

The Association Between General Childhood Psychopathology and Adolescent Suicide Attempt and Self-Harm: A Prospective, Population-Based Twin Study

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Few quantitative behavior genetic studies have examined why psychopathology is associated with suicide attempt (SA) and self-harm (SH) in adolescence. The present study analyzed data from the Child and Adolescent Twin Study in Sweden to examine the extent to which genetic and environmental factors explain SA/SH and its association with psychopathology in childhood, an often-cited risk factor of subsequent SA/SH. When children were 9 or 12 years old ($n = 30,444$), parents completed the Autism–Tics, AD/HD and other Comorbidities Inventory (Larson et al., 2010) regarding their children's psychiatric problems as part of an ongoing, longitudinal study. At age 18 years ($n = 10,269$), adolescents completed self-report questionnaires, including SA/SH assessments. In a bifactor model of childhood psychopathology, a general factor of psychopathology was a statistically significant predictor of adolescent SA/SH at a higher magnitude (β , 0.25, 95% confidence interval [CI; 0.15, 0.34] for suicide attempt), as compared with specific factors of inattention, impulsivity, oppositional behavior, and anxiety/emotion symptoms. Quantitative genetic modeling indicated that the additive genetic influences on the general factor accounted for the association with each outcome (β , 0.24, 95% CI [0.13, 0.34] for suicide attempt). The results remained virtually identical when we fit a higher order factors model. Two additional outcomes demonstrated comparable results. The results extend current literature by revealing the shared genetic overlap between general psychopathology during childhood and adolescent SA/SH.

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General Scientific Summary

This study suggests that children with more nonspecific psychiatric problems in childhood are more likely to endorse having made a suicide attempt or engaged in self-harm in adolescence. This association is primarily due to an overlap in genetic influences.

Keywords: suicide attempt, self-harm, adolescence, twin design, general psychopathology factor

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Suicidal behavior is a major public health problem, especially in adolescence (Patton et al., 2009). Suicide is currently the second leading cause of death among adolescents and young adults in the US, and rates of adolescent suicidal behavior have remained relatively stable over the past few decades (Center for Disease Control, 2018; Kessler, Berglund, Borges, Nock, & Wang, 2005). Studies suggest that 4% to 10% of adolescents make a suicide attempt (SA; Nock et al., 2013). Depending on how self-harm (SH) is defined or measured, approximately 12% to 25% of adolescents self-harm (Muehlenkamp, Claes, Havertape, & Plener, 2012; Shain et al., 2016). The prevalence of SA/SH remains low before puberty but dramatically increases between the ages of 9 and 12 and continues to rise through late adolescence (Nock, Borges, Bromet, Cha, et al., 2008; Nock et al., 2013). Given the prevalence of and developmental trends in SA/SH, adolescence is a crucial developmental period to study in order to deepen our understanding of how risk and protective factors operate.

The National Action Alliance for Suicide Prevention, Research Prioritization Task Force (2014) and the World Health Organization (2014) have highlighted a major gap in our understanding of how individuals become suicidal. Prior research is limited by small sample sizes, retrospective inquiries about suicidal behavior and the inability to test plausible alternative hypotheses for why risk factors are associated with SA/SH (Hawton & van Heeringen, 2009; Nock, Borges, Bromet, Cha, et al., 2008; Nock et al., 2013; Nock, Hwang, Sampson, & Kessler, 2010). Regarding the latter limitation, the majority of studies examining risk factors for SA/SH are observational studies of unrelated individuals. Many of these studies include measured covariates (e.g., parental suicidal behavior) or statistically match individuals to rule out potential confounders of the association between risk and protective factors and SA/SH. However, reliance on measured covariates to make causal inferences is frequently inadequate because of error in the measurement of confounding factors and the inability to account for unmeasured confounding factors (i.e., genetic and shared environmental factors; Westfall & Yarkoni, 2016). As such, the use of genetically informative designs can help to examine underlying processes by specifically testing the extent to which associations are due to genetic and environmental factors (McGue, Osler, & Christensen, 2010).

The need to use genetically informative designs is particularly relevant given that previous twin (Fu et al., 2002; Roy & Segal, 2001), adoption (Brent & Mann, 2005; Wender et al., 1986), extended family (Tidemalm et al., 2011), and molecular genetic studies (Baldessarini & Hennen, 2004; Bondy, Buettner, & Zill, 2006) have demonstrated that nonsuicidal self-injury and suicidality are heritable (approximately 50%) in young and middle

adulthood (Maciejewski et al., 2014; Richmond-Rakerd et al., 2019; Statham et al., 1998). Additionally, there are shared environmental factors that may influence psychopathology in adolescents, including suicide (Burt, 2009; Tidemalm et al., 2011). However, very few quantitative behavior genetics studies have examined SA/SH in adolescence. The existing twin studies have shown that adolescent SA/SH is heritable (Glowinski et al., 2001), but the relative rarity of suicidal behavior has made achieving adequate statistical power difficult (Cho, Guo, Iritani, & Hallfors, 2006). Given that previous research has demonstrated the role of shared familial factors (both genetic and environmental) influencing SA/SH (Althoff et al., 2012; Brent & Mann, 2005; Glowinski et al., 2001; Hawton, Saunders, & O'Connor, 2012), genetically informative designs are required to help separate the extent to which shared covariance between risk factors and SA/SH is due to genetic and environmental factors (McGue et al., 2010).

