Development and Psychopathology (2023), **35**, 1371–1381
doi:10.1017/S0954579421001267

CAMBRIDGE UNIVERSITY PRESS

Regular Article

Parsing between- and within-person effects: Longitudinal associations between irritability and internalizing and externalizing problems from early childhood through adolescence

Emma Chad-Friedman[1], Maria M. Galano[2], Edward P. Lemay[1], Thomas M. Olino[3], Daniel N. Klein[4] and Lea R. Dougherty[1]

[1]University of Maryland, College Park, MD, USA, [2]University of Massachusetts Amherst, MA, USA, [3]Temple University, Philadelphia, PA, USA and [4]Stony Brook University, New York, USA

Abstract

Introduction: This report examines between- and within-person associations between youth irritability and concurrent and prospective internalizing and externalizing symptoms from early childhood through adolescence. Distinguishing between- and within-person longitudinal associations may yield distinct, clinically relevant information about pathways to multifinality from childhood irritability.
Methods: Children's irritability and co-occurring symptoms were assessed across five waves between ages 3 and 15 years using the mother-reported Child Behavior Checklist ($N = 605$, 46% female). Parental history of depressive disorders was assessed with a clinical interview.
Results: Results demonstrated that between- and within-person irritability were uniquely associated with concurrent depressive, anxiety, and defiance symptoms, but not ADHD. Prior wave within-person irritability also predicted next wave depressive, anxiety, and defiance symptoms, controlling for prior symptoms; these prospective associations were bidirectional. Child sex and parental depressive disorders moderated associations.
Discussions: Findings identify pathways from within- and between-person irritability to later internalizing and externalizing psychopathology. Results demonstrate the importance of parsing within- and between-person effects to understand nuanced relations among symptoms over childhood.

Keywords: between-person effects; childhood irritability; externalizing problems; internalizing problems; within-person effects

(Received 16 April 2021; revised 28 September 2021; accepted 29 September 2021; First Published online 27 December 2021)

Childhood irritability, characterized by low frustration tolerance and temper outbursts, is common, impairing and a frequent reason for psychiatric referral (Brotman et al., 2017). Longitudinal studies consistently support links between youth irritability and later internalizing disorders, particularly depression and anxiety, and suicide in later childhood and adulthood (Orri et al., 2019; Stringaris et al., 2009; Vidal-Ribas et al., 2016). Additionally, studies have found that irritability predates the emergence of externalizing problems and the co-occurrence of internalizing and externalizing disorders in later childhood and adolescence (Eyre et al., 2019; Hawes et al., 2019; Humphreys et al., 2019) and in young children (Dougherty et al., 2013; Wakschlag et al., 2015). These findings suggest that irritability may be a nonspecific risk factor for multiple psychiatric problems (Beauchaine & Tackett, 2020).

Importantly, prior longitudinal work has largely relied on between-person approaches that compare average levels of irritability across individuals in a sample. However, it is unknown whether within-person effects are also important and exhibit similar relations to other symptom dimensions as between-person effects. Parsing within-person effects would reveal whether a child's increase in irritability relative their own mean would lead to an increase in other symptoms. In some ways, within-person effects are more clinically useful than between-person effects, as clinicians are generally concerned with change in individual patient's symptoms over time (e.g., detecting and predicting worsening symptoms, identifying and making use of factors associated with improvement). These different sources of variability are independent of one another and within-person effects may yield distinct, more specific relations between irritability and later psychopathology (Curran & Bauer, 2011).

Associations between youth irritability and psychiatric symptoms

In terms of concurrent associations, irritability consistently co-occurs with depression, anxiety, oppositional defiant disorder (ODD), and attention-deficit/ hyperactivity disorder (ADHD; Brotman et al., 2017). Prospectively, robust evidence supports irritability as a predictor of later internalizing disorders, yet the literature has not reached consensus on whether irritability is a meaningful risk factor for later ODD or ADHD after accounting

Corresponding author: Lee R. Dougherty, email: ldougher@umd.edu
Cite this article: Chad-Friedman, E., *et al.* (2023). Parsing between- and within-person effects: Longitudinal associations between irritability and internalizing and externalizing problems from early childhood through adolescence. *Development and Psychopathology* **35**: 1371–1381, https://doi.org/10.1017/S0954579421001267

for item-overlap and prior symptoms. According to a recent meta-analysis, children with high levels of irritability incur an almost two-fold risk of developing later internalizing psychopathology (Vidal-Ribas et al., 2016). While this meta-analysis also found that children with high levels of irritability are at increased risk for ODD, the authors noted shared item overlap may explain this link. Furthermore, there was minimal support for prospective links between irritability and later ADHD (Vidal-Ribas et al., 2016). Similarly, we previously reported in the current sample that chronic irritability at age 3 predicted ADHD at age 6 years old, but the association was no longer significant after adjusting for a prior diagnosis of ADHD (Dougherty et al. 2013). Thus, irritability may not be a unique predictor of later ADHD after accounting prior ADHD and co-occurring symptoms.

Despite prior work on associations between irritability and psychiatric symptoms, little work has examined unique associations, controlling for co-occurring psychopathology, from early childhood through adolescence. This is important because irritability is a symptom of multiple disorders, including depression, ODD, and anxiety. Therefore, it is necessary to separate irritable from non-irritable symptoms to determine their unique predictive validity over and above non-irritable symptoms, on later psychopathology; otherwise, associations could merely reflect overlap with co-occurring internalizing and externalizing problems. Furthermore, little work has examined the directionality of these associations. Prior findings show that irritability in middle childhood predicts later internalizing symptoms in adolescence, but not vice versa, whereas irritability and internalizing problems demonstrate bidirectional associations in later adolescence and early adulthood (Savage et al., 2015). A bidirectional association has also been found between irritability and externalizing symptoms at ages 3 and 12 years, controlling for age 3 internalizing symptoms, but only in the context of blunted diurnal cortisol (Kessel et al., 2019). More work is needed examining the directionality of associations between irritability and non-irritable symptoms of internalizing and externalizing symptoms throughout childhood and adolescence to identify unique and shared pathways to psychological dysfunction.

Between- and within-person effects

Between- and within-person effects provide complementary, distinct, and sometimes opposite information (Curran & Bauer, 2011; Wang & Maxwell, 2015). Between-person variability reflects individual differences in irritability and psychopathology between individuals. In contrast, within-person variability captures how irritability and other psychopathology fluctuate within the same individual over time (Curran & Bauer, 2011). Despite prior models largely relying on between-person data, a fundamental question in irritability and developmental psychopathology research more generally, is a within-person question: *when* a child experiences an increase in irritability, are they more likely to experience an increase in other symptoms? This question can only be answered with a within-person design. For example, a child may exhibit high levels of irritability and depressive symptoms relative to their peers (between-person effect); however, we cannot infer from this between-person effect that *when* children experience irritability, they are more likely to experience depression symptoms (within-person effect). By examining change in repeated assessments over time, within-person models can test this within-person hypothesis, which may elucidate transient factors that may be responsible for changes in the severity of psychiatric symptoms. Thus, parsing within-person effects could yield unique information about how the child's irritability compared to their typical functioning contributes to developmental pathways of psychopathology.

Prior work examining within-person change in irritability have used latent class analyses to identify distinct trajectories of irritability across childhood (Ezpeleta et al., 2016; Forte et al., 2021; Galera et al., 2021; Orri et al., 2018, 2019; Pagliaccio et al., 2018; Wiggins et al., 2014). These studies linked different developmental trajectories of irritability (increasing, declining, and stable) to mental health outcomes in childhood, adolescence, and early adulthood (Caprara et al., 2007; Ezpeleta et al., 2016; Galera et al., 2021; Orri et al., 2018, 2019; Pagliaccio et al., 2018). While these prior studies focused on classes of irritability trajectories over time, no study, to our knowledge, has examined whether within-person change predicts within-person change in other symptoms over time. This fine-grained approach captures the dynamic unfolding of irritability alongside other symptoms over time. Furthermore, no work has parsed both within- and between-person levels of irritability and examined their unique effects on later psychiatric symptoms across childhood and adolescence.

