

## Special Issue Article

# Intergenerational transmission of psychopathology: An examination of symptom severity and directionality

Kristine Marceau<sup>1</sup> , Li Yu<sup>1</sup>, Valerie S. Knopik<sup>1</sup> , Jody M. Ganiban<sup>2</sup>  and Jenae M. Neiderhiser<sup>3</sup> 

<sup>1</sup>Department of Human Development and Family Studies, Purdue University, West Lafayette, IN, USA, <sup>2</sup>Department of Psychological and Brain Sciences, George Washington University, Washington, DC, USA and <sup>3</sup>Department of Psychology, The Pennsylvania State University, University Park, PA, USA

### Abstract

The present study examined the intergenerational transmission of internalizing and externalizing symptom severity, which indexes comorbidity, and symptom directionality, which indicates differentiation toward externalizing versus internalizing problems. Data are from 854 male and female, same-sex adult twin pairs born between 1926 and 1971 (32–60 years old,  $M = 44.9$  years,  $SD = 4.9$  years) from the Twin and Offspring Study in Sweden and their adolescent offspring (11–22 years old,  $M = 15.7$  years,  $SD = 2.4$  years, 52% female). Children-of-twins models revealed additive (9%) and dominant (45%) genetic and nonshared environmental (47%) influences on twins' symptom severity, and additive genetic (39%) and nonshared environmental (61%) influences on twins' symptom directionality. Both comorbid problems and preponderance of symptoms of a particular – internalizing versus externalizing – spectrum were correlated across parent and child generations, although associations were modest especially for directionality (i.e., transmission of specific symptom type). By interpreting findings alongside a recent study of adolescent twins, we demonstrate that the intergenerational transmission of symptom severity and symptom directionality are both unlikely to be attributable to genetic transmission, are both likely to be influenced by direct phenotypic transmission and/or nonpassive  $rGE$ , and the intergenerational transmission of symptom severity is also likely to be influenced by passive  $rGE$ .

**Keywords:** children-of-twins; comorbidity; directionality; externalizing; intergenerational transmission; internalizing; severity

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There is a long history of empirical work establishing intergenerational transmission of psychopathology, from studies establishing correlations of parent and youth psychopathology (Weissman et al., 1984; Wickersham et al., 2020) to studies defining specific mechanisms by which psychopathology is passed on through the generations (Jami et al., 2021). Following substantial work in the field of developmental psychopathology (Cicchetti, 2016), here we consider psychopathology at the spectrum-level, specifically internalizing problems (i.e., symptoms of internalizing disorders such as anxiety, depression, and phobias), and externalizing problems (i.e., delinquency and aggression; symptoms of externalizing disorders such as oppositional/defiant, conduct, and antisocial personality). A major goal of empirical work on intergenerational transmission of psychopathology is to discover the most important, plausibly causal pathways in order to be able to successfully break the intergenerational cycle of psychopathology.

In broad strokes, psychopathology could run in families because being exposed to a parent with elevated symptoms of psychopathology is in itself a causal risk factor for the offspring developing symptoms (e.g., modeling, direct phenotypic transmission). Or, the wider family environment (i.e., patterns of interactions or family customs) could influence psychopathology symptoms similarly in multiple

generations (i.e., extended family effects). A third mechanism is that parents with elevated psychopathology symptoms may contribute to a less warm, more hostile or disengaged family interpersonal environment, and/or engage in parenting practices that put youth at risk for developing psychopathology (Branje et al., 2020; Goodman et al., 2020). Finally, a large literature has established the heritability of psychopathology symptoms and disorders across the lifespan (Jami et al., 2021), and thus genetic transmission and/or gene–environment correlation are likely to play an important role in the intergenerational transmission of psychopathology.

The present study leverages a powerful design, the children-of-twins design, for disentangling three of the possible mechanisms of the intergenerational transmission of psychopathology: direct phenotypic association, extended family (environmental) effects, and genetic transmission. We further provide a relatively novel lens through which to understand the transmission of comorbid and specific problem types by leveraging the severity and directionality model of psychopathology. Finally, integrating findings with a recently published twin study of symptom severity and directionality (Marceau & Neiderhiser, 2022), we shed further light on possible gene–environment mechanisms underlying the intergenerational transmission of psychopathology. Specifically, considering the contributions of parents' genetic and environmental influences and adolescents' genetic and environmental influences to psychopathology informs on whether phenotypic associations between parent and offspring psychopathology represent passive  $rGE$ , nonpassive  $rGE$ , and/or there is evidence of genetic transmission. Passive

**Corresponding author.** Kristine Marceau, Email: [kristinemarceau@purdue.edu](mailto:kristinemarceau@purdue.edu)

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rGE occurs when the rearing environment that genetically related parents provide is influenced by genes that the parent and child share: relevant genes and environmental influences are passed together from parent-to-child generations. Nonpassive rGE encompasses both evocative (parents' psychopathology symptoms are evoked by adolescents' genetically influenced psychopathology symptoms) and/or active (children with genetically influenced psychopathology seeking out environments consistent with their predisposition) forms of rGE. In this case, evocative explanations are more likely than active, although they cannot be disentangled empirically outside of an experimental design.