Psychiatric traits of disorders in childhood, such as impulsivity and inattention, oppositional behavior, conduct problems, anxiety, and depression are consistently cited as risk factors for SA/SH (Bentley et al., 2016; Brent et al., 2015; Bridge, Goldstein, & Brent, 2006; Hawton, Rodham, Evans, & Weatherall, 2002; Mann et al., 2009; Nock et al., 2013). At the same time, these traits are highly comorbid with each other (Brown & Barlow, 2009), and recent research has demonstrated that a general factor of psychopathology explains a large portion of the covariation among various disorders (Lahey et al., 2012). Additionally, a general factor predicts greater impairment and poorer overall functioning while adjusting for specific factors (Caspi et al., 2014). A dimensional and factorial approach to psychopathology across disorders allows for the examination of what is shared among disorders and the association with suicidality related outcomes. Research has debated the utility of modeling general psychopathology through the use of a bifactor model, as these models are prone to overfitting and may not represent the underlying structure of psychopathology (Bonifay, Lane, & Reise, 2016; Reise, Kim, Mansolf, & Widaman, 2016). However, bifactor models are particularly advantageous to examine the extent to which what is shared among versus unique to disorders is predictive of given outcomes, which can impact clinical intervention. Previous research has demonstrated that a general factor of psychopathology is predictive of suicidal ideation and suicide attempt within an adult sample (Hoertel et al., 2015), but we know of no genetically informative studies of general psychopathology liability and SA/SH within an adolescent sample. Therefore, we used data from a Swedish adolescent twin sample to investigate the degree to which (1) general and specific factors of childhood psychopathology are associated with adolescent SA/SH and (2) the associations between childhood psychopathology and

adolescent SA/SH are due to common genetic and environmental influences. In consideration of the limitations of our analytic approach, we also explored a higher order factors model.

Method

Sample

The Child and Adolescent Twin Study in Sweden (CATSS) is an ongoing, population-based, longitudinal study of physical and mental health targeting all child and adolescent twins living in Sweden beginning in 2004. Twins are assessed longitudinally at three time points (ages 9, 15, and 18). During the first three years of the study (i.e., birth years between July 1992 through June 1995), twins aged 12 years also participated in the first wave of data collection (Anckarsäter et al., 2011). There were 30,444 twins at ages 9 or 12 and 10,269 twins followed through age 18. Given that data collection is ongoing, not all twins included at ages 9 or 12 are old enough at present to complete age 18 data collection. Therefore, we included only twins that completed both ages 9 or 12 and 18 in the analyses, which included youth born between 1992 and 1998. Extensive details about the study, including recruitment, measurement, and follow-up are available elsewhere (Anckarsäter et al., 2011; Lichtenstein et al., 2002; Lichtenstein et al., 2006). Notably, previous research has demonstrated that the overall response rate of CATSS was 80%, and nonresponders at ages 9 or 12 data collection are more likely than responders to have a parent (1) with a psychiatric history, (2) who has been convicted of a felony, (3) who is divorced, and (4) of low socioeconomic status. However, when merging CATSS with population-based registers, missing information appeared to minimally influence the associations with particular outcomes (Anckarsäter et al., 2011). To address concerns of biasing our results due to nonrandom attrition, we predicted each SA/SH outcome from an indicator of missing at ages 9 or 12 (see Table 1 in the online supplemental material). Results suggest that missing at ages 9 or 12 is not associated with elevated SA/SH at age 18. However, those with missing items indexing SA/SH had elevated childhood psychopathology, except for anxiety, compared with those who completed at least one item indexing SA/SH (see Table 2 in the online supplemental material).¹

To minimize potential sex differences, we included only monozygotic (MZ) and same-sex dizygotic (DZ) twins for the current analyses. Zygosity was determined from a DNA sample analysis of 48 single nucleotide polymorphisms. For twins without a DNA sample, zygosity was determined from five questions indexing twin similarity, which has been shown to assign zygosity with accuracy greater than 95% probability (Anckarsäter et al., 2011).

Childhood Psychiatric Problems

When twins enrolled in the study at age 9 or 12 years, parents completed the Autism–Tics, AD/HD and other Comorbidities Inventory (A-TAC; Larson et al., 2010). The A-TAC is a valid and reliable 96-item questionnaire administered to parents via telephone regarding their twins' mental health, which largely correspond to *DSM–IV* criteria for psychiatric diagnoses (Anckarsäter et al., 2011; Halleröd et al., 2010; Hansson et al., 2005; Larson et al., 2010). Biological mothers (84.84%) com-

pleted most questionnaires, followed by biological fathers (14.71%). The A-TAC questions are grouped according to theoretical problem areas (e.g., concentration and attention, impulsiveness and activity), rather than discrete disorders (e.g., ADHD). This allows researchers to measure symptom dimensions (Anckarsäter et al., 2011). Given our focus on common childhood psychopathology, we utilized 43 questions from the inattention (e.g., “Does s/he often seem not to listen when directly spoken to?”), impulsivity (e.g., “Is s/he often ‘on the go’ or does s/he often act as if ‘driven by a motor’?”), oppositional (e.g., “Does s/he often lie or cheat?”), anxiety (e.g., “Is s/he often particularly nervous or anxious?”), and emotionality (e.g., “Does s/he have poor self-confidence?”) domains. All items were assessed on a three-point scale (i.e., no, yes to a certain degree, and yes). We a priori chose the items based on a similar approach as Pettersson, Lahey, Larsson, and Lichtenstein (2018), previous research examining a general factor of psychiatric disorders from internalizing and externalizing domains (Caspi et al., 2014), and our focus on common psychiatric problems. See Table 3 in the online supplemental material for a summary of the included items and their respective frequencies.

Adolescent SA/SH

When the twins were 18 years old, they completed the Lifetime History of Aggression (LHA) questionnaire, which contained assessment of suicide attempt and self-harm. The LHA included the following questions: “Have you ever deliberately attempted to kill yourself when you were angry or despondent?” and “Have you ever deliberately attempted to injure yourself physically when you were angry or despondent?” The response scale indicated six options ranging from 1 (*never*) to 6 (*more times than I can count*). We dichotomized each SA/SH item into absent (0) or ever present (1).