Current study

We filled this important gap by examining the effects[1] of time-invariant between-person differences and time-varying within-person changes in childhood irritability on depressive, anxiety, ADHD, and defiance symptoms from early childhood through adolescence. We examined these aims in a community sample of 605 children from the Stonybrook Temperament Study (Klein & Finsaas, 2017). At ages 3, 6, 9, 12, and 15 years old, mothers completed the parent-report Child Behavior Checklist (CBCL) which yielded non-overlapping measures of irritability, depression, anxiety, ADHD, and defiance (Achenbach & Rescorla 2001). We examined 1) concurrent between- and within-person associations between irritability and depressive, anxiety, ADHD, and defiance symptoms, adjusting for co-occurring symptoms across five waves and 2) prospective bidirectional within-person associations between childhood irritability and internalizing and externalizing symptoms, adjusting for prior symptoms.

We hypothesized that higher levels of between-person and greater variability in within-person irritability would be concurrently associated with greater depressive, anxiety, ADHD, and defiance symptoms and that greater within-person irritability would predict greater next wave depression, anxiety, and defiance, controlling for prior levels of internalizing and externalizing symptoms and these effects may be bidirectional, though prior literature is sparse. We did not expect within-person irritability to predict next wave ADHD, given findings that prior ADHD accounts for longitudinal links between irritability and later ADHD (Dougherty et al. 2013; Vidal-Ribas et al. 2016).

We also explored the moderating roles of child sex and parental depressive disorders on associations between irritability (between- and within-person effects) and internalizing and externalizing symptoms. Some findings support sex differences in associations between irritability and internalizing and externalizing problems at different developmental periods. In childhood, males showed stronger co-occurring trajectories of irritability and internalizing symptoms than females (Orri et al., 2018). In adolescence, females showed stronger concurrent associations between irritability and internalizing symptoms than males, but similar concurrent and longitudinal associations between irritability and externalizing

[1]The use of the word "effect" does not imply causation.

https://doi.org/10.1017/S0954579421001267 Published online by Cambridge University Press

symptoms (Humphreys et al., 2019). In addition, prior findings in the current sample demonstrated sex-specific pathways at an earlier assessment: chronic irritability in early childhood predicted anxiety disorders for males only and ADHD for females only at age 9 (Dougherty et al., 2015). Given limited prior work, we did not have specific hypotheses about the moderation of sex.

A history of parental depression has also been linked to childhood irritability in the current sample (Dougherty et al., 2013) and other samples (Krieger et al., 2013; Wiggins et al., 2014); it is also a well-established risk factor for both internalizing and externalizing problems in offspring (Goodman, 2007; Goodman & Gotlib, 1999; Klein et al., 2005; Weijers et al., 2018; Weissman et al., 2006, 2016). Given that parents with depression are more likely to have both irritability and other forms of psychopathology (Steffen et al., 2020), associations between youth irritability and other symptoms may be strongest in high-risk offspring. Parents with depression may also use less positive parenting, more negative parenting, and less engagement with their children, which may limit their abilities to support the development of emotion regulation in their children (England & Sim 2009; Lovejoy et al. 2000; Tsotsi et al. 2019), placing their offspring at greater risk for maladjustment. Thus, we hypothesized that between- and within-person effects of irritability on internalizing and externalizing symptoms would be stronger in children of parents with a history of parental depressive disorders.

Methods

Participants

Participants were selected from the Stony Brook Temperament Study, a longitudinal study examining the role of early childhood temperament on the development of internalizing disorders (for detailed description see Klein and Finsaas, 2017). Families with a 3-year-old child were recruited within 20 contiguous miles of Stony Brook University and identified via commercial mailing lists. Eligible families had a child between 3 and 4 years old with no developmental disabilities or serious medical conditions and at least one English-speaking biological parent. The study was approved by the human subjects review committee. Parents provided informed consent, and after age 9 children provided assent. Families were compensated for participating in the study.

Participants were assessed at ages 3, 6, 9, 12, and 15 years-old. At baseline, 559 families entered the study and 547 mothers completed the CBCL. At the age 6 assessment, an additional 50 minority/non-White families were recruited to increase the diversity of the sample, and 467 mothers completed the CBCL; 490, 472 and 454 mothers contributed CBCL data at the age 9, age 12, and age 15 assessments, respectively. The current study included all children whose mothers completed at least one CBCL at any timepoint ($n = 605$, 45.6% female; Table 1).

Measures

Childhood psychiatric symptoms

At all timepoints, mothers completed the parent-report CBCL (Achenbach, 2000; Achenbach & Rescorla, 2001), which has been used extensively to assess children's internalizing and externalizing symptoms in longitudinal studies (Achenbach & Ruffle, 2000). The CBCL captures the past 6 months. At age 3, mothers completed the CBCL 1.5–5 (Achenbach, 2000) and at ages 6 and older, mothers completed the CBCL 6–18 version (Achenbach & Rescorla, 2001). Items on the CBCL are rated by parents on a 3-point scale (0 = never/not true; 1 = sometimes; 2 = often/very true). Scales have been previously derived from the CBCL to examine irritability and related problems without overlap. Factor analyses have identified separate empirically derived irritability and defiance factors from the CBCL (Evans et al., 2020). Research has shown that these separate dimensions (irritability and oppositionality/defiance) predict unique outcomes (Evans et al., 2020; Johnston et al., 2020; Stringaris & Goodman, 2009). To assess child irritability, we used the empirically-derived CBCL-irritability factor score (Evans et al., 2020; Roberson-Nay et al., 2015; Stringaris et al., 2012). The CBCL-irritability factor score sums three items assessing irritable mood, sudden changes in mood, and temper outbursts. The parent-report CBCL-irritability factor score has been used with children ranging from preschool-age through adolescence and demonstrates acceptable reliability, convergent validity, and structural invariance over time (Aebi et al., 2013; Roberson-Nay et al., 2015; Stringaris, Zavos, et al., 2012; Tseng et al., 2017; Wiggins et al., 2014). Internal consistency of the irritability score was acceptable across assessments (median $\alpha = .73$, range: $\alpha = .68$–$.77$). We calculated children's defiance with the three-item empirically-derived CBCL-defiance factor score, which sums three items assessing disobedience at home, disobedience at school, and a tendency to argue from the CBCL 6–18 form (Evans et al., 2020). The defiance scale items are not included in the CBCL-1.5-5 version and thus were not assessed at age 3. The defiance scale had acceptable internal consistency across assessments (median: $\alpha = .62$, range: $\alpha = .62$–$.69$).

We used the Diagnostic and Statistical Manual (DSM)-oriented CBCL scales to assess children's symptoms of depression (Affective Problems scale), anxiety (Anxiety Problems scale), and ADHD (ADHD Problems scale) (Achenbach, 2000; Achenbach & Rescorla, 2001). These scales contained no overlapping items with the CBCL-irritability factor scale. These scales had acceptable internal consistency at each timepoint (Affective Problems: median: $\alpha = .68$, range: $\alpha = .62$–$.78$; Anxiety Problems: median: $\alpha = .72$, range: $\alpha = .64$–$.76$; ADHD Problems: median: $\alpha = .83$, range: $\alpha = .76$–$.85$). Given that the different versions of the CBCL include different items, we converted the raw DSM-oriented scales into age- and sex-based T-scores, with higher scores indicating more frequent symptoms (Achenbach, 2000; Achenbach & Rescorla, 2001). Unlike standardized z-scores, T-scores are sample independent and do not remove between-person and within-person variability.

Parental lifetime depressive disorder

Children's biological parents were interviewed using the non-patient Structured Clinical Interview for DSM-IV (SCID; First et al., 2002) to assess parent's lifetime history of any depressive disorder (major depressive disorder and/or dysthymic disorder). Clinical interviews with parents were conducted at study entry, which was at the age 3 assessment for most participants and at age 6 for the additional 50 minority/non-White participants recruited at age 6. The Kappa for interrater reliability was based on 30 audio recordings and was excellent for lifetime depressive disorder (age 3 kappa = .93). Two hundred and forty children (42.2%) had at least one biological parent with a lifetime depressive disorder (215 mothers and 109 fathers).

