ODD).

Due to concerns about administration time, in the first 53.2% of this sample ( $n = 246$ ) at age 3 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 age 6, 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.<sup>26</sup> This is less biased than pairwise and listwise deletion procedures, even with large amounts of missing data.<sup>27</sup>

**Functional Impairment**—The PAPA interviewer completed the Children’s Global Assessment Scale (CGAS) and functional impairment ratings following the administration of the PAPA. The CGAS is a global measure of children’s level of functioning.<sup>28</sup> Scores range from 0–100, where 0 indicates the worst functioning and 100 indicates superior functioning. The interrater reliability (ICC) for the CGAS ratings was .92 and .86 at ages 3 and 6, respectively. At age 3, impairment was also 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 age 6, 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 age 3 assessment, children’s biological parents were interviewed using the Structured Clinical Interview for *DSM-IV*, Non-patient version (SCID-NP).<sup>29</sup> Interviews were conducted by telephone, which yields similar results as face-to-face interviews,<sup>30</sup> by 2 Masters-level raters. SCIDs were obtained from 459 (99.4%) mothers and 385 (83.3%) fathers. When parents were unavailable, family history interviews were conducted with the coparent (one mother and 70 fathers). Based on audiotapes of 30 SCID interviews, kappas for inter-rater reliability of lifetime diagnoses were .93 for any depressive disorder; .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; 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 four psychiatric diagnoses (any depressive disorder, any anxiety disorder, ADHD and ODD). Odds ratios (OR) provide the effect size estimate. Separate models were run for each of the four diagnoses. The irritability measure 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 age 6 were adjusted for all four groups of baseline disorders at age 3 (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, we used non-overlapping symptom scales of depression, anxiety, ADHD and ODD with all irritability items removed as outcomes in four additional linear regression models.

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

## Results

Table 2 shows significant concurrent associations between irritability at age 3 with all age 3 diagnoses and functional impairment. There were significant concurrent associations between age 6 irritability and any depression, ADHD, and ODD and greater functional impairment at age 6. Symptoms of chronic irritability demonstrated moderate stability (Spearman's  $\rho=.38$ ,  $p<.001$ ).

### Parent-rated Irritability at Age 3 as Predictor of Psychiatric Disorders at Age 6

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

### Irritability at Age 3 as Predictor of Nonoverlapping Symptom Scores at Age 6

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

### Irritability at Age 3 as Predictor of Functional Impairment at Age 6

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

### Associations With Parental Psychopathology

Irritability at age three was significantly associated with parental lifetime depressive (OR=1.32,  $p=.01$ , 95% CI=1.09–1.60) and anxiety (OR=1.35,  $p<.01$ , 95% CI=1.11–1.64) disorders. No significant association was observed for parental lifetime substance use disorder (OR=1.14,  $p=.18$ , 95% CI=.94–1.38). Child irritability at age 6 was significantly associated with a parental lifetime depressive disorder (OR=1.23,  $p=.03$ , 95% CI=1.02–1.48). No significant associations were observed for parental lifetime anxiety (OR=1.13,  $p=.22$ , 95% CI=.93–1.36) or substance use disorder (OR=1.16,  $p=.12$ , 95% CI=.96–1.41).



## Discussion

While 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.<sup>1,3</sup> Using data from a large, community sample of preschoolers, we examined symptoms of chronic irritability from ages 3 to 6, including concurrent and longitudinal associations between preschool irritability and psychopathology, functional impairment, and family history of psychopathology.

We 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 age 3 predicted only depression and ODD at age 6. Moreover, in parallel longitudinal analyses utilizing dimensional scales that excluded any overlapping items between irritability and psychiatric diagnoses, we found that irritability continued to predict only symptoms of depression and ODD, suggesting that our findings were not due to content overlap. We also found that irritability at baseline predicted children's functional impairment three years later; this association remained after controlling for diagnoses at baseline and concurrent diagnoses at follow-up. Lastly, child irritability was associated with a family history of depression and anxiety.