Additionally, we linked all individuals in CATSS via a unique identification number to the National Patient Registers that record all contact with psychiatric inpatient mental health services since 1973 and specialized outpatient services since 2001. Specifically, we had access to all intentional self-harm behaviors and self-harm events of undetermined intent (i.e., *International Classification of Disease–10* codes X60 through X84 and Y10 through Y34, respectively; Tidemalm et al., 2011) assigned by the attending physician. Given the small sample size ($n = 179$, 2.07%) of this outcome, we did not include inpatient/outpatient suicide attempt as a primary outcome. However, this measure of suicide attempt was strongly correlated with self-reported suicide attempt (tetrachoric $r[r_1] = 0.63$ [SE , 0.03]) and self-harm ($r_t = 0.47$ [0.03]; see Table 4 in the online supplemental material), which suggests that self-reported SA/SH and suicide attempt appearing in an inpatient/outpatient setting are capturing a similar underlying construct.

Twin Methodology

Although detailed descriptions of twin methods can be found elsewhere (Boomsma, Busjahn, & Peltonen, 2002), we highlight a

¹ Indiana University, Bloomington considers the proposed project exempt from institutional review board review for the use of human subjects as the data are de-identified. The Regional Ethical Review Board in Stockholm, Sweden also approved this study.

few essential elements here. MZ twins share 100% and DZ twins share, on average, 50% of their segregating alleles. Similarities and differences between MZ and DZ twin correlations allow researchers to decompose the observed variance of a phenotype into four potential latent factors: (1) additive genetic (A path), (2) dominance genetic (D path), (3) shared environmental (C path; environmental factors that make twins similar), and/or (4) nonshared environmental (E path; environmental factors that make twins dissimilar and measurement error). The E path also represents the within-pair regression coefficient reflected in a sibling-comparison analysis (Turkheimer & Harden, 2014). Because not all four latent factors can be modeled simultaneously due to lack of information, traditional twin models include either C (ACE models) or D (ADE models), which is determined based on the difference between the MZ and DZ twin correlations. If the MZ twin correlation is at least twice that of the DZ correlation, D is estimated. Each twin is compared with his or her cotwin, thereby allowing all factors that make those twins similar to be captured as familial factors in A, D, or C. If MZ twins are more highly correlated on a phenotype than DZ twins, there is evidence of genetic influences on the phenotype. If MZ twins are correlated as much as DZ twins, there are shared environmental influences on the phenotype. If MZ twins are not perfectly correlated, there are nonshared environmental influences on the phenotype. Multivariate quantitative genetic modeling can then be applied to explore why the general psychopathology factor and SA/SH are associated. The design can provide information about the degree to which genetic, shared environmental, and nonshared environmental factors underlie these associations. Shared factors (A, C, or D) are viewed as common familial factors (e.g., genotype, home environment); they represent what makes twins within pairs similar to one another and could potentially explain the association between psychopathology and SA/SH that is not due to psychopathology. Nonshared environmental factors (E) represent what is uncorrelated between twins with a pair (i.e., what makes them different) and are the closest approximation to a causal pathway independent of additive genetic and shared environmental confounding (Turkheimer & Harden, 2014). We conducted univariate twin analyses to estimate the heritability of each SA/SH outcome (see Table 5 in the online supplemental material). The variance of LHA items were primarily attributable to additive genetic and nonshared environment influences.

Analyses

We completed all data management and summary statistics in SAS 9.4 (SAS Institute Inc., 2016) and all structural equation modeling in Mplus Version 8 (Muthén & Muthén, 1998–2010). We used the weighted least square mean and variance adjusted estimator (ESTIMATOR = WLSMV, which uses a diagonal weight matrix with standard errors and adjusts chi-square based on mean and variance), as all outcomes were dichotomous and simulation research has demonstrated the preferred performance of WLSMV compared with WLSM (Muthén, du Toit, & Spisic, 1997). We standardized the variances to 1 and means to 0 for each latent ACE factor. Finally, we estimated the paths from the ACE factors to the SA/SH items and constrained the cross-twin correlation between A to 1.0 for MZ twins and 0.5 for DZ twins and between C to 1.0 for both MZ and DZ twins (Prescott, 2004).

As a first step toward examining the association between childhood psychopathology and adolescent SA/SH (Aim 1), we conducted a confirmatory factor analysis on the childhood psychopathology symptoms. We modeled a bifactor structure, in which each item was loaded onto a general factor and specific factors captured residual item variance. Prior research in other samples has demonstrated that a bifactor model best explained the factor structure of *DSM-IV* diagnoses and explained significantly more variance than the inclusion of factors such as fear, distress, and externalizing alone (Lahey et al., 2012). Additionally, a similar structure fit the CATSS data well (Pettersson et al., 2018). Therefore, we allowed the 43 A-TAC items to load onto a general factor. We additionally derived specific factors from the A-TAC domains and included an inattention specific factor consisting of 11 items, an impulsivity specific factor consisting of 10 items, an oppositional specific factor consisting of 10 items, and an anxiety/emotionality specific factor consisting of 12 items. We held each specific factor orthogonal to each other and to the general factor (Chen, Hayes, Carver, Laurenceau, & Zhang, 2012). We allowed the general and specific factors to correlate across twins (e.g., attention for Twin 1 with attention for Twin 2). For the inattention and impulsivity factors, consistent with previous research in CATSS and elsewhere, we included between-twin regression paths to account for potential sibling contrast effects (Kuntsi, Gayán, & Stevenson, 2000; Quinn et al., 2016). These effects capture potential rater bias caused by the perception of behavior to be either more or less extreme when compared with that of a sibling. We then separately regressed each SA/SH item onto the general and specific factors. To estimate reliability, we computed coefficient H, which is the squared correlation between the latent variable and the optimum weighted linear composite of the observed factor indicators (see Table 6 in the online supplemental material; Hancock & Mueller, 2001). Three of the four specific factors had unsatisfactory reliability, which converges with past bifactor model reliability research (Rodríguez, Reise, & Haviland, 2016). Note that we circumvented issues related to unreliability by regressing the outcome onto error-free latent variables.