### *Homotypic and heterotypic intergenerational continuity of psychopathology*

Familial aggregation of specific forms of psychopathology, either at the disorder or spectra level, that has high fidelity (i.e., parent depression to specifically child depression) reflects homotypic continuity (Branje *et al.*, 2020). Heterotypic continuity, on the other hand, is the transmission of *different* forms of psychopathology across generations (i.e., parent depression to child externalizing) (Branje *et al.*, 2020). A robust literature from diverse study types has shown that the intergenerational transmission of psychopathology is marked by both homo- and heterotypic continuity (e.g., Jami *et al.*, 2021; Kendler *et al.*, 1997).

#### *Mechanisms of homotypic transmission*

Parental internalizing symptoms have been found to predict offspring internalizing symptoms (Goodman *et al.*, 2011; McAdams *et al.*, 2015), and parental externalizing symptoms predict offspring externalizing symptoms (Salvatore *et al.*, 2015; Smith & Farrington, 2004). This homotypic transmission could reflect one or multiple processes, for example, genetic transmission, extended family effects, and direct phenotypic transmission (e.g., modeling). Children-of-twins study designs have yielded evidence of all three processes.

When examining externalizing problems, genetic and family environmental mechanisms were supported for associations of parent antisocial behavior with child conduct problems, but only genetic transmission was found for associations with child attention deficit/hyperactivity disorder (ADHD) (Silberg *et al.*, 2012). Genetic transmission also played a key role in associations of parental alcoholism and offspring externalizing problems (Waldron *et al.*, 2009) and between paternal alcohol dependence and children's alcohol dependence, conduct disorder, nicotine dependence (Koenig *et al.*, 2010), and attention deficit-hyperactivity problems (Knopik *et al.*, 2006; Knopik *et al.*, 2009). D'Onofrio *et al.* (2007) found that shared genetic liability explains the intergenerational transmission of conduct problems, but only to females. The transmission of conduct problems to male offspring, however, was largely explained by environmental factors relating to parents' conduct disorder.

For internalizing problems, findings largely support the influence of phenotypic associations and environmental factors rather than genetic factors for depression (Silberg *et al.*, 2010; Singh *et al.*, 2011), anxiety (Eley *et al.*, 2015), and broadband internalizing symptoms (McAdams *et al.*, 2015). Only one study so far has detected genetic transmission, in the association between maternal *prenatal* depressive symptoms and offspring internalizing symptoms, with shared genetic factors explaining a substantial

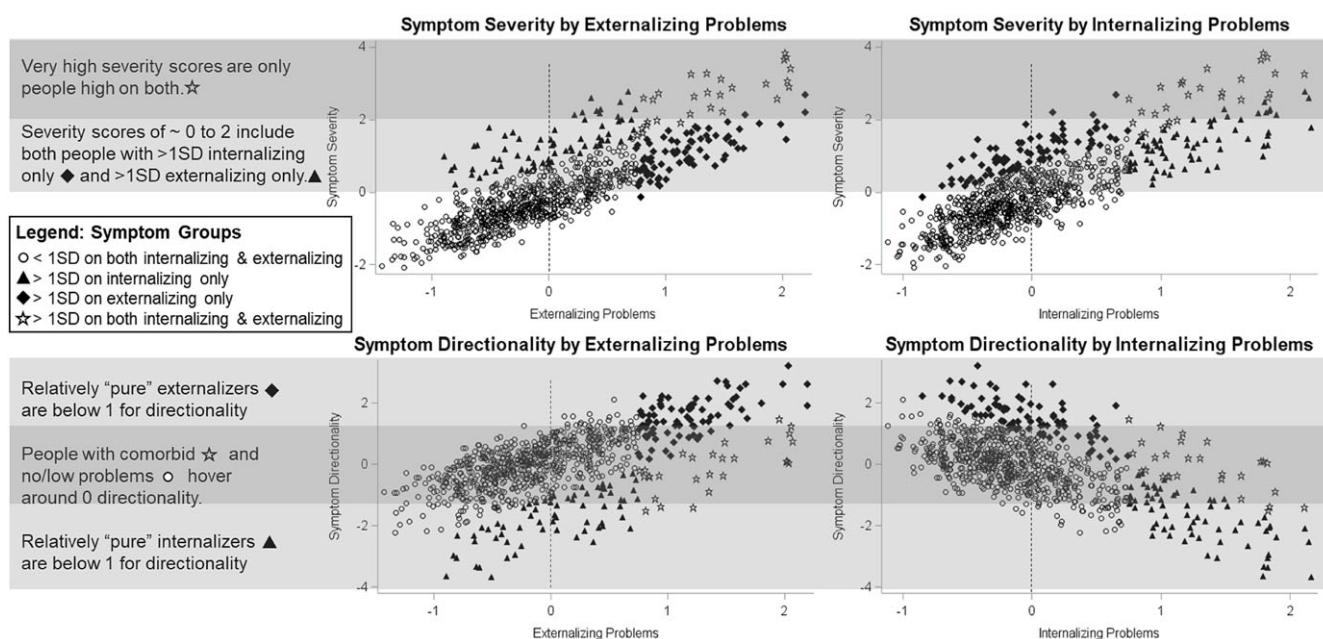
proportion of variance in children's internalizing symptoms (Hannigan *et al.*, 2018). Therefore, while homotypic transmission has been observed, the underlying mechanisms may vary by disorder spectra (i.e., externalizing vs. internalizing), by specific disorder, and by child sex. Neither solely genetic nor environmental factors completely explain homotypic transmission, though genetic transmission may be more important for externalizing problems, whereas phenotypic transmission may be more important for internalizing problems.