Data analysis plan

To examine between-person and within-person associations between irritability and childhood internalizing and externalizing

https://doi.org/10.1017/S0954579421001267 Published online by Cambridge University Press

Table 1. Sample characteristics ($n = 605$)

	Age 3	Age 6	Age 9	Age 12	Age 15
	$n = 547$	$n = 467$	$n = 490$	$n = 472$	$n = 454$
Child mean age: years SD; range	3.52 (26)	6.11 (.44)	9.23 (4.19)	12.66 (.46)	15.25 (.40)
	2.92–4.17	5.13–7.67	8.38–11.00	11.50–14.17	14.44–17.65
Mother's mean age: years SD; range	35.99 (4.44)				
	20–49				
Father's mean age: years SD; range	38.26 (5.38)				
	22–60				
Child sex: female *n* (%)	254 (46.4)	208 (44.5)	224 (45.7)	222 (47)	218 (48)
Child race: *n* (%)					
White	516 (94.3)	409 (87.6)	436 (89)	423 (89.6)	409 (90.1)
Black/African-American	15 (2.7)	43 (9.2)	40 (8.2)	33 (7)	29 (6.4)
Asian	11 (2)	14 (3)	13 (2.7)	13 (2.8)	13 (2.9)
Multiracial/other	5 (.9)	1 (.2)	1 (.2)	1 (.2)	3 (.2)
Child Hispanic ethnicity[a]: *n* (%)	50 (9.1)	58 (12.4)	61 (12.4)	62 (13.1)	58 (12.8)
Biological parents' marital status[a]: *n* (%)					
Married	542 (89.6)				
Divorced, separated, or widowed	18 (3)				
Never married	43 (7.1)				
At least one parent with a 4-year college degree[a]: *n* (%)	395 (65.3)				
Household income[a]: median	$70,000–$90,000				
Parental lifetime depression	240 (42.2%)				
Maternal depression	215 (35.5%)				
Paternal depression	109 (18%)				
CBCL scores: M (SD) range					
Irritability	1.66 (1.44)	.98 (1.2)	.91 (1.28)	.76 (1.19)	.69 (1.12)
	0–6	0–5	0–6	0–6	0–6
Depression	52.71 (11.55)	48.25 (8.80)	48.73 (9.47)	47.35 (8.60)	48.47 (10.01)
	39.5–99.50	42.63–147.89	42.63–116.32	42.08–92.73	42.08–104.58
Clinical range[a]: n (%)	69 (12.4%)	19 (4%)	29 (5.8%)	69 (6.6%)	37 (8%)
Anxiety	51.25 (11.16)	47.63 (9.93)	48.58 (11.56)	47.58 (10.22)	46.93 (9.77)
	36.40–94.18	39.38–100.67	39.38–114.00	41.25–97.50	41.25–103.75
Clinical range: n (%)	57 (10.4%)	28 (5.9%)	42 (8.4%)	42 (8.8%)	27 (5.9%)
ADHD	48.01 (9.06)	45.29 (7.91)	45.94 (8.73)	46.84 (9.55)	45.43 (9.03)
	32.14–75.00	37.24–78.62	37.24–80.16	38.97–88.80	38.97–88.80
Clinical range: n (%)	21 (4%)	13 (2.9%)	20 (4.1%)	31 (5.8%)	21 (4.6%)
Defiance	–	1.16 (1.28)	1.18 (1.23)	.86 (1.14)	.75 (1.10)
		0–6	0–6	0–6	0–6

Notes: Sample includes any child whose mother completed an irritability measure at any timepoint ($N = 605$). CBCL = Child Behavior Checklist; ADHD = Attention-Deficit Hyperactivity Disorder.
[a]Clinical range is 1.5 SD above the mean.

psychopathology, we used linear mixed models (LMM; West, 2009) in IBM SPSS Statistics Version 24. LMM accounts for the unique statistical properties of repeated-measures data and uses restricted maximum likelihood to estimate conditional parameters and accommodate missing data (West, 2009). While all data were included in concurrent analyses, 70 participants with only one wave of data were excluded from prospective models.

To assess between-person effects of the time-varying predictor variables (i.e., irritability, depression, anxiety, ADHD, and defiance), we calculated the participant's average score across all time points. These person-means were centered on the grand mean and entered as predictors in the models. Given that they vary across people, but not across waves, effects of these predictors reflect only between-person effects (Enders & Tofighi, 2007). To assess within-

https://doi.org/10.1017/S0954579421001267 Published online by Cambridge University Press

person effects of these time-varying predictors, we used person-mean centering for which each assessment at a particular time point was centered on the participant's mean value across all of his/her assessments. Each of the symptom scores thus reflected the difference between the child's overall individual average score across all timepoints and the score at a given timepoint. These person-centered variables vary within people across time, but do not contain between-person variance, and so they have a zero-correlation with all between-person variables (Enders & Tofighi, 2007; Raudenbush & Bryk, 2001). Hence, effects of these variables reflect only within-person effects over time. In all models, we allowed intercepts to vary randomly across individuals to model the multiple assessments as nested within person. Across all models, parental education and child sex[2] (level 2 variables), and co-occurring symptoms (depressive, anxiety, ADHD, and defiance; level 1 variables) were included as covariates to examine unique associations between irritability and each problem scale.[3] Parental education was included as a covariate, given links between low socioeconomic status and psychiatric symptoms across development (Conger et al., 2010).

We first examined between- and within-person associations between irritability and concurrent depressive, anxiety, ADHD, and defiance in separate models. In each model, we controlled for between- and within-person effects of the other internalizing and externalizing symptoms (e.g., for a model predicting depressive symptoms we controlled for anxiety, ADHD, and defiance). The equation representing concurrent associations between irritability and depression is described below:

Level 1: η_{ij}(depression) = β_{0j} + β_{1j}(Person-centered irritability) + β_{2j}(Person-centered anxiety) + β_{3j}(Person-centered ADHD) + β_{4j}(Person-centered defiance) + β_{5j}(Person-centered age) + r_{ij}.

Level 2: $\beta_{0j} = \gamma_{00} + \gamma_{01}$(Person-mean irritability) + γ_{02}(Person-mean anxiety) + γ_{03}(Person-mean ADHD) + γ_{04} (Person-mean defiance) + γ_{05}(child sex) + γ_{06}(parental education) + u_{0j}; $\beta_{1-5j} = \gamma_{1-50}$, where *ij* reflects wave *i* for person *j*.

We next examined prospective within-person associations between irritability and children's later depression, anxiety, ADHD, and defiance in separate models. For these analyses, we lagged depressive, anxiety, ADHD, and defiance symptoms by one wave, such that children's prior wave irritability predicted their later psychiatric symptoms in separate models. We assessed whether irritability on a particular wave (measured on wave *w*) was associated with later symptoms (measured on wave *w*+1), controlling for prior symptoms (also measured on wave *w*) as well as time, parental education and child sex. In order to examine the effects of the time-varying predictor variables independently of how these variables change over time, we created difference scores (wave *w* + 1 − wave *w*) capturing change from one wave to the next in these predictor variables and included them as covariates in the model. For prospective models, we did not include between-person effects because these variables do not vary across time and their effects are the same as what was presented in the concurrent models described above.[4] We continued the practice of centering all time-varying predictors on person-means in these lagged models. The equation for prospective associations between irritability and depression is described below:

Level 1: η_{ij}(lagged depression$_i$) = β_{0j} + β_{1j}(person-centered irritability$_{i-1}$) + β_{2j}(person-centered depression$_{i-1}$) + β_{3j}(person-centered anxiety$_{i-1}$) + β_{4j}(person-centered ADHD$_{i-1}$) + β_{5j}(person-centered defiance$_{i-1}$) + β_{6j}(person-centered age) + r_{ij}.

Level 2: $\beta_{0j} = \gamma_{00} + \gamma_{01}$(child sex) + γ_{02}(parental education) + u_{0j}. ($\beta_{1j} = \gamma_{10}$) where *ij* reflects wave *i* for person *j*, *i* reflects later symptoms, *i*−1 reflects prior symptoms.