Second, to determine the extent to which the associations in Aim 1 were due to genetic or environmental factors (Aim 2), we regressed the SA/SH items onto both the additive genetic and nonshared environmental components of the general factor. We simultaneously included regression paths from each of the specific factors to SA/SH. However, these specific factors were not decomposed into ACE components, as results from Aim 1 suggested that the general factor was the largest predictor of SA/SH. We also decomposed the residual variance in each SA/SH item unaccounted for by the associations with the general and specific factors. Figure 1 presents a graphical representation of Aim 2. Paths a_g , e_g , a_s , and e_s represent the direct paths of latent additive genetic or nonshared environmental factors onto the general factor or SA/SH item, respectively. Paths β_a and β_e represent the direct path from A_g and E_g to the SA/SH item. Finally, $\beta_{\text{inattention}}$, $\beta_{\text{impulsivity}}$, $\beta_{\text{oppositional}}$, and $\beta_{\text{anxiety/emotion}}$ represent the direct paths from the specific factors to the SA/SH item.

Sensitivity Analyses

Previous researchers have raised concerns about the utility and overfitting of a bifactor model (Bonifay et al., 2016; Reise et al.,

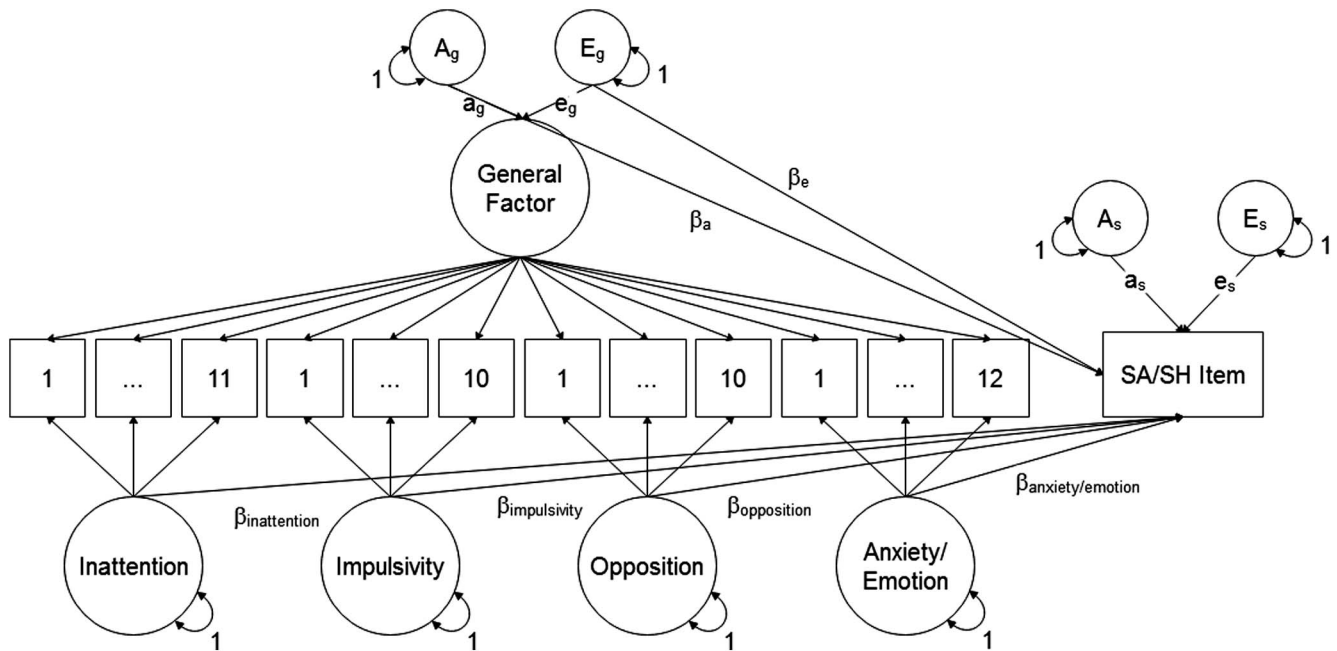


Figure 1. Representation of Aim 2. Each suicide attempt/self-harm (SA/SH) item was regressed on the additive genetic latent factor of the general factor, nonshared environmental factor of the general factor, and each specific factor. Figure represents one twin per twin pair.

2016) and given that our general factor is comprised of more externalizing items, we ran the multivariate behavior genetic models using a theoretically derived structure of higher order factors (i.e., we modeled externalizing and internalizing latent factors instead of a general factor, see Figure 1 in the online supplemental material). Inattention, impulsivity, and opposition items were set to load onto an externalizing factor, and anxiety and emotion items were set to load onto an internalizing factor. We fit a higher order factors model in order to estimate genetic and environmental factors that were shared between externalizing and internalizing, as well as unique to each (Yung, Thissen, & McLeod, 1999). As such, we derived six latent factors (i.e., unique A and E to externalizing and internalizing, and common A and E); externalizing and internalizing were both loaded onto common A and E. We imposed model constraints to set the common A paths to internalizing and externalizing to be equivalent and common E paths to internalizing and externalizing to be equivalent (Loehlin, 1996). The SA/SH outcomes were then regressed onto the latent genetic and/or environmental factors that accounted for a statistically significant portion of variance in externalizing and internalizing. We did not include C as there was no evidence of shared environmental influence in the bifactor models.

We used the higher order factors model because in multiple regression, the unique regression paths are directly estimated but the shared effect of the paths is not. In a higher order factors model, however, the shared effect is directly estimated via a common latent factor. For two and three higher order factors, the multiple regression and the higher order factors model are parametrically equivalent. In other words, they are merely reparameterizations of the other (Yung et al., 1999). The higher order factors model also fits fewer parameters and, thus, is less prone to overfitting.