#### *Mechanisms of heterotypic transmission*

There is also empirical evidence of heterotypic transmission. For example, there are associations between parental internalizing symptoms and offspring externalizing symptoms (Hannigan *et al.*, 2018; Kim *et al.*, 2009; Schulz *et al.*, 2021) and between parental externalizing symptoms and offspring internalizing symptoms (Kim *et al.*, 2003; Schulz *et al.*, 2021; Silberg *et al.*, 2012). Findings from several types of genetically informed designs have shown that the association between biological parents' internalizing symptoms and offspring externalizing symptoms is at least partially accounted for by genetic mechanisms (e.g., in toddlerhood: Kerr *et al.*, 2013; Marceau *et al.*, 2013; Pemberton *et al.*, 2010; in adolescence: Silberg *et al.*, 2010; Singh *et al.*, 2011). In a study using the Twin and Offspring Study in Sweden (TOSS) data, however, no genetic transmission in the association between parental depression and child externalizing problems was detected (McAdams *et al.*, 2015). In contrast to these mixed findings, the association between parent externalizing to child internalizing symptoms shows a consistent pattern across studies. Specifically, children-of-twins models linking paternal alcohol dependence to offspring suicidal behavior and linking parental antisocial behavior and child depression highlight the influence of environmental effects, especially extended family effects on associations (Glowinski *et al.*, 2004; Silberg *et al.*, 2012), and the absence of genetic influences. In all, heterotypic transmission is present, but the underlying genetic and environmental processes that underlie transmission are poorly understood.

### **Comorbidity of internalizing and externalizing problems**

The presence of heterotypic transmission raises conceptual issues about whether it reflects the transmission of underlying vulnerabilities common to multiple forms of psychopathology or the transmission of two separate sets of symptoms (i.e., transmission of comorbidities). Substantial evidence has demonstrated that the rates of comorbidity within internalizing problems, within externalizing problems, and between internalizing and externalizing problems all far exceed the chance rate that different symptoms co-occur (Beauchaine & McNulty, 2013; Caron & Rutter, 1991; Willner *et al.*, 2016). Further, a substantial body of work has led to a general consensus that there is an underlying hierarchical structure to psychopathology symptoms, consistent with the notion that heterotypic continuity may reflect the transmission of a general vulnerability for psychopathology (Hartman, 2021). Across myriad models, input variables (i.e., symptoms and/or diagnostic indicators from different constellations of disorders), and data sets, there is general support of psychopathology symptoms forming two larger internalizing and externalizing factors, as well as a larger "general," or "*p*-factor" encompassing symptoms from disorders across these spectra (Caspi & Moffitt, 2018; Hartman, 2021; Lahey *et al.*, 2021). Therefore, extant evidence suggests that



**Figure 1.** Data visualization of symptom severity and directionality scores.

heterotypic transmission is likely to reflect the transmission of a general vulnerability to psychopathology that could be expressed as internalizing or externalizing symptoms.

### *Etiology of comorbid and spectra-specific psychopathology*

In adults, there is also evidence of separate genetic vulnerabilities for internalizing and externalizing subdomains (e.g., Kendler et al., 2003), although this study did not investigate the potential for an overarching general “*p*-factor.” More recently, in adults a general “*p*-factor” had a heritability of 48%, and the separate internalizing and externalizing factors were also heritable (estimates from different models were 35% and 41% for internalizing; 37% and 43% for externalizing) with no evidence of shared environmental influences (Rosenström et al., 2019). Twin studies of comorbidity have examined underlying genetic and environmental factors linking the various symptoms (i.e., common pathways models) and genetic and environmental influences on phenotypically defined factors (i.e., independent pathways models), most typically during adolescence. Across the various methods of modeling comorbidity and the underlying etiology, twin studies examining the hierarchical nature of psychopathology have generally shown familial influences on the general “*p*-factor” (i.e., genetic and sometimes shared environmental), as well as separate sets of genetic and environmental influences on each subdomain (i.e., internalizing and externalizing), though these studies are predominantly done in child and adolescent (not adult) populations (e.g., Allegrini et al., 2020; Cosgrove et al., 2011; Lahey et al., 2011; Pettersson et al., 2018).

### **Symptom severity and directionality**

The severity-directionality model provides a unique lens into comorbidity of problems, wherein individuals’ composite internalizing and externalizing scores are reorganized into two orthogonal factors. The first, *symptom severity*, is what the two scores have in common and is an expression of how severe an individual’s total problems are, since the highest severity scores can only be attained

by having more symptoms of both internalizing and externalizing problems. This is very akin to a “*p*-factor” from a hierarchical or second-order factor model, in that it is a factor loaded on already created internalizing and externalizing composite scores rather than symptom- or disorder-level scores. The second, *symptom directionality*, is the differentiation of internalizing versus externalizing scores and indicates the individual’s tendency toward externalizing problems rather than internalizing problems, regardless of severity (Essex et al., 2003; Marceau & Neiderhiser, 2022). Although conceptually symptom severity is similar to the “*p*-factor,” directionality is a qualitatively different measure (Marceau & Neiderhiser, 2022). That is, directionality captures differentiation of problem type rather than phenotype-specific residual variation (as in the predominant models of comorbidity on which the above literature is based).