Finally, we explored the cross product of the level-2 moderators (child sex, parental depressive disorders) and between- and within-person irritability on the concurrent and prospective associations detailed above in separate models. In each model, we controlled for all concurrent or prior internalizing and externalizing symptoms, time, and parental education. We additionally controlled for child sex in models examining parental depression as the moderator. Significant interactions were probed using simple slopes analyses (Aiken & West, 1991).

Results

Descriptive statistics

As detailed in Supplementary Table 1, boys showed greater symptoms of irritability at age 9, anxiety at age 6, depression at age 12, defiance at age 6, defiance at age 9, and defiance at age 12 than girls. Children's whose parents did not have a 4-year college degree had higher levels of irritability at ages 6 and 9, depressive symptoms at ages 3 and 6, anxiety symptoms at ages 3, 6, and 9, ADHD symptoms at ages 3, 6, and 9, and defiance at age 9 than children who had at least one parent with a college degree. As shown in Supplementary Table 2, all corresponding symptoms were moderately stable over time. All concurrent correlations (*r*s = .26–.60) and prospective correlations between symptoms were significantly positively correlated (*r*s = .10–.72), with the exception of age 3 anxiety and age 15 depression (r = .09, p = .06; Supplementary Table 2).

Concurrent associations between irritability and psychiatric symptoms

Unconditional models (1-ICC) indicated that 58% of the variance in irritability, 65% of the variance in depression, 59% of the variance in anxiety, 45% of the variance in ADHD, and 48% of the variance in defiance was attributable to within-person factors. Variance and covariance results demonstrated significant between-person variation (intercept variance) and within-person variance across waves (*p*s < .001).

[2]The goal of our analyses was to model change from one time point to the next (not change across all timepoints). Because of this, the use of a sex- and age-adjusted T-scores did not alter the interpretation of the findings. The inclusion of age and sex as covariates provided information about whether the change from one time point to the next was age- or sex-dependent, not whether the score was age- or sex-dependent.

[3]We also examined child race/ethnicity (1 = White, non-Hispanic, 2 = Non-White or Hispanic) as a possible covariate; it was only correlated with ADHD symptoms at age 6 (White non-hispanic M = 44.49, SD = 7.56, non-white and/or Hispanic M = 48.24, SD = 8.49, t(146) = −4.02, p < .001), and age 9 (White non-hispanic M = 45.32, SD = 8.43, non-white and/or Hispanic M = 48.29, SD = 9.46, t(146) = −2.88, p = .005). At these ages, having an ethno-racial identity that was non-white or Hispanic was associated with higher ADHD scores. When controlling for race/ethnicity in models predicting ADHD, results were similar.

[4]In addition, in the prospective analyses, the time-varying predictors are centered on each person's mean. These person-centered predictors have no between-person variance, so they have a zero-correlation with all between-person variables. Given this zero-correlation, controlling for between-person variables would not alter the prospective effects of the time-varying predictors, or any other effects of time-varying predictors.

https://doi.org/10.1017/S0954579421001267 Published online by Cambridge University Press

Table 2. Concurrent and prospective associations between irritability and psychiatric symptoms from ages 3–15 years old

	Concurrent Depression	Next-wave Depression	Concurrent Anxiety	Next-wave Anxiety	Concurrent Defiance	Next-wave Defiance	Concurrent ADHD	Next-wave ADHD
	b (SE)	b (SE)	b (SE)	b (SE)	b (SE)	b (SE)	b (SE)	b (SE)
Between-person:								
Irritability	1.93 (0.34)***	–	0.54 (0.05)***[d]	–	0.56 (0.04)***[e]	–	−0.85 (0.43)[e]	–
Depression	–	–	0.54 (0.05)***	–	−.00 (0.01)	–	.19 (0.05)**	–
Anxiety	0.35 (0.03)***	–	–	–	−.01 (0.00)	–	.13 (0.05)**	–
Defiance	0.03 (0.35)	–	−1.32 (0.46)**	–	–	–	4.74 (0.37)***	–
ADHD	0.13 (0.04)**	–	.21 (0.05)***	–	.05 (0.00)***	–	–	–
Within-person[a]:								
Irritability	1.72 (0.29)***	1.70 (0.53)**	1.31 (0.29)***	2.09 (0.54)***	0.28 (0.03)***	0.37 (0.05)***	0.40 (0.21)[e]	0.44 (0.38)
Depression	–	−0.23 (0.05)***	0.36 (0.05)***	0.31 (0.07)***	0.01 (0.00)**	0.00 (0.01)	0.10 (0.03)***	0.01 (0.05)
Anxiety	0.20 (0.03)	0.35 (0.05)***	–	−0.17 (0.04)***	0.00 (0.00)	0.00 (0.01)	0.07 (0.02)***	0.17 (0.04)***
Defiance	0.47 (0.24)	1.15 (0.48)*	0.61 (0.27)*	0.67 (0.53)	–	−0.16 (0.03)***	1.85 (0.19)***	1.99 (0.34)***
ADHD	0.18 (0.03)	.22 (0.06)**	0.10 (0.04)*	0.12 (0.07)	.04 (.00)***	0.04 (0.01)***	–	−.12 (0.04)**
Child sex[b]	−0.53 (0.44)	−1.58 (.68)*	−0.78 (0.58)	−0.65 (0.81)	−.20 (.05)***	−0.24 (0.09)**	1.81 (0.53)**	0.62 (0.77)
Parent education[c]	−0.26 (0.47)	−1.40 (.75)	0.05 (0.62)	−1.34 (0.88)	−0.03 (0.06)	−0.22 (0.10)*	−0.29 (0.57)**	−1.13 (0.84)
Age centered	0.06 (0.04)	0.17 (0.07)*	−0.02 (0.04)	−0.06 (0.08)	−0.04 (0.00)	−0.06 (.01)***	0.14 (0.03)	0.09 (0.05)

Notes. * $p < .05$, ** $p < .01$, *** $p < .001$.

[a]We controlled for difference scores (wave $w+1$ − wave w) to independently examine effects of time-varying predictors from how they change over time. Across all models, the inverse effect of prior within-person symptoms on the corresponding next wave symptom scales indicated that symptoms fluctuated around each individual's mean over time.

[b]0 = male, 1 = female.

[c]0 = neither parent with college degree, 1 = at least one parent with 4-year college degree.

[d]Effect moderated by parental lifetime depression; see Supplementary Table 3.

[e]Effects moderated by child sex; see Supplementary Table 2.

Between- and within-person irritability were both uniquely associated with concurrent depressive, anxiety, and defiance symptoms, controlling for co-occurring symptoms, parental education, and child sex (see Table 2). However, irritability was not associated with concurrent ADHD symptoms at the between- or within-persons levels.

Co-occurring symptoms also demonstrated significant concurrent associations among themselves. As seen in Table 2, greater between-person anxiety and ADHD, but not between-person defiance, were uniquely associated with concurrent depressive symptoms. However, at the within-person level, no co-occurring symptoms were uniquely related to concurrent depressive symptoms. Additionally, between- and within-person depression, defiance, and ADHD were uniquely associated with anxiety symptoms. Furthermore, between-person ADHD was concurrently associated with defiance, whereas within-person depression and ADHD, but not within-person anxiety, were associated with defiance. Finally, between-person depression, anxiety, and defiance were concurrently associated with ADHD, whereas within-person anxiety and defiance, but not within-person depression, were associated with ADHD.

Prospective associations between within-person irritability and later psychiatric symptoms

Similar to the within-person concurrent effects, within-person irritability was associated with next wave depressive, anxiety, and defiance symptoms, but not ADHD symptoms, controlling for all prior symptoms, time, parental education, and child sex (Table 2).

We further tested the directionality of the prospective associations with irritability in one model. Within-person depression ($b = .02$ $SE = .01$, $t = 3.57$, $p < .001$, CI [.01, .04]), anxiety ($b = .02$ $SE = .01$, $t = 4.14$, $p < .001$, CI [.01, .03]), and defiance ($b = .45$ $SE = .06$, $t = 7.83$, $p < .001$, CI [.34, .57]), but not within-person ADHD symptoms, were associated with next wave irritability, controlling for prior irritability, child sex, and parental education.