To test the generalizability of our results, we used an additional questionnaire, the Brief Obsessive Compulsive Scale (BOCS), which included the following question: "I do things that injure my body" endorsed as "No"; "Yes, in the past"; or "Yes, currently." We dichotomized the item into absent (0) or ever present (1). Given the high correlations among the self-reported SA/SH items (range = 0.68, 0.83; see Table 4 in the online supplemental material), we also created a dichotomous outcome variable that indicated the endorsement of any of the SA/SH items (labeled "any SA/SH"). We examined these two outcomes in separate models.

Results

Summary Statistics

As is shown in Table 1, 4.93% and 21.44% of adolescents attempted to kill or injure themselves, respectively, when angry or despondent. Of note in Table 1, those included in the category "missing" were those without a response to the specific SA/SH items, which does not specify whether individuals were missing the LHA questionnaire or did not complete any of the data collection at age 18. Of the adolescents who turned 18 years old and thus were eligible to complete data collection, 12.63% did not participate (i.e., did not complete any self-report questionnaire administered). Of those who participated (i.e., completed at least one questionnaire included at age 18 data collection), 3.24% did not complete the LHA questionnaire.

Bifactor Model

See Table 6 in the online supplemental material for the bifactor model loadings of each item onto both the general and specific

Table 1
Distribution of Items Indexing Adolescent SA/SH: Twin Report at Age 18 (N = 10,269)

Item and response option	n (%)
Have you ever deliberately attempted to kill yourself when you were angry or despondent? (SA)	
Never	8,146 (79.33)
Once	300 (2.92)
2–3 times	120 (1.17)
4–9 times	37 (0.36)
10+ times	18 (0.18)
More times than I can count	31 (0.30)
Missing	1,617 (15.75)
Have you ever deliberately attempted to injure yourself physically when you were angry or despondent? (SH)	
Never	6,461 (62.92)
Once	797 (7.76)
2–3 times	661 (6.44)
4–9 times	303 (2.95)
10+ times	199 (1.94)
More times than I can count	241 (2.35)
Missing	1,607 (15.65)

Note. Items and response options were derived from the Lifetime History of Aggression Questionnaire. SA = suicide attempt; SH = self-harm.

factors, $\chi^2(8, 276) = 31,835, p < .01$, (root mean square error of approximation = 0.024; 90% confidence interval [CI; 0.024, 0.024]; comparative fit index/Tucker–Lewis index = 0.924/0.923; weighted root mean square residual = 4.034). Most items moderately or highly loaded onto the general factor (range = 0.27, 0.74, mean: 0.59). Furthermore, the loadings on the specific factors were low to moderate (inattention range = 0.32, 0.61, $M = 0.45$; impulsivity range = 0.14, 0.38, $M = 0.32$; oppositional range = 0.16, 0.34, $M = 0.27$; anxiety/emotion range = 0.09, 0.47, $M = 0.34$). See Table 7 in the online supplemental material for the tetrachoric correlations among the SA/SH items by zygosity and sex.

Aim 1: Associations Between General and Specific Psychopathology and Adolescent SA/SH

Table 2 presents the associations between the general and specific factors and SA/SH items as standardized regression coefficients. The general factor was the only statistically significant predictor of suicide attempt ($\beta = 0.25, 95\% \text{ CI } [0.15, 0.34]$). The

general factor ($\beta = 0.11, 95\% \text{ CI } [0.04, 0.18]$) and the opposition specific factor ($\beta = 0.13, 95\% \text{ CI } [0.01, 0.26]$) also predicted self-harm as measured by LHA.

Aim 2: Genetic and Environmental Factors Explaining the Association Between General Psychopathology and SA/SH

Table 8 in the online supplemental material presents the cross-twin cross-trait (CTCT) correlations between the general factor and each of the SA/SH items, which are the correlations across twins within a twin pair between the general psychopathology factor and SA/SH. Larger MZ CTCT correlations compared with DZ CTCT correlations suggest that genetic factors partly account for the associations. Given that we found little evidence that the specific factors predicted SA/SH, we focused our analyses in Aim 2 on the general factor.

We decomposed the general factor variance and regressed the SA/SH items onto the additive genetic factor (for suicide attempt, $\beta_a = 0.24, 95\% \text{ CI } [0.13, 0.34]$) and nonshared environmental factor of the general factor ($\beta_e = 0.11, 95\% \text{ CI } [-0.11, 0.32]$). Additionally, we regressed each SA/SH item onto the inattention, impulsivity, oppositional, and anxiety/emotion specific factors. None of these paths were statistically significant, except for opposition predicting self-harm ($\beta_{\text{opposition}} = 0.12, 95\% \text{ CI } [0.01, 0.24]$). See Table 3 for the results when regressing SA/SH on the decomposed general factor and the specific factors. Note that we constrained the shared environmental influence on the general factor to zero due to an estimate of no shared environment (0.01, 95% CI [-0.08, 0.09]) when we decomposed the variance of the general factor into ACE. To formally estimate model fit, we compared the freely estimated model (ACE) to the constrained model (AE), and there was no loss in model fit when excluding C, Satorra-Bentler scaled, $\Delta\chi^2(1) = 0.04, p = .86$, supporting the use of an AE model for the general factor. Table 9 in the online supplemental material presents the decomposed variance of the general factor and the residual variance decomposition for each of the SA/SH items. The variance of the general factor was primarily due to additive genetic factors ($a^2 = 0.87, 95\% \text{ CI } [0.84, 0.89]$). Finally, to capture the percent of variance of each SA/SH item either shared with childhood psychopathology or unique to the SA/SH item, we calculated the percent of the total variance due to the genetic and nonshared environmental factor of the general factor, the specific factors, and the genetic, shared, and/or non-shared environmental factor of the SA/SH items. Psychopathology