Figure 1 is a heuristic that demonstrates how severity and directionality scores are related to the underlying spectra dimensions of internalizing and externalizing problems. The figure depicts scatter plots of symptom severity by externalizing (upper left) and internalizing problems (upper right), as well as symptom directionality by externalizing (lower left) and internalizing problems (lower right). Markers in the scatterplots were determined by a standard deviation cutoff (i.e., star markers indicate individuals with comorbid problems – scoring over one standard deviation on both internalizing and externalizing problems). The figure shows that only individuals who score above one standard deviation on both internalizing and externalizing problems can score highly on the severity measure, confirming that severity is an index of comorbidity. Individuals who score above zero (i.e., average) on internalizing and/or externalizing have severity scores above zero. Directionality, on the other hand, distinguishes “pure” externalizers – individuals who score over one standard deviation on externalizing problems only – have symptom directionality scores greater than one, whereas those who score over one standard deviation on internalizing problems only (“pure” internalizers) have directionality scores less than negative one. Both individuals with balanced, low symptoms and balanced high symptoms

(i.e., those who are comorbid) score between  $-1$  and  $1$  on symptom directionality. Thus, directionality indexes differentiation of problem type regardless of level or severity of problems.

### Present study

The present study examines the intergenerational transmission of psychopathology symptom severity and directionality using a children-of-twins design. A critical limitation of children-of-twins models thus far is that they have focused on *either* internalizing *or* externalizing problems in the parent and offspring generations, despite ample evidence of comorbidity at the phenotypic, genetic, and environmental levels in both adults and adolescents. Although bivariate children-of-twins extensions have been proposed (Silberg *et al.*, 2010), it is particularly challenging to implement children-of-twins models that are layered on more complex models of comorbidity, particularly without extended kinship models. The severity-directionality model thus provides an important and different conceptual lens for understanding how psychopathology symptomatology is passed down through generations. Symptom severity is a measure of within-person comorbidity, and thus allows for investigation of intergenerational transmission of *comorbid* psychopathology using a standard children-of-twins model. A children-of-twins analysis of directionality tests the specificity of homotypic intergenerational continuity, above and beyond comorbid problems, and the contributions of the general liability of psychopathology.

It is important to note that children-of-twins models are quite powerful for assessing genetic and environmental influences on parent psychopathology, but much less accurate in estimating offspring etiology (due to the low contrast in the percentage of segregating genes shared by cousins of MZ twins [25%] vs. cousins of DZ twins [12.5%]). However, “dual study” designs, which interpret findings from a children-of-twins model in conjunction with parallel findings from a sample of twin children (Neiderhiser *et al.*, 2004), and several extensions to the children-of-twins design (adding a child twin sample, ECoT, MCoT, McAdams *et al.*, 2018; Narusyte *et al.*, 2008; adding multiple sibling offspring of twin parents) have increased interpretation and power (respectively) for understanding intergenerational transmission of psychopathology. The ECoT design is inappropriate for the current data because it was designed to interrogate parent-offspring correlations when the adult phenotype is a parenting behavior that can vary across offspring twins, rather than a parent characteristic which is the same for both offspring twins as is the case for parent psychopathology (McAdams *et al.*, 2018). We are unable to fit the MCoT model because the TOSS sample includes only one adolescent per family. Thus, we interpret our findings in the context of a “dual study” design by leveraging the previously published adolescent twin decomposition of severity and directionality<sup>1</sup> (Marceau & Neiderhiser, 2022).

### The dual-study framework

Theoretically, if variation in an adolescents’ genotype contributes to their parents’ phenotype, nonpassive (likely evocative) *rGE* could drive the offspring-to-parent correlation (assuming the association operates with this direction of effects). However, this would only be the case if there were environmental influences on the parents’ phenotype (i.e., if the parents’ phenotype was entirely

heritable, genetic transmission would be the more likely the explanation). In contrast, if variation in both a parents’ genotype and environment contributes to their own phenotype, the conditions would be met for possible passive *rGE* as an explanation for the parent-to-offspring correlation (assuming this direction of effects). In the dual-study design, what would differentiate passive *rGE* from genetic transmission is the presence of shared environmental influences in the offspring (i.e., in the child-based twin study). That is, for passive *rGE* to occur, the combined influence of parents’ genes and environments would yield a phenotype in parents that via modeling, patterns of interaction, and/or extended family effects would increase the likelihood of psychopathology similarly across children in a family. Note that these interpretations rely on information about parents’ and offspring’s genetic and environmental influences. Since basic children-of-twins studies are inaccurate for obtaining these estimates for youth, the dual-sample design can aid in interpretations, increasing the impact of findings from basic children-of-twins models.

A key feature of the sample used in the present study, the Twin and Offspring in Sweden Study (TOSS), is that it has been used in conjunction with a sample of adolescent twins and siblings: the Nonshared Environment in Adolescent Development (NEAD) Study (Neiderhiser *et al.*, 2007; Neiderhiser, Reiss, Lichtenstein, *et al.*, 2007; Neiderhiser *et al.*, 2004). NEAD was designed specifically to be interpreted together with TOSS. We purposely conducted this analysis following the procedures used in Marceau and Neiderhiser (2022), which was a univariate decomposition of adolescents’ severity and directionality in the NEAD sample. In that sample, genetic, shared, and nonshared environmental influences contributed to adolescents’ symptom severity, whereas only genetic and nonshared environmental influences contributed to adolescents’ symptom directionality. We will interpret the findings of the current study together the findings from Marceau and Neiderhiser (2022), lending further insight into the mechanisms of intergenerational transmission of psychopathology symptom severity and directionality in a “dual-sample” framework (Neiderhiser *et al.*, 2004).