As seen in Table 2, within-person anxiety, defiance, and ADHD were associated with next wave depression, controlling for covariates; within-person depression, but not within-person defiance or ADHD, was associated with next wave anxiety; within-person ADHD, but not within-person depression or anxiety, was associated with next wave defiance; and within-person anxiety and defiance, but not within-person irritability or depression, was associated with next wave ADHD. Across all models, the inverse effect of prior within-person symptoms on the corresponding next wave symptom scales (e.g., prior depression and next wave depression) indicated that symptoms fluctuated around each individual's mean over time (Table 2).

Moderators of concurrent associations over time

Child sex

Child sex moderated the between- and within-person associations between irritability and ADHD (between-person: $b = 1.49$, $SE = .58$, $t = 2.57$, $p = .010$, 95% CI [.35, 2.63]; within-person: $b = .81$, $SE = .32$, $t = 2.55$, $p = .012$, 95% CI [.18, 1.43]). Between-person irritability was associated with fewer ADHD

https://doi.org/10.1017/S0954579421001267 Published online by Cambridge University Press

symptoms for males ($b = -1.68$, $SE = .55$, $t = -3.06$, $p = .002$, 95% CI [−2.76, −.60] but not for females, whereas within-person irritability was associated with greater ADHD symptoms for females ($b = .76$, $SE = .24$, $t = 3.15$, $p = .002$, 95% CI [.28, 1.24]) but not for males. Child sex also moderated the between-person association between irritability and defiance ($b = -.19$, $SE = .06$, $t = -3.18$, $p = .002$, 95% CI [−.31, −.07]). The between-person association between irritability and defiance was stronger for males ($b = .69$, $SE = .05$, $t = 13.84$, $p < .001$, 95% CI [.59, .73]) than for females ($b = .49$, $SE = .05$, $t = 9.48$, $p < .001$, 95% CI [.39, .60]). Child sex did not moderate any other between- or within-person effects (Supplementary Table 3).

Parent lifetime depressive disorder

Parent lifetime depressive disorder moderated the concurrent between-person association between irritability and anxiety ($b = 1.59$, $SE = .69$, $t = 3.00$, $p = .022$, 95% CI [.23, 2.95]). Between-person irritability was more strongly associated with greater anxiety symptoms for children whose parents had a depressive disorder ($b = 2.65$, $SE = .54$, $t = 4.95$, $p < .001$, 95% CI [1.60, 3.70], than children whose parents did not ($b = 1.45$, $SE = .68$, $t = 2.14$, $p = .033$, 95% CI [.12, 2.79]. Parental depressive psychopathology did not moderate any other between- or within-person concurrent effects (Supplementary Table 4).

Moderators of prospective associations

Child sex

Child sex did not significantly interact with within-person prior irritability to predict later depressive, anxiety, ADHD, or defiance symptoms.

Parent lifetime depressive disorder

Parental lifetime depressive disorder did not interact with within-person irritability to predict later depressive, anxiety, ADHD, or defiance symptoms.

Discussion

This was the first study to examine unique between- and within-person associations between irritability and psychiatric symptoms from early childhood through adolescence. With regard to between-person effects, we found that children with high levels of irritability relative to their peers experienced greater concurrent depressive, anxiety, and defiance symptoms, relative to their peers. With regard to within-person effects, children who experienced high levels of irritability at a particular point in time, relative to their own baseline, experienced heightened depression, anxiety, and defiance symptoms at that point in time, relative to their typical levels. Importantly, these findings emerged while controlling for co-occurring symptoms, which demonstrates an important predictive effect of irritability that is not attributable to its overlap with other psychiatric symptoms. These findings emphasize the importance of considering both a child's irritability relative to their peers as well as their changes in irritability relative to their own baseline when assessing risk for internalizing and externalizing psychopathology across development. Our within-person findings provide support for conceptualizing irritability as a clinical problem in its own right that is uniquely associated with the development of other later problems.

Concurrent and prospective effects of irritability on psychopathology

Our findings align with prior literature documenting concurrent and prospective links between irritability and depression, anxiety, and ODD (e.g., Orri et al., 2018; Stringaris et al., 2009, 2012; Vidal-Ribas et al., 2016). We extend prior work by showing distinct between- and within-person patterns of effects with irritability and internalizing and externalizing symptomatology. Studies of the etiology of childhood psychopathology often focus on between-person differences in individuals and effects of environmental characteristics on risk for disorders. While these studies are necessary and informative, our findings suggest the importance of simultaneously considering how changes within a child's symptoms contribute to risk for psychopathology. Our between- and within-person findings highlight that elevated levels of irritability compared to one's peers and change within oneself are both important risk factors; these findings highlight that within-person differences provide unique information about children's risk. The bidirectional findings with irritability and internalizing and defiance symptoms underscore the negative downward spiral that can occur when within-person increases in irritability are left unaddressed. Our novel findings that both between- and within-person irritability predicts later psychiatric symptoms have implications for identification of, and clinical intervention, for at-risk youth. From a prevention and early detection perspective, our results are the first to demonstrate that we should be most concerned both about children who are high in irritability compared to their peers and also about the times when children are elevated compared to their own baseline. This approach has the potential to identify a larger proportion of youth who are at risk for long term psychiatric problems.

Consistent with other findings, later depression is predicted by a number of earlier problems, including irritability, anxiety and externalizing problems (Blain-Arcaro & Vaillancourt, 2019; Weeks et al., 2016). Yet, our findings add to this work by demonstrating that these findings also hold for within-person effects over time. We also found that next wave anxiety was predicted by prior within-person irritability and depression, but not externalizing problems; this aligns with work showing anxiety is predated by irritability and mood problems, but not necessarily externalizing problems (Humphreys et al., 2012). In line with some prior work that did not parse between- from within-person effects (Dougherty et al. 2013; Harvey et al. 2016), we found that next wave within-person defiance was predicted by irritability and ADHD symptoms, but not depressive or anxiety symptoms; additionally, next wave within-person ADHD symptoms were predicted by anxiety and defiance, but not irritability or depressive symptoms. Our lack of within-person findings with irritability and ADHD are consistent with prior work showing that despite a co-occurrence between irritability and ADHD, irritability does not predict ADHD (Costello et al., 2003; Spencer et al., 2007). Overall, our findings demonstrate similar patterns of effects at the between- and within-person level and the importance of disaggregating effects to understand more nuanced relations among irritability and internalizing and externalizing psychopathology in youth across development and pathways to later symptomatology.

Multiple factors may explain links between irritability and other psychiatric problems. Several studies demonstrated support for shared genetic factors between irritability and internalizing and externalizing psychopathology (Merwood et al., 2014; Riglin et al., 2017; Savage et al., 2015; Stringaris et al., 2012,

https://doi.org/10.1017/S0954579421001267 Published online by Cambridge University Press

2018). In addition, aberrant reward processing has been proposed as a common neural correlate of affective processing underlying irritability, internalizing, and externalizing disorders (Stringaris et al., 2018). These links may also be explained by the evocative hypothesis, which posits that children's behaviors evoke negative experiences in their environments, such as negative parenting and peer responses, which further contribute to increasing irritability and other forms of psychiatric problems (Stringaris et al., 2018; Yan et al., 2020). Further research testing these mechanistic pathways between irritability and other forms of psychopathology is needed, especially research that aims to analyze the extent to which these pathways operate at the within-person level, between-person level, or both.

Moderators of the associations between irritability and psychopathology

We found that child sex moderated the association between irritability and externalizing psychopathology (ADHD, defiance), but not depression or anxiety. Concurrently, child sex moderated the between- and within-person associations between irritability and ADHD. Higher irritability relative to peers (between-person) was associated with fewer ADHD symptoms for males, but was not associated with irritability for females, whereas higher irritability relative to one's own baseline (within-person) was associated with greater ADHD symptoms for females, but was not associated with irritability for males. These findings suggest sex-specific pathways may differ across between- and within-person longitudinal associations. These findings also highlight differences when disaggregating between- and within-person effects. We previously reported that chronic irritability at age 3 predicted a diagnosis of ADHD at age 9 in females but not males (Dougherty et al., 2015). Our between-person effects were not consistent with the previous findings, perhaps because the previous findings confounded between- and within-person findings. Our new findings suggest that these female-specific associations were in fact driven by within-person effects. Notably, prior work on sex differences in the links between youth irritability and ADHD has demonstrated that relations between irritability and ADHD vary based on both sex and subtype of ADHD (Ambrosini et al., 2013). Ambrosini and colleagues (2013) found that irritable females had the highest rates of ADHD-inattentive type, while irritable males had the lowest rates. In contrast, irritable males had the highest rates of ADHD-combined type and irritable girls had the lowest rate. Our measure of ADHD symptoms did not distinguish between different ADHD subtypes; however, our findings may be related to differences in ADHD symptom presentation in males versus females and at different levels of effects.