Table 2
The Associations Between General and Specific Childhood Psychopathology and Adolescent SA/SH

Outcome	General factor	Inattention	Impulsivity	Opposition	Anxiety/emotion
	β [95% CI]	β [95% CI]	β [95% CI]	β [95% CI]	β [95% CI]
SA LHA ^a	0.25 [0.15, 0.34]	0.03 [-0.09, 0.14]	-0.09 [-0.22, 0.05]	0.01 [-0.16, 0.18]	0.06 [-0.09, 0.21]
SH LHA ^b	0.11 [0.04, 0.18]	0.04 [-0.05, 0.12]	-0.03 [-0.12, 0.06]	0.13 [0.01, 0.26]	0.09 [-0.02, 0.19]

Note. Data are based on 9,903 observations. Inattention, impulsivity, opposition, and anxiety/emotion-specific factors were derived from the Autism–Tics, AD/HD and Other Comorbidities Inventory. SA = suicide attempt; SH = self-harm; CI = confidence interval; LHA = Lifetime History of Aggression Questionnaire.

^a Model fit: $\chi^2(7,641) = 29,399.67, p < .01$; root mean square error of approximation (RMSEA) = 0.024, 95% CI [0.024, 0.024], comparative fit index/Tucker–Lewis index (CFI/TLI) = 0.928/0.928, weighted root mean square residual (WRMR) = 4.235. ^b Model fit: $\chi^2(7,641) = 29,570.24, p < .01$; RMSEA = 0.024, 95% CI [0.024, 0.024], CFI/TLI = 0.928/0.928, WRMR = 4.23 8.

Table 3

The Associations Between General and Specific Childhood Psychopathology and Adolescent SA/SH, Decomposing General Factor Variance Into Additive and Nonshared Environmental Variance

Outcome	β_a [95% CI]	β_e [95% CI]	$\beta_{\text{Inattention}}$ [95% CI]	$\beta_{\text{Impulsivity}}$ [95% CI]	$\beta_{\text{Opposition}}$ [95% CI]	$\beta_{\text{Anxiety/Emotion}}$ [95% CI]
SA LHA ^a	0.24 [0.13, 0.34]	0.11 [−0.11, 0.32]	0.01 [−0.13, 0.14]	−0.15 [−0.33, 0.03]	0.03 [−0.13, 0.18]	0.06 [−0.09, 0.21]
SH LHA ^b	0.10 [0.02, 0.18]	0.09 [−0.08, 0.25]	0.02 [−0.08, 0.12]	−0.06 [−0.17, 0.06]	0.12 [0.01, 0.24]	0.07 [−0.03, 0.17]

Note. Data are based on 9,903 observations. All results represent the theta parameterization and are standardized regression coefficients. β_a refers to the regression path between additive genetic factors of the general factor and the suicide attempt/self-harm (SA/SH) item; β_e refers to the regression path between nonshared environmental factors of the general factor and the SA/SH item; $\beta_{\text{Inattention}}$ refers to the regression path between the inattention specific factor and the SA/SH item; $\beta_{\text{Impulsivity}}$ refers to the regression path between the impulsivity specific factor and the SA/SH item; $\beta_{\text{Opposition}}$ refers to the regression path between the opposition specific factor and the SA/SH item; and $\beta_{\text{Anxiety/Emotion}}$ refers to the regression path between the anxiety/emotion-specific factor and the SA/SH item. The general factor monozygotic correlation was 0.91 ($SE = 0.02$) and dizygotic correlation was 0.47 ($SE = 0.02$). SA = suicide attempt; SH = self-harm; CI = confidence interval; LHA = Lifetime History of Aggression Questionnaire.

^a Model fit: $\chi^2(7,726) = 26,261.75$, $p < .01$; root mean square error of approximation (RMSEA) = 0.022, 95% CI [0.022, 0.022], comparative fit index/Tucker–Lewis index (CFI/TLI) = 0.939/0.939, weighted root mean square residual (WRMR) = 4.288. ^b Model fit: $\chi^2(7,726) = 26,383.05$, $p < .01$; RMSEA = 0.022, 95% CI [0.022, 0.022], CFI/TLI = 0.939/0.939, WRMR = 4.292.

(both general and specific paths) in childhood explained 4.0% to 9.6% of the variance in SA/SH items. When examining only what was shared between childhood psychopathology and adolescent SA/SH, additive genetic factors of general psychopathology explained between 23.6% to 57.1% of the shared variance (see Figure 2).

Sensitivity Analyses

When decomposing the variance of the externalizing and internalizing factors into higher order A and E components, the proportion of variance in externalizing and internalizing due to common A was 0.75 (95% CI [0.70, 0.80]) and 0.72 (95% CI [0.67, 0.77]), respectively. The proportion due to common E in externalizing and internalizing was 0.03 (95% CI [0.00, 0.07]) and 0.03 (95% CI [0.00, 0.07]), respectively. The decomposition of the unique variance in externalizing and internalizing suggested that

the residual variance in externalizing was due to nonshared environmental factors and that of internalizing was due to additive genetic factors (see Table 10 in the online supplemental material). Therefore, when including the outcome, we regressed each item onto the common A, unique externalizing E, and unique internalizing A. We found that the common A was the largest and only statistically significant predictor of each outcome (e.g., 0.12, 95% CI [0.05, 0.20] for any SA/SH; see Table 11 in the online supplemental material).

When examining two additional outcomes, the results demonstrated that the additive genetic component of general psychopathology was the only statistically significant predictor of a self-harm item derived from BOCS ($\beta_a = 0.16$, 95% CI [0.06, 0.27]) and any SA/SH ($\beta_a = 0.13$, 95% CI [0.04, 0.22]; see Table 12 in the online supplemental material).