### Hypotheses

Based on the above findings for intergenerational transmission within and across internalizing and externalizing disorders, we hypothesize that there will be genetic and phenotypic transmission of both severity and directionality. Due to evidence of shared environmental influences on adolescents’ symptom severity, we posit that there may also be a role of extended family effects on severity.

### Method

#### Participants

The present study analyzed data from the Twin and Offspring Study in Sweden (TOSS; Neiderhiser & Lichtenstein, 2008), a sample of 909 same-sex twin pairs recruited through the use of the Swedish Twin Registry in two cohorts within 3 years of each other. The first cohort included 326 female twin pairs born between 1926 and 1966, and the second included 583 male and female twin pairs born between 1944 and 1971. For both cohorts, inclusion criteria were (1) the twins each had an adolescent child that was the same sex and within 4 years of age of the co-twin’s adolescent child and (2) the twins each were in a long-term relationship with a partner who resided in the same home (so that the current living experiences of the twin parents were similar to those of the co-twin).

<sup>1</sup>See limitations section for discussion of why we did not use the Silberg *et al.* (2010) extension to COT models.

All study procedures were approved by institutional review boards (IRB) in Sweden and the United States, informed consent was provided by all participants, and the Purdue University IRB approved this secondary data analysis.

Zygoty was established using a validated questionnaire, on which twins were rated for physical similarity (Nichols & Bilbro, 1966). DNA was used to confirm zygoty for 89% of the sample (11% of twins either refused to provide DNA or the sample was unusable; agreement with the questionnaire was 96%). In the case of disagreement between DNA and questionnaire zygoty, DNA was prioritized. The analysis sample consists of 854 families for whom we have zygoty information, covariate data (age and sex of the twins; age, sex, and age difference of the twins' adolescent offspring), as well as data on both internalizing and externalizing problems for at least one person in the extended family unit (128 MZ fathers, 185 DZ fathers, 253 MZ mothers, and 288 DZ mothers). At the time of assessment, adult twins were 32–60 years old ( $M = 44.9$  years,  $SD = 4.9$  years). The adult twins' adolescent offspring were 11–22 years old ( $M = 15.7$  years,  $SD = 2.4$  years) and were 52% female.

## Measures

### Twin internalizing problems

Adult twins' internalizing problems were measured by standardizing and averaging the following scores: Total depressive symptoms were assessed via the Center for Epidemiological Studies Depression Scale, a 20-item measure of the frequency of symptoms of depression in the past week,  $\alpha = .90$  (CES-D; (Gatz et al., 1993; Radloff, 1977)). Psychic anxiety (10 items, i.e., "even if I know I'm right I find it difficult to stand up for myself";  $\alpha = .80$ ) and somatic anxiety (10 items, i.e., "sometimes I get a feeling that there is not enough air to breathe,"  $\alpha = .87$ ) were assessed on the Karolinska Institute Personality, which asked twins to "think about what answer best fits with the way you usually act and feel" (Schalling & Edman, 1993). The total number of phobias was assessed via a DSM measure. First, participants rated a list of 18 common phobias whether: (a) they give up things because of their fear; (b) whether they have an exaggerated fear of [each checkbox]; and (c) whether their fear of each thing is uncontrollable. After these questions, they rated for each fear, on a scale of 1 (no fear) to 10 (very afraid) for each fear. The average score across all items was used to index phobias,  $\alpha = .85$  (Fredrikson et al., 1996). Finally, continuous indicators of DSM anxiety and depression symptoms were created from the Composite International Diagnostic Inventory (CIDI; (Kessler & Üstün, 2004, available only in the second cohort)). Specifically, for depression symptoms, the continuous score was the sum of 8 symptoms, and one additional point each was added for each of the following diagnostic indicators: (1) symptoms interfering with daily tasks; (2) symptoms lasting all or most of the day long; and (3) feeling like this every day or almost every day. For anxiety, the continuous score was the sum of nine symptoms plus an additional point for symptoms interfering with daily tasks. All of these scale scores were correlated (range:  $r = .21$  to  $r = .68$ ), and Cronbach's alpha for the composite indicated a reliable score ( $\alpha = .80$ ) that was roughly normally distributed around 0,  $M = .008$ ,  $SD = 0.74$ , range =  $-1.51$  to  $3.31$ , Skewness = 1.11, Kurtosis = 1.31. The presence of a few ( $n = 16$ ) moderate outliers affected this distribution and were winsorized to  $+3$  SD of the distribution (2.24), yielding a normal distribution (Skewness = 0.99, Kurtosis = 0.66).