Concurrently, child sex also moderated the between-person association between irritability and defiance. Higher irritability relative to peers was more strongly associated with concurrent defiance for males than for females. In contrast, Humphreys and colleagues (2019) reported similar concurrent associations between irritability and externalizing symptoms between males and females in adolescence; however, different levels of variance were not parsed and between- and within-person effects were thus confounded, suggesting that aggregating between- and within-person levels of variance may obscure important information.

Parent lifetime depressive disorder moderated the between-person association between irritability and anxiety, building on prior work linking greater irritability in youth and parental depression (Dougherty et al., 2013; Krieger et al., 2013; Wiggins et al., 2014). Between-person irritability was more strongly associated with greater anxiety symptoms for children whose parents had a depressive disorder, whereas the association was weaker for children whose parents did not. A number of factors may explain this moderation effect. First, a broad genetic predisposition for internalizing psychopathology may lead irritable youth to manifest increased anxiety behaviors. Second, parents with depression may have difficulty in supporting self-regulation due to less use of positive and greater use of negative parenting skills, and less engagement with their children (England & Sim 2009; Lovejoy et al. 2000; Tsotsi et al. 2019), placing their youth at greater risk for maladjustment. Thus, having a parent with depression may compound the effects of irritability, increasing risk for co-occurring anxiety in their children relative to others. We did not observe moderators of longitudinal within-person prospective associations; this is an important avenue for future work.

Strengths and limitations

This work has several strengths, including the use of longitudinal data tracking outcomes from the preschool period to adolescence and the parsing of between- and within-person effects. Moreover, because we assessed multiple forms of psychopathology concurrently, we were able to examine unique between- and within-person associations between irritability and internalizing and externalizing psychopathology. We also used non-overlapping measures of irritability and defiance to examine symptoms separately.

This work is not without limitations. First, this work was conducted with a community sample of largely White and educated families, limiting the generalizability of our findings to more diverse samples and clinical settings. Second, although the CBCL is an adequate measure of irritability, especially in younger samples, other measures, such as the Affective Reactivity Index are better at assessing irritability, especially at more severe levels (Dougherty et al., 2021). More rigorous assessment of irritability would help to further disentangle the complex relations between irritability and the development of childhood psychopathology. Third, we used a single reporter (mothers) to measure irritability and psychiatric symptoms, which may bias our findings due to shared method variance and omit important symptomatology from the youth's perspective. Fourth, although we used previously developed T-scores that allowed us to model symptoms over a wide age range, T-scores are limited by their use of population means that are not necessarily representative of the whole population. T-scores may also restrict or change the variance in the outcomes. Fifth, although we used non-overlapping, empirically-derived scales from the CBCL, items in the defiance scale (i.e., tendency to argue) overlap with facets of irritability. Future research should continue to examine the distinction between these constructs, especially with ODD. Finally, although we used a longitudinal design, our approach did not examine unique relations at different stages in development. This is an important avenue for future research. Future research should also examine trajectories (slope and curvature) of irritability and their effects on the slope of other symptom scales over time.

Conclusions

The results of this study provide further evidence that irritability has a significant role in the etiology and maintenance of psychopathology across development. This study also demonstrates the importance of parsing between- and within-person effects of risk

https://doi.org/10.1017/S0954579421001267 Published online by Cambridge University Press

factors for psychopathology, as they these effects are confounded in traditional designs and can have distinct effects in each domain. This study highlights the need to further examine mechanisms that may explain effects of within-person irritability on later psychiatric symptoms (e.g., tests of the evocative hypothesis). Furthermore, this study uncovered bi-directional effects of within-person irritability and psychiatric symptoms; future research should investigate factors that maintain these bi-directional associations over time.

Supplementary material. For supplementary material accompanying this paper visit https://doi.org/10.1017/S0954579421001267

Funding statement. Support for this research was provided by funding through NIMH R01 MH069942 (Klein) and the National Science Foundation Graduate Research Fellowship Program (Chad-Friedman). We assert that all procedures contributing to this work comply with APA ethical standards and Stony Brook University's institutional review board and with the Helsinki Declaration of 1975, as revised in 2008. Written informed consent was obtained by parents after the procedures had been fully explained.

Conflict of interest. The authors report no conflicts of interest.

References

Achenbach, T. M. (2000). *Child behavior checklist for ages 1 1/2–5*.

Achenbach, T. M., & Rescorla, L. A. (2001). *Manual for the ASEBA school-age forms and profiles*. Burlington, VT: University of Vermont Research Center for Children, Youth, & Families.

Achenbach, T. M., & Ruffle, T. M. (2000). The child behavior checklist and related forms for assessing behavioral/emotional problems and ompetencies. *Pediatrics in Review*, *21*(8), 265–271. https://doi.org/10.1542/pir.21-8-265

Aebi, M., Plattner, B., Metzke, C. W., Bessler, C., & Steinhausen, H.-C. (2013). Parent- and self-reported dimensions of oppositionality in youth: Construct validity, concurrent validity, and the prediction of criminal outcomes in adulthood. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *54*(9), 941–949. https://doi.org/10.1111/jcpp.12039

Aiken, L. S., & West, S. G. (1991). *Multiple regression: Testing and interpreting interactions*. Newbury Park, CA: Sage.

Ambrosini, P. J., Bennett, D. S., & Elia, J. (2013). Attention deficit hyperactivity disorder characteristics: II. Clinical correlates of irritable mood. *Journal of Affective Disorders*, *145*(1), 70–76. https://doi.org/10.1016/j.jad.2012.07.014

Beauchaine, T. P., & Tackett, J. L. (2020). Irritability as a transdiagnostic vulnerability trait: Current issues and future directions. *Behavior Therapy*, *51*(2), 350–364. https://doi.org/10.1016/j.beth.2019.10.009

Blain-Arcaro, C., & Vaillancourt, T. (2019). Longitudinal associations between externalizing problems and symptoms of depression in children and adolescents. *Journal of Clinical Child and Adolescent Psychology: The Official Journal for the Society of Clinical Child and Adolescent Psychology, American Psychological Association, Division 53*, *48*(1), 108–119. https://doi.org/10.1080/15374416.2016.1270830

Brotman, M. A., Kircanski, K., & Leibenluft, E. (2017). Irritability in children and adolescents. *Annual Review of Clinical Psychology*, *13*(1), 317–341. https://doi.org/10.1146/annurev-clinpsy-032816-044941

Caprara, G. V., Paciello, M., Gerbino, M., & Cugini, C. (2007). Individual differences conducive to aggression and violence: Trajectories and correlates of irritability and hostile rumination through adolescence. *Aggressive Behavior*, *33*(4), 359–374. https://doi.org/10.1002/ab.20192

Conger, R. D., Conger, K. J., & Martin, M. J. (2010). Socioeconomic status, family processes, and individual development. *Journal of Marriage and the Family*, *72*(3), 685–704. https://doi.org/10.1111/j.1741-3737.2010.00725.x

Costello, E. J., Mustillo, S., Erkanli, A., Keeler, G., & Angold, A. (2003). Prevalence and development of psychiatric disorders in childhood and adolescence. *Archives of General Psychiatry*, *60*(8), 837–844. https://doi.org/10.1001/archpsyc.60.8.837

Curran, P. J., & Bauer, D. J. (2011). The disaggregation of within-person and between-person effects in longitudinal models of change. *Annual Review of Psychology*, *62*, 583–619. https://doi.org/10.1146/annurev.psych.093008.100356

Dougherty, L. R., Smith, V. C., Bufferd, S. J., Kessel, E., Carlson, G. A., & Klein, D. N. (2015). Preschool irritability predicts child psychopathology, functional impairment, and service use at age nine. *Journal of Child Psychology and Psychiatry*, *56*(9), 999–1007. https://doi.org/10.1111/jcpp.12403

Dougherty, L. R., Smith, V. C., Bufferd, S. J., Stringaris, A., Leibenluft, E., Carlson, G. A., & Klein, D. N. (2013). Preschool irritability: Longitudinal associations with psychiatric disorders at age 6 and parental psychopathology. *Journal of the American Academy of Child and Adolescent Psychiatry*, *52*(12). https://doi.org/10.1016/j.jaac.2013.09.007

Dougherty, L. R., Galano, M. M., Chad-Friedman, E., Olino, T. M., Bufferd, S. J., & Klein, D. N. (2021). Using item response theory to compare irritability measures in early adolescent and childhood samples. *Assessment, 28*(3), 918–927. doi: 10.1177/1073191120936363

Enders, C. K., & Tofighi, D. (2007). Centering predictor variables in cross-sectional multilevel models: A new look at an old issue. *Psychological Methods*, *12*(2), 121–138. https://doi.org/10.1037/1082-989X.12.2.121

England, M., & Sim, L. (Eds.). (2009). *Depression in parents, parenting, and children*. US: National Academies Press.