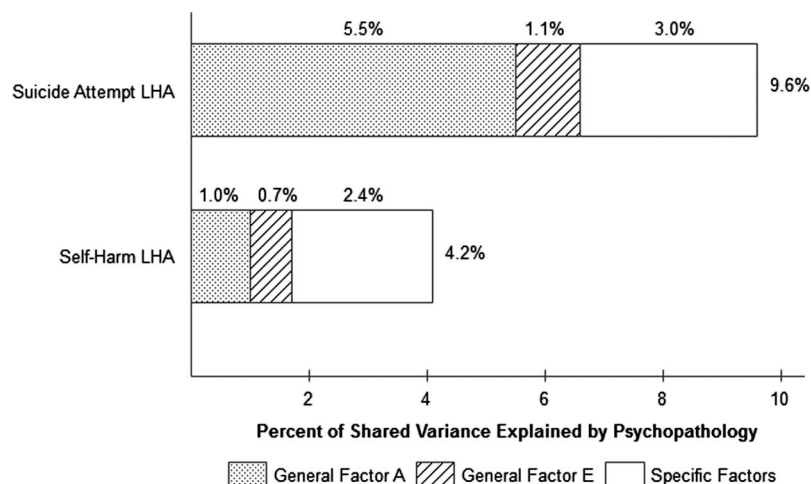


Figure 2. Representation of the decomposition of shared variance between general and specific childhood psychopathology and adolescent suicide attempt/self-harm (SA/SH). Note that (from left to right) the dotted bars represent additive genetic factors of general psychopathology; diagonal striped bars represent nonshared environmental factors of general psychopathology; and the open bars represent specific factors (i.e., inattention, impulsivity, oppositional, anxiety/emotion). The total shared variance may not equal 9.6% or 4.2% for SA and SH lifetime history of aggression (LHA), respectively, due to rounding.

Discussion

This study examined the association between childhood psychopathology and adolescent SA/SH and demonstrated two main findings. First, the general factor of childhood psychopathology was the only statistically significant predictor of adolescent SA/SH as compared with the specific factors of inattention, impulsivity, oppositional, and anxiety/emotion, apart from the association between opposition and self-harm. Our results are consistent with research among adults, which supports that a general factor is associated with increased risk for suicidal ideation and attempt rather than individual psychiatric disorders (Hoertel et al., 2015). Research has consistently demonstrated that symptoms cluster in factors such as internalizing (e.g., distress, fear) and externalizing, which are highly correlated (Krueger & Markon, 2006) and are associated partly due to additive genetic factors (Rhee, Lahey, & Waldman, 2015). As proposed by Lahey, Krueger, Rathouz, Waldman, and Zald (2017a), the structure of a latent general factor, latent specific factors, and observed items reflects a hierarchical taxonomy, in which nonspecific genetic and environmental factors increase risk for all dimensions of psychopathology, other causal factors increase risk for the specific factors, and still other causal factors increase risk for specific items. The current findings call into question the strength of parent-reported individual psychopathology items in childhood predicting later self-reported SA/SH, indicating instead that the association is largely driven by what is shared among these symptoms/problem areas. However, our results do suggest that specific factors account for approximately half of the shared variance in SA/SH outcomes, although these estimates do not take into account the imprecision of the specific factor regression paths.

Second, to determine why childhood psychopathology and adolescent SA/SH were associated, we decomposed the association into additive genetic and nonshared environmental contributions. Consistent with prior research, we found genetic influences on the general factor of psychopathology (Waldman, Poore, van Hulle, Rathouz, & Lahey, 2016). As discussed by Lahey, Krueger, Rathouz, Waldman, and Zald (2017b), factors that influence general psychopathology are likely nonspecific and increase risk for all disorders. The association between the general psychiatric problems and SA/SH was also largely explained by genetic factors, which we replicated with two additional SA/SH items. These results support an interpretation of shared genetic influences between childhood psychopathology and adolescent SA/SH, rather than an independent (i.e., causal) association as represented by the nonshared environmental path. The general factor likely captures the common variance across various disorders due to shared genetic influences, which is shared with suicidality roughly nine years later. However, we cannot distinguish pleiotropic effects on both psychopathology and SA/SH from genes that influence the general factor, which, in turn, have causal effects on SA/SH. Although researchers debate whether the general factor is represented genotypically (Bonifay et al., 2016; Pettersson, Larsson, & Lichtenstein, 2016), when we decomposed the association between externalizing and internalizing into a higher order factors model, the common additive genetic factor was the largest predictor of each SA/SH outcome. Therefore, results from the bifactor model and the higher order factors model suggested that what is shared among the included A-TAC items is due to additive genetic

factors, which predicts adolescent SA/SH. Importantly, this association remains irrespective of the latent factor structure. The current results add to a growing body of literature demonstrating that genetic factors largely explain the continuity in symptoms across time (both within and across domains). In contrast, nonshared environmental influences explain changes in symptoms across time (Lahey et al., 2017a; Wertz et al., 2015). It is also worth noting that childhood psychopathology, both general and specific, accounts for a small proportion of variance in the SA/SH items at age 18 (approximately 4% to 9%). The stability of a genetic liability for both psychopathology and SA/SH does not preclude the role of environmental risk factors influencing and being influenced by genetic factors along this developmental trajectory.

Implications

Prominent suicide theories propose potential mechanisms for the development of suicidal ideation and behaviors. For example, genetically driven childhood psychopathology may indicate the presence of or increase potential mechanisms of hopelessness and pain (Klonsky & May, 2015). General psychopathology may fit well into psychological theories of suicide, as pain and hopelessness may operate transdiagnostically and are not unique to specific domains. Given that the general factor of psychopathology likely captures an increased vulnerability for poor overall functioning and impairment (Caspi et al., 2014), an individual could seek out or elicit environmental circumstances that perpetuate this vulnerability and reduce connections with peers and family. This would be consistent with an environmentally mediated genetic explanation between general psychopathology and SA/SH. Inherent in this interpretation is the role of development, which should be considered in psychological theories. Additionally, the three-step theory of suicide emphasizes the importance of distinguishing between suicidal ideation without action and suicidal behavior, which is critical to the prevention of suicidality (Klonsky & May, 2015). Future research should examine the role of general psychopathology within this context of distinguishing between suicidal ideation and suicidal behavior.