### Twin externalizing problems

In TOSS, externalizing in twins was measured primarily by measures of aggression. Thus, twin externalizing problems were indexed by standardizing and averaging indirect aggression (5 items, i.e., "I sometimes get so angry that I throw things"), verbal aggression (5 items, i.e., "When I get angry I sometimes say nasty things"), and aggression – irritability (5 items, i.e., "Sometimes I get irritated just having people around me") subscales of the Karolinska Institute Personality (Schalling & Edman, 1993). Correlations ranged from  $r = .31$  to  $r = .43$ , and Cronbach's alpha for the composite indicated acceptable reliability ( $\alpha = .64$ ) that was normally distributed around 0,  $M = .0003$ ,  $SD = 0.76$ , range =  $-2.61$  to  $3.05$ , Skewness = 0.12, Kurtosis =  $-0.04$ . To be consistent with our treatment of the internalizing composite, outliers ( $n = 4$ ) were winsorized to  $+3$  SD of the distribution (2.29), which did not largely affect the distribution (Skewness = 0.10, Kurtosis =  $-0.18$ ).

### Adolescent internalizing problems

Adolescent internalizing problems were assessed by standardizing and averaging the following scores. Twin, spouse, and youth reported on internalizing problems over the past 6 months using the CBCL internalizing subscale (Achenbach & Edelbrock, 1979). The internalizing measure was constructed from 7 withdrawn items, 14 anxious/depressed items, and 9 somatic compliant items,  $\alpha$ 's across raters  $> .82$ . Additionally, the following four measures were included that were only available in the second cohort: Youth self-reported total depressive symptoms in the past week on the CES-D,  $\alpha = .75$  (Gatz et al., 1993; Radloff, 1977). The total number of phobias was assessed as described above for twins, via youth self-report  $\alpha = .80$  (Fredrikson et al., 1996). Twins and spouses also reported on adolescents' depressive symptoms in the last weeks using the Child Depression Inventory (Kovacs, 1985), which asks parents to choose which of three sentences best describes how their child feels (27 items),  $\alpha$ 's across raters  $> .82$ . Finally, using the Eating Disorders Inventory – 2 (Garner, 1991), youth self-reported symptoms of three eating disorder subscales on a scale of always (1) to never (6): drive for thinness (7 items), susceptibility to bulimia (7 items), and body dissatisfaction (8 items),  $\alpha$ 's across scales  $> .74$ . All of these scale scores were correlated (range:  $r = .12$  to  $r = .70$ ), and Cronbach's alpha for the composite indicated a reliable score ( $\alpha = .83$ ) that was right-skewed and leptokurtotic around 0,  $M = -0.02$ ,  $SD = 0.67$ , range =  $-1.06$  to  $4.18$ , Skewness = 1.69, Kurtosis = 4.28. The presence of outliers ( $n = 36$ ) affected this distribution and were winsorized to  $+3$  SD of the distribution (1.99), which improved the distribution (Skewness = 1.24, Kurtosis = 1.46) sufficiently to proceed with the creation of severity and directionality scores (see below).

### Adolescent externalizing problems

Adolescent externalizing was assessed by standardizing and averaging the following scores: Youth self-reported their aggression – assertiveness (10 items, i.e., "When a teacher or coach or similar is unfair to me, I get angry and protest,"  $\alpha = .67$ ), aggression (12 items, i.e., "It's ok to make life difficult for a teacher, coach or similar who is stupid,"  $\alpha = .74$ ), and aggression – irritability (8 items, i.e., "Sometimes I'm so furious that I just hit someone,"  $\alpha = .78$ ), on the childhood aggression scale (no timeframe specified; Olweus et al., 1988). Twin, spouse, and youths reported on externalizing problems over the past 6 months using the CBCL externalizing subscale (Achenbach & Edelbrock, 1979). The externalizing measure was constructed from 19 aggressive and 11 delinquent behavior items,  $\alpha$ 's across raters  $> .82$ . Finally, youth in the second cohort

only self-reported how often (daily = 5 to never = 1) they commit relational aggression on 13 items (i.e., “Try to make others not like a certain person by spreading rumors about them”; (Crick & Bigbee, 1998)), and were victimized on 11 items. All 24 items were factor analyzed, with oblique rotation, recovering victimized, and victimizing scores as anticipated ( $r = .57$ ); only the victimizing scale was used here (Eigenvalue = 1.84;  $\alpha = .67$ , additional information available upon author request). Correlations for all of these subscales ranged from  $r = .11$  to  $r = .57$ , and Cronbach’s alpha indicated an acceptably reliable composite score ( $\alpha = .65$ ), which was normally distributed around 0,  $M = 0.002$ ,  $SD = 0.70$ , range =  $-1.53$  to  $3.91$ , Skewness = 0.86, Kurtosis = 1.08. As above, a few ( $n = 11$ ) outliers were winsorized to  $+3$  SD of the distribution (2.09), which improved Kurtosis (Skewness = 0.71, Kurtosis = 0.25).

### Analytic strategy

Data preparation decisions, code, and output supporting this paper can be found here: <https://osf.io/ure8z/>.

### Data preparation

We adjusted for covariates using linear regression. For each twin (1 and 2) and adolescent offspring (of twin 1 and 2), we regressed the age and sex of the twin as well as the age of both adolescents, adolescent sex (entered once, as it was always the same for each twin pair), and the age difference between the adolescents onto each score (i.e., twin internalizing, twin externalizing, adolescent internalizing, and adolescent externalizing). The residuals were saved as an index of the focal variables less the variance attributable to covariates, as commonly done in analyses of this kind (Neiderhiser, Reiss, Lichtenstein, et al., 2007; Neiderhiser et al., 2004).