Using this sample, we previously reported that the rates of disorders and patterns of homotypic and heterotypic continuity are similar to those observed in samples of older children.<sup>8,20</sup> The present study extends these findings by showing that chronic irritability in preschool predicted the emergence of new cases of depressive disorders and ODD at age 6, 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 our findings, studies of older youth have reported that irritability is concurrently<sup>7</sup> and longitudinally<sup>6</sup> associated with both 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.<sup>4,7</sup> 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. Our finding that preschool irritability predicted ODD even after controlling for age three diagnoses is particularly striking since ODD predicts depression in adulthood over and above depression in childhood.<sup>13</sup> Thus, irritability also likely plays a role in concurrent and longitudinal associations between ODD and depression.<sup>9,10</sup>

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

Preschool irritability was also 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 age 6. These findings strongly argue for the early identification of irritability in young children and the importance of intervening as early as possible. Furthermore, understanding the processes

by which irritability in young children lead 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 may then promote additional maladaptive child behaviors.

We also examined whether early chronic irritability is associated with parental psychopathology. We found that irritability was specifically linked to family histories of depression and anxiety. Similarly, Krieger *et al.*<sup>33</sup> 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 are also consistent with evidence linking youth irritability to subsequent depressive and anxiety disorders,<sup>4,7</sup> and supports conceptualizing irritability as being closely related to mood and anxiety disorders. Based on an adult twin study, Stringaris *et al.*<sup>11</sup> 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 both parents and offspring.

This study had several strengths. First, we assessed child psychopathology and irritability using a comprehensive interview, which allowed us to take into account the intensity, frequency, and duration of irritability. Second, we used a dimensional construct of youth irritability, as the boundaries between clinically significant irritability and normative irritability, particularly in preschoolers, continue to be investigated.<sup>17</sup> This approach is consistent with the National Institute of Mental Health (NIMH) Research Domain Criteria project, which aims to identify new ways to classify behavior based on dimensional measures of behavior and neurobiological processes.<sup>34</sup> Third, we used a community sample of preschoolers, which is important as irritability is common in the course of typical development.

The study also had several limitations. First, assessments of irritability and psychiatric diagnoses were both 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 measure of chronic irritability for preschoolers; we derived a measure of chronic irritability based on responses in a diagnostic interview. Third, the children who participated in the age 6 assessment were less likely to have a depressive disorder at baseline. The implications of this attrition are unknown but raise the possibility that our 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 comprises at least 2 dimensions with different outcomes; an irritability dimension associated with depression and a headstrong/hurtful dimension associated with antisocial behaviors.<sup>7,9,10</sup>

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

In closing, our 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 us refine how we classify and treat preschool mental health problems. Specifically, more longitudinal work is needed to delineate the processes through which preschool irritability develops into adolescent and adult phenotypes. Finally, future research needs to examine the mechanisms involved in early chronic irritability, including genetic and environmental influences, as well as associated affective and cognitive processes and neural circuitry.

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Table 1

## Demographic and Clinical Characteristics of the Study Sample

	Age 3 Assessment	Age 6 Assessment
<i>Demographic Characteristics</i>		
Child mean age, years (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)
Mean child irritability (0–7) (SD) range	.69 (1.27)	0–7
0–6		.80 1.35
<i>Child psychopathology n (%)</i>		
Depressive Disorder	6 (1.3)	25 (5.4)
Anxiety Disorder	89 (19.3)	72 (15.6)
ADHD	11 (2.4)	25 (5.4)
Oppositional defiant disorder	47 (10.2)	41 (8.9)
<i>Child functioning</i>		
Child mean GAF (1–100) (SD; range)	84.5 (13.76)	45–100
75.31 (11.18)		42–100
Child mean impairment ratings (SD; range)	.84 (1.45)	0–8
5.40 (3.87)		0–18
Received referrals for treatment n (%)	12 (2.6)	
<i>Parental lifetime psychopathology n (%)</i>		
Depressive Disorder	194 (42.5)	
Anxiety Disorder	210 (45.7)	

	Age 3 Assessment	Age 6 Assessment
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.