The finding that the general psychopathology factor predicted SA/SH above and beyond the specific factors included in the model has important clinical implications. The general factor may be more indicative of a marker of risk, rather than a specific risk factor itself. Treatments that address transdiagnostic features (e.g., emotion regulation), rather than specific disorders, and risk across domains (e.g., home environment) may prove particularly important for suicidality treatment and prevention. The continuous assessment of symptoms and functioning throughout treatment may shed light onto the complex interplay among these processes and may help guide treatment (e.g., if there is no change in a general factor score, clinicians may alter the treatment method). More formally, the development of an easily implemented general factor algorithm would have significant utility in risk assessment, given that the general factor predicts a variety of adverse outcomes (Pettersson et al., 2018). This may also have practical implications for the number of sessions allotted for insurance reimbursement; if an individual is elevated on the general factor, a maximum of eight sessions, for example, may be insufficient for symptom alleviation. Coordination between policymakers and mental health providers is

essential for providing the appropriate care for individuals at elevated risk across domains.

Strengths and Limitations

To date, this study is the largest twin study of adolescent suicide attempt and self-harm. We have advanced the current literature by examining bivariate phenotypic associations between a general factor of psychopathology and SA/SH. Continued behavior genetic research using adolescent samples is needed to compare against adult populations. As previously mentioned, adolescence is a vulnerable period for the onset of suicidality, as it coincides with important developmental changes (e.g., self-regulatory challenges) and the steepest increase in suicidal ideation across the life span (Czyz & King, 2015; Nock, Borges, Bromet, Alonso, et al., 2008). The examination of twins can account for unmeasured confounding due to the ability to rule out genetic and environmental factors that make twins similar. Unexposed twins serve as a superior counterfactual condition compared with matched controls because the twin design can adjust for unmeasured confounding that makes twins similar (Turkheimer & Harden, 2014). Finally, this study is also strengthened by the use of different raters (i.e., parent and adolescent), which helped to reduce shared method variance and rater bias (Bank, Dishion, Skinner, & Patterson, 1990).

Several limitations are important to highlight when interpreting the results. First, the analysis of twin data relies on various assumptions (e.g., equal environmental influences for both MZ and DZ twins, minimal assortative mating among the twins' parents) and does not take into account gene-environment correlations or interactions (D. M. Evans & Martin, 2000; Verweij, Mosing, Zietsch, & Medland, 2012). Research has demonstrated that the equal environment assumption is unlikely to greatly bias estimates (Felson, 2014) and the presence of assortative mating underestimates heritability, thereby strengthening our results.

Second, our indices of SA/SH were limited by numerous factors. Given that LHA and BOCS were not designed to measure suicidality, SA/SH items were constrained to the context of anger/despondence or obsessive-compulsive behaviors, thereby limiting the generalizability of the findings. Without direct information indexing intent to die for the self-harm items, we were unable to clearly distinguish nonsuicidal self-injury (NSSI) from suicide attempt. Recent research investigating the latent structure of NSSI and suicidality in adulthood supported a bifactor model, in which the variance among self-harm items was best captured by a general factor and two specific factors (i.e., NSSI and suicidality; C. M. Evans & Simms, 2019). Future research is needed to extend the current findings with precise measures of psychopathology would display a different association with NSSI. We also lacked items indicating suicidal ideation without action. Numerous researchers suggest that the distinction between suicidal thoughts and behaviors is critical for the advancement of our understanding of these outcomes and to inform intervention efforts (Burke & Alloy, 2016; Klonsky & May, 2015).

Third, our construction of the general psychopathology factor was primarily neurodevelopmental problems (inattention, impulsivity) and externalizing symptoms. It is possible that the general factor represented by more internalizing symptoms may differentially predict adolescent SA/SH. Of note, however,

prior research that has examined both internalizing and externalizing latent factors suggest that negative emotionality may best represent a shared construct across both dimensions, as it is highly associated with the general factor (Lahey et al., 2017a; Tackett et al., 2013). Therefore, it is also possible that a general factor composed of more internalizing symptomatology than ours may similarly predict adolescent SA/SH.

Finally, childhood psychopathology accounted for 4% to 9% of the variance in adolescent SA/SH, which emphasizes the importance of examining other risk factors in closer temporal proximity. However, explaining minimal variance does not necessarily negate the importance of childhood psychopathology as an indicator of risk, as prior research supports the role of general psychopathology as predictive of numerous adverse outcomes, including suicidality (Hoertel et al., 2015; Pettersson et al., 2018). The current findings highlight the need to examine the potential mediating roles of various risk factors in order to investigate the complex interplay between stable genetic factors and time-specific nonshared environmental factors (Abelson, 1985; O'Grady, 1982).

Conclusions

We found that additive genetic factors largely explained the association between general childhood psychopathology and adolescent SA/SH. When modeling latent externalizing and internalizing factors in sensitivity analyses, the genetic factors of what is shared among these factors similarly predicted SA/SH. Taken together, children who are elevated on psychopathology broadly, as compared with specific symptomatology, are at increased risk for SA/SH in adolescence. Clinicians should closely monitor suicidal ideation and behavior in order to appropriately intervene. Additionally, most of the variance in adolescent SA/SH is not shared with childhood psychopathology. This may indicate the complex role between environmental processes and genetic influences on adolescent SA/SH. Future research is needed to examine potential mediators between the general factor and SA/SH in adolescence and develop intervention strategies for vulnerable youth as indicated by greater general psychopathology.

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