Next, following Marceau and Neiderhiser (2022) and prior studies (Essex et al., 2003; Shirtcliff & Essex, 2008), severity and directionality scores were computed via a principal component analysis (PCA), conducted separately within zygosity group (though scores were correlated  $> .99$  whether done with the full sample or separately by zygosity, analysis available upon request). Specifically, the internalizing and externalizing composites were simultaneously entered into a PCA with two factor scores extracted and saved (i.e., as the severity and directionality scores)<sup>2</sup>. This effectively reorganizes the variance into two completely orthogonal scores, the first comprising what the scores have in common, reflecting severity of total problems regardless of type, and the second loads each score in opposite directions in exactly the same strength – comprising what differentiates the scores, called directionality, with positive scores indicating stronger differentiation towards (or more pure) externalizing problems and negative scores indicating a stronger differentiation toward (or more pure) internalizing problems.

### Analysis

Prior to conducting the children-of-twins model, we conducted intra-class correlations (ICCs) separately by zygosity. Correlations between twin 1 and 2 that are twice as large among MZ twins than DZ twins indicate the presence of additive genetic

influences; if the MZ twin correlation ( $r_{MZ}$ ) is more than twice that of the DZ twin correlation ( $r_{DZ}$ ), then dominant genetic influences are indicated. Briefly, additive genetic influences comprise the influence of all genes on the phenotype that operate together in a linear or additive way, whereas dominant genetic influences include nonadditive, typically interactive, effects of different alleles both within a locus (i.e., genetic dominance) and across loci (epistasis) (Rettew et al., 2008). If  $r_{MZ}$  is less than twice the size of  $r_{DZ}$ , then shared environmental influences are indicated. Finally, to the extent that  $r_{MZ}$  is not 1, nonshared environmental influences are indicated. Examining ICC’s is a critical first step, because in a children-of-twins design where only MZ and DZ twins are included, as is the case here, there is not power to simultaneously estimate additive genetic (A), dominant genetic (D), shared environmental (C), and nonshared environmental (E) influences – we can only estimate ADE or ACE models. Thus, the twin correlations are used to choose the baseline model. In addition to twin correlations, we also estimated parent–offspring and avuncular (twin-niece/nephew) correlations, which helps to set expectations about genetic transmission. That is, if the  $r_{MZ}$  for parent–offspring correlations are twice that of  $r_{DZ}$  for parent–offspring correlations, and higher than avuncular correlations, genetic transmission is expected. Regardless of zygosity, if parent–offspring correlations are higher than avuncular correlations, phenotypic transmission is expected. Highly similar parent–offspring and avuncular correlations regardless of zygosity would indicate the likelihood of extended family effects.

### Children-of-twins model

The children-of-twins design leverages data on families of adult twins and their children. Using biometric models (McAdams et al., 2018), correlations between parent and child psychopathology are explained by a combination of genetic transmission (Figure 2:  $a_i \cdot .50 \cdot a_{ta}$ ), extended family effects (Figure 2:  $c_{ta}$ ), and phenotypic influences (labeled “p” in Figure 2). The phenotypic path may indicate a *potentially* causal “exposure effect.” That is, exposure to parents’ or children’s genetically influenced psychopathology would be directly associated with the others’ psychopathology influences either from parent to child or child to parent, after accounting for shared genetic influences and any extended family effects (i.e., the twin parents’ rearing environment influencing offspring psychopathology). However, it is much more likely that the phenotypic path reflects some form of gene–environment correlation and/or the presence of a third variable that either induces or explains the association – either an environmental causal factor (not captured by extended family effects), leading to both parent and adolescent psychopathology, or unmeasured mediators (i.e., parenting, genetic nurture).

### Base model selection

ICC results are presented in Table 1. The twin correlations for both severity and directionality indicated  $r_{MZ}$  were more than twice  $r_{DZ}$ , and so the base model chosen for the children-of-twins analyses was ADE models. The correlations for the children-of-twins for severity were equal for children of MZ and children of DZ twins suggesting no genetic influences on severity in the children. Whereas, for directionality, the correlations for the children of MZ twins were twice that of children of DZ twins (though both correlations were very small). For both severity and directionality, parent–offspring correlations were higher than avuncular correlations, but not higher among MZ twin families than DZ twin families, suggesting that phenotypic transmission will explain the

<sup>2</sup>Given that the second cohort ( $n = 1092$ ) had more measures than the first cohort ( $n = 652$ ), we also created “reduced” scores for adolescent internalizing and externalizing problems by including only the scores that were measured in both cohorts. The correlations of the full and reduced scores in cohort 2 ranged from  $r = .87$  to  $.98$  for internalizing, externalizing, severity, and directionality. We judged it more important to include a better range of variables for the youth for whom we were able (the majority of the sample).