Evans, S. C., Bonadio, F. T., Bearman, S. K., Ugueto, A. M., Chorpita, B. F., & Weisz, J. R. (2020). Assessing the irritable and defiant dimensions of youth oppositional behavior using CBCL and YSR items. *Journal of Clinical Child and Adolescent Psychology: The Official Journal for the Society of Clinical Child and Adolescent Psychology, American Psychological Association, Division 53*, *49*(6), 804–819. https://doi.org/10.1080/15374416.2019.1622119

Eyre, O., Hughes, R. A., Thapar, A. K., Leibenluft, E., Stringaris, A., Davey Smith, G., Stergiakouli, E., Collishaw, S., & Thapar, A. (2019). Childhood neurodevelopmental difficulties and risk of adolescent depression: The role of irritability. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *60*(8), 866–874. https://doi.org/10.1111/jcpp.13053

Ezpeleta, L., Granero, R., de la Osa, N., Trepat, E., & Domènech, J. M. (2016). Trajectories of oppositional defiant disorder irritability symptoms in preschool children. *Journal of Abnormal Child Psychology*, *44*(1), 115–128. https://doi.org/10.1007/s10802-015-9972-3

First, M., Spitzer, R., Gibbon, M., & Williams, J. (2002). *Structured clinical interview for DSM-IV-TR Axis I disorders, research version, non-patient edition. (SCID-I/NP)*. New York: New York State Psychiatric Institute.

Forte, A., Orri, M., Turecki, G., Galera, C., Pompili, M., Boivin, M., Tremblay, R. E., Côté, S. M., & Geoffroy, M.-C. (2021). Identifying environmental pathways between irritability during childhood and suicidal ideation and attempt in adolescence: Findings from a 20-year population-based study. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*. https://doi.org/10.1111/jcpp.13411

Galera, C., Orri, M., Vergunst, F., Melchior, M., der Waerden, J. V., Bouvard, M. P., Collet, O., Boivin, M., Tremblay, R. E., & Côté, S. M. (2021). Developmental profiles of childhood attention-deficit/hyperactivity disorder and irritability: Association with adolescent mental health, functional impairment, and suicidal outcomes. *Journal of Child Psychology and Psychiatry*, *62*(2), 232–243. https://doi.org/10.1111/jcpp.13270

Goodman, S. H., & Gotlib, I. H. (1999). Risk for psychopathology in the children of depressed mothers: A developmental model for understanding mechanisms of transmission. *Psychological Review*, *106*(3), 458–490. https://doi.org/10.1037/0033-295x.106.3.458

Goodman S. H. (2007). Depression in mothers. *Annual Review of Clinical Psychology*, *3,* 107–135. doi: 10.1146/annurev.clinpsy.3.022806.091401

Harvey, E. A., Breaux, R. P., & Lugo-Candelas, C. I. (2016). Early development of comorbidity between symptoms of attention deficit hyperactivity disorder and oppositional defiant disorder. *Journal of Abnormal Psychology*, *125*(2), 154–167. https://doi.org/10.1037/abn0000090

Hawes, M. T., Carlson, G. A., Finsaas, M. C., Olino, T. M., Seely, J. R., & Klein, D. N. (2019). Dimensions of irritability in adolescents: Longitudinal associations with psychopathology in adulthood. *Psychological Medicine*, 1–9. https://doi.org/10.1017/S0033291719002903

Humphreys, K. L., Aguirre, V. P., & Lee, S. S. (2012). Association of anxiety and ODD/CD in children with and without ADHD. *Journal of Clinical Child and Adolescent Psychology : The Official Journal for the Society of Clinical Child and Adolescent Psychology, American Psychological Association, Division 53*, *41*(3), 370–377. https://doi.org/10.1080/15374416.2012.656557

Humphreys, K. L., Schouboe, S. N. F., Kircanski, K., Leibenluft, E., Stringaris, A., & Gotlib, I. H. (2019). Irritability, externalizing, and internalizing psychopathology in adolescence: Cross-sectional and longitudinal associations and moderation by sex. *Journal of Clinical Child and Adolescent Psychology: The Official Journal for the Society of Clinical Child and Adolescent Psychology, American Psychological Association, Division 53*, *48*(5), 781–789. https://doi.org/10.1080/15374416.2018.1460847

Johnston, O. G., Cruess, D. G., & Burke, J. D. (2020). Irritability and behavioral symptom dimensions of oppositional defiant disorder in young adults: Associations with DSM-5 pathological personality traits. *Journal of Psychopathology and Behavioral Assessment*, *42*(3), 424–435. https://doi.org/10.1007/s10862-020-09786-8

Kessel, E. M., Frost, A., Goldstein, B. L., Black, S. R., Dougherty, L. R., Carlson, G. A., & Klein, D. N. (2019). Developmental pathways from preschool irritability to multifinality in early adolescence: The role of diurnal cortisol. *Psychological Medicine*, 1–9. https://doi.org/10.1017/S0033291719003684

Klein, D. N., & Finsaas, M. C. (2017). The Stony Brook temperament study: Early antecedents and pathways to emotional disorders. *Child Development Perspectives*, *11*(4), 257–263. https://doi.org/10.1111/cdep.12242

Klein, D. N., Lewinsohn, P. M., Rohde, P., Seeley, J. R., & Olino, T. M. (2005). Psychopathology in the adolescent and young adult offspring of a community sample of mothers and fathers with major depression. *Psychological Medicine 35*(3), 353–365. doi: 10.1017/s0033291704003587

Krieger, F. V., Polanczyk, V. G., Goodman, R., Rohde, L. A., Graeff-Martins, A. S., Salum, G., Gadelha, A., Pan, P., Stahl, D., & Stringaris, A. (2013). Dimensions of oppositionality in a Brazilian community sample: Testing the DSM-5 proposal and etiological links. *Journal of the American Academy of Child and Adolescent Psychiatry*, *52*(4), 389–400.e1. https://doi.org/10.1016/j.jaac.2013.01.004

Lovejoy, M. C., Graczyk, P. A., O'Hare, E., & Neuman, G. (2000). Maternal depression and parenting behavior: A meta-analytic review. *Clinical Psychology Review*, *20*(5), 561–592. https://doi.org/10.1016/s0272-7358(98)00100-7

Merwood, A., Chen, W., Rijsdijk, F., Skirrow, C., Larsson, H., Thapar, A., Kuntsi, J., & Asherson, P. (2014). Genetic associations between the symptoms of attention-deficit/hyperactivity disorder and emotional lability in child and adolescent twins. *Journal of the American Academy of Child and Adolescent Psychiatry*, *53*(2), 209–220.e4. https://doi.org/10.1016/j.jaac.2013.11.006

Orri, M., Galera, C., Turecki, G., Boivin, M., Tremblay, R. E., Geoffroy, M.-C., & Côté, S. M. (2019). Pathways of association between childhood irritability and adolescent suicidality. *Journal of the American Academy of Child and Adolescent Psychiatry*, *58*(1), 99–107.e3. https://doi.org/10.1016/j.jaac.2018.06.034

Orri, M., Galera, C., Turecki, G., Forte, A., Renaud, J., Boivin, M., Tremblay, R. E., Côté, S. M., & Geoffroy, M.-C. (2018). Association of childhood irritability and depressive/anxious mood profiles with adolescent suicidal ideation and attempts. *JAMA Psychiatry*, *75*(5), 465–473. https://doi.org/10.1001/jamapsychiatry.2018.0174

Pagliaccio, D., Pine, D. S., Barch, D. M., Luby, J. L., & Leibenluft, E. (2018). Irritability trajectories, cortical thickness, and clinical outcomes in a sample enriched for preschool depression. *Journal of the American Academy of Child and Adolescent Psychiatry*, *57*(5), 336–342.e6. https://doi.org/10.1016/j.jaac.2018.02.010

Raudenbush, S. W., & Bryk, A. S. (2001). *Hierarchical linear models: Applications and data analysis methods* (2nd ed.). Thousand Oaks, CA: SAGE Publications, Inc.