Table 2

Concurrent Associations of Parent-Rated Irritability and *DSM-IV* Diagnoses and Functioning at Ages 3 and 6

Age 3 Diagnosis	Age 3 Irritability OR (95% CI)	Age 6 Diagnosis	Age 6 Irritability OR (95% CI)
Depressive Disorder	3.38*** (1.83–6.26)	Depressive Disorder	2.17*** (1.59–2.96)
Anxiety Disorder	1.47*** (1.20–1.81)	Anxiety Disorder	1.167 (.92–1.48)
ADHD	1.53* (1.01–2.30)	ADHD	1.46* (1.06–2.00)
ODD	4.30*** (3.10–5.97)	ODD	4.76*** (3.28–6.92)
<b>Age 3 Functional Impairment</b>			
GAF	$r = -.52$ ***	GAF	$r = -.53$ ***
Impairment rating	$r = .56$ ***	Impairment rating	$r = .51$ ***

Note: All logistic regression models controlled for age, sex, and parental education. Age 3  $n=541$ ; Age 6  $n=462$ . ADHD=attention-deficit/hyperactivity disorder; GAF=Global Assessment of Functioning; ODD=oppositional defiant disorder; OR=odds ratio.

\*  $p < .05$ ;

\*\*  $p < .01$ ;

\*\*\*  $p < .001$ .

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

Disorder at Age 6	Not Adjusted		Adjustment for Emotional and Behavioral Disorders at Age 3 <sup>a</sup>	
	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 <sup>†</sup>	.97–1.76
ADHD	1.39*	1.02–1.91	.90	.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 ages 3 included depression, anxiety, attention-deficit/hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD).

<sup>†</sup>  $p < .10$ ;

\*  $p < .05$ ;

\*\*  $p < .01$ ;

\*\*\*  $p < .001$ .



**Table 4**

Irritability at Age 3 as Predictor of Non-Overlapping Symptom Scores at Age 6

Symptoms at age 6	Not Adjusted		Adjustment for corresponding age 3 scale	
	B (SE)	$\beta$	B (SE)	$\beta$
Depressive symptom scale	.22 (.05)	.22***	.14 (.05)	.14**
Anxiety symptom scale	.16 (.05)	.16**	.02 (.04)	.02
ADHD symptom scale	.17 (.05)	.17***	.01 (.04)	.01
ODD symptom scale	.36 (.04)	.36***	.10 (.05)	.10*

Note: All linear regression models controlled for age, sex, and parental education. ADHD=attention-deficit/hyperactivity disorder; ODD=oppositional defiant disorder.

\*  $p < .05$ ,

\*\*  $p < .01$ ,

\*\*\*  $p < .001$ .

**Table 5**

## Irritability at Age 3 as Predictor of Functional Impairment at Age 6

Adjustment for Disorders	Impairment ratings at age 6		GAF at age 6	
	B (SE)	$\beta$	B (SE)	$\beta$
Not adjusted	1.20 (.17)	.31***	-3.38 (.49)	-.30***
Adjusted for Disorders at age 3	.95 (.21)	.25***	-2.95 (.62)	-.26**
Adjusted for Disorders at age 6	.51 (.14)	.13***	-1.35 (.41)	-.12**

Note: All linear regression models controlled for age, sex, and parental education. Adjustment for disorders at ages 3 and 6 included depression, anxiety, attention-deficit/hyperactivity disorder, and oppositional defiant disorder. GAF=Global Assessment of Functioning; SE = standard error.

\*\*  
 $p < .01$ ,

\*\*\*  
 $p < .001$ .