Riglin, L., Eyre, O., Cooper, M., Collishaw, S., Martin, J., Langley, K., Leibenluft, E., Stringaris, A., Thapar, A. K., Maughan, B., O'Donovan, M. C., & Thapar, A. (2017). Investigating the genetic underpinnings of early-life irritability. *Translational Psychiatry*, *7*(9), e1241. https://doi.org/10.1038/tp.2017.212

Roberson-Nay, R., Leibenluft, E., Brotman, M. A., Myers, J., Larsson, H., Lichtenstein, P., & Kendler, K. S. (2015). Longitudinal stability of genetic and environmental influences on irritability: From childhood to young adulthood. *American Journal of Psychiatry*, *172*(7), 657–664. https://doi.org/10.1176/appi.ajp.2015.14040509

Savage, J., Verhulst, B., Copeland, W., Althoff, R. R., Lichtenstein, P., & Roberson-Nay, R. (2015). A genetically informed study of the longitudinal relation between irritability and anxious/depressed symptoms. *Journal of the American Academy of Child and Adolescent Psychiatry*, *54*(5), 377–384. https://doi.org/10.1016/j.jaac.2015.02.010

Spencer, T. J., Biederman, J., & Mick, E. (2007). Attention-deficit/hyperactivity disorder: Diagnosis, lifespan, comorbidities, and neurobiology. *Ambulatory Pediatrics: The Official Journal of the Ambulatory Pediatric Association*, *7*(1 Suppl), 73–81. https://doi.org/10.1016/j.ambp.2006.07.006

Steffen, A., Nübel, J., Jacobi, F., Bätzing, J., & Holstiege, J. (2020). Mental and somatic comorbidity of depression: A comprehensive cross-sectional analysis of 202 diagnosis groups using German nationwide ambulatory claims data. *BMC Psychiatry*, *20*(1), 142. https://doi.org/10.1186/s12888-020-02546-8

Stringaris, A., Cohen, P., Pine, D. S., & Leibenluft, E. (2009). Adult outcomes of youth irritability: A 20-year prospective community-based study. *The American Journal of Psychiatry*, *166*(9), 1048–1054. https://doi.org/10.1176/appi.ajp.2009.08121849

Stringaris, A., & Goodman, R. (2009). Three dimensions of oppositionality in youth. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *50*(3), 216–223. https://doi.org/10.1111/j.1469-7610.2008.01989.x

Stringaris, A., Vidal-Ribas, P., Brotman, M. A., & Leibenluft, E. (2018). Practitioner review: Definition, recognition, and treatment challenges of irritability in young people. *Journal of Child Psychology and Psychiatry*, *59*(7), 721–739. https://doi.org/10.1111/jcpp.12823

Stringaris, A., Zavos, H., Leibenluft, E., Maughan, B., & Eley, T. (2012). Adolescent irritability: Phenotypic associations and genetic links with depressed mood. *The American Journal of Psychiatry*, *169*(1), 47–54. https://doi.org/10.1176/appi.ajp.2011.10101549

Tseng, W.-L., Moroney, E., Machlin, L., Roberson-Nay, R., Hettema, J. M., Carney, D., Stoddard, J., Towbin, K. A., Pine, D. S., Leibenluft, E., & Brotman, M. A. (2017). Test-retest reliability and validity of a frustration paradigm and irritability measures. *Journal of Affective Disorders*, *212*, 38–45. https://doi.org/10.1016/j.jad.2017.01.024

Tsotsi, S., Broekman, B. F. P., Sim, L. W., Shek, L. P., Tan, K. H., Chong, Y. S., Qiu, A., Chen, H. Y., Meaney, M. J., & Rifkin-Graboi, A. (2019). Maternal anxiety, parenting stress, and preschoolers' behavior problems: The role of child self-regulation. *Journal of Developmental and Behavioral Pediatrics*, *40*(9), 696–705. https://doi.org/10.1097/DBP.0000000000000737

Vidal-Ribas, P., Brotman, M. A., Valdivieso, I., Leibenluft, E., & Stringaris, A. (2016). The status of irritability in psychiatry: A conceptual and quantitative review. *Journal of the American Academy of Child and Adolescent Psychiatry*, *55*(7), 556–570. https://doi.org/10.1016/j.jaac.2016.04.014

Wakschlag, L. S., Estabrook, R., Petitclerc, A., Henry, D., Burns, J. L., Perlman, S. B., Voss, J. L., Pine, D. S., Leibenluft, E., & Briggs-Gowan, M. (2015). Clinical implications of a dimensional approach: The normal: Abnormal spectrum of early irritability. *Journal of the American Academy of Child and Adolescent Psychiatry*, *54*(8), 626–634. https://doi.org/10.1016/j.jaac.2015.05.016

Wang, L. P., & Maxwell, S. E. (2015). On disaggregating between-person and within-person effects with longitudinal data using multilevel models. *Psychological Methods*, *20*(1), 63–83. https://doi.org/10.1037/met0000030

Weeks, M., Ploubidis, G. B., Cairney, J., Wild, T. C., Naicker, K., & Colman, I. (2016). Developmental pathways linking childhood and adolescent internalizing, externalizing, academic competence, and adolescent depression. *Journal of Adolescence*, *51*, 30–40. https://doi.org/10.1016/j.adolescence.2016.05.009

Weijers, D., van Steensel, F. J. A., & Bögels, S. M. (2018). Associations between psychopathology in mothers, fathers and their children: A structural modeling approach. *Journal of Child and Family Studies*, *27*(6), 1992–2003. https://doi.org/10.1007/s10826-018-1024-5

Weissman, M. M., Wickramaratne, P., Gameroff, M. J., Warner, V., Pilowsky, D., Kohad, R. G., Verdeli, H., Skipper, J., & Talati, A. (2016). Offspring of depressed parents: 30 years later. *American Journal of Psychiatry*, *173*(10), 1024–1032. https://doi.org/10.1176/appi.ajp.2016.15101327

Weissman, M. M., Wickramaratne, P., Nomura, Y., Warner, V., Pilowsky, D., & Verdeli, H. (2006). Offspring of depressed parents: 20 years later. *The American Journal of Psychiatry*, *163*(6), 1001–1008. https://doi.org/10.1176/ajp.2006.163.6.1001

West, B. T. (2009). Analyzing longitudinal data with the linear mixed models procedure in SPSS. *Evaluation & the Health Professions*, *32*(3), 207–228. https://doi.org/10.1177/0163278709338554

Wiggins, J. L., Mitchell, C., Stringaris, A., & Leibenluft, E. (2014). Developmental trajectories of irritability and bidirectional associations with maternal depression. *Journal of the American Academy of Child and Adolescent Psychiatry*, *53*(11), 1191–1205.e4. https://doi.org/10.1016/j.jaac.2014.08.005

Yan, N., Ansari, A., & Peng, P. (2020). Reconsidering the relation between parental functioning and child externalizing behaviors: A meta-analysis on child-driven effects. *Journal of Family Psychology*, *35*(2), 225–235. https://doi.org/10.1037/fam0000805

https://doi.org/10.1017/S0954579421001267 Published online by Cambridge University Press