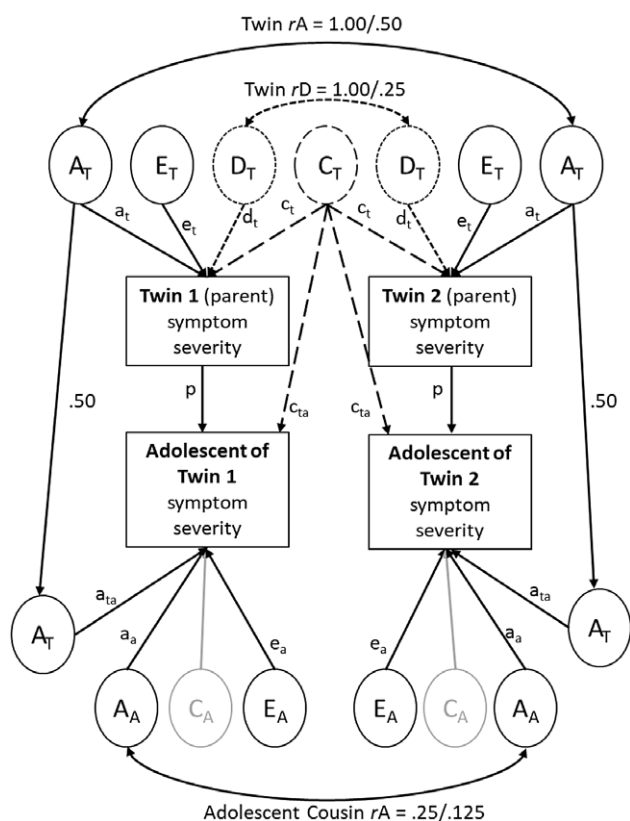


Figure 2. Children-of-twins model.

intergenerational transmission of severity and directionality of psychopathology symptoms.

As noted above, our base model includes additive genetic ( $A_T$ ), dominant genetic ( $D_T$ ), and nonshared environmental influences ( $E_T$ ) on twins' severity and directionality, as well as additive genetic ( $A_A$ ) and nonshared environmental influences ( $E_A$ ) on adolescent offspring's severity and directionality. Additionally, the children-of-twins model includes a path,  $a_{ta}$ , that begins with parents' additive genetic influences through offspring's additive genetic influences (fixed at .50 because parents pass 50% of their segregating genes on to their offspring) to the offspring's phenotype.  $a_{ta}$  indicates genetic transmission. There is also a direct path from parent to offspring phenotype,  $p$ , which indicates phenotypic transmission. Importantly, although this phenotypic path is modeled in the structural equation model as a directional path, it is actually correlational in nature and could go in either direction. Because  $C_T$  was not estimated based on the patterns of correlations from the ICCs, extended family effects ( $c_{ta}$ ) are not possible and thus not included in the model (McAdams et al., 2018). Our model-fitting steps included fitting this *baseline model* (Figure 2) with confidence intervals. Then, we systematically set the following paths to zero to confirm their importance:  $d_t$ ,  $a_{ta}$ ,  $p$ . If there was a decrement in model fit as measured by the difference in the  $-2\text{LogLikelihood}$  function under a chi-square distribution and/or a higher AIC value when constraining the path to zero ("dropping" the path), and confidence intervals included zero, this constitutes strong evidence of the paths' importance. The *final model* is the model deemed most parsimonious model (i.e., with unimportant paths set to zero) with the best fit (i.e., lowest AIC value).

## Results

### Severity

Unstandardized parameter estimates, 95% confidence intervals from the baseline model, and variance components from the baseline and final models are presented in the top panel of Table 2. Parameter estimates from the baseline model suggested that 9% of the variance in twins' severity was attributable to additive genetic influences, though confidence intervals included zero, 44% of the variance in twins' severity was attributable to dominant genetic influences (95% confidence intervals did not include zero for  $D_T$  or  $E_T$ ). Further, there were genetic ( $A_A = 52\%$ ) and nonshared environmental ( $E_A = 40\%$ ) influences on adolescents' symptom severity, although 95% confidence intervals included zero for  $A_A$ . There was no evidence of genetic transmission ( $A_{TA} < 1\%$ , with a negative unstandardized estimate of  $-0.04$ ), but there was evidence of phenotypic transmission ( $p = 8\%$  of the variance in adolescent offspring's symptom severity). The estimated phenotypic correlation between parent and offspring symptom severity was  $r = .29$ ,  $-2\%$  of which was attributable to genetic transmission and  $102\%$  of which was attributable to phenotypic transmission. Consistent with these results, there was a decrement in model fit when we attempted to fix  $d_t$  or  $p$  to zero, but no decrement in model fit when we fixed  $a_{ta}$  to zero (Table 3, top panel). Thus, the final, best-fitting model included small additive genetic influences ( $A_T = .09$ , 95% CI [ $3.6e^{-10}$ , .43]), relatively larger but still moderate dominant genetic influences ( $D_T = .45$ , 95% CI [.08, .59]), and moderate nonshared environmental influences ( $E_T = .47$ , 95% CI [.41, .54]) for twins' psychopathology symptom severity, additive genetic ( $A_A = .52$ , 95% CI [.20, .83]) and nonshared environmental ( $E_A = .40$ , 95% CI [.09, .71]) influences on adolescents' psychopathology symptom severity, and  $100\%$  phenotypic transmission to offspring symptom severity.

### Directionality

Unstandardized parameter estimates and 95% confidence intervals from the baseline models and variance components from the baseline and final models are presented on the bottom panel of Table 2. Parameter estimates from the baseline model suggested that 20% of the variance in twins' directionality was attributable to additive genetic influences, though 95% confidence intervals included zero, and 20% of the variance in twins' directionality was attributable to dominant genetic influences, though this was a negative unstandardized estimate, and 95% confidence intervals included zero. The majority (60%) of the variance was attributable to nonshared environmental influences (95% confidence intervals did not include zero for  $E_T$ ). Further, there were genetic ( $A_A = 22\%$ ) and nonshared environmental ( $E_A = 70\%$ ) influences on adolescents' directionality, although confidence intervals included zero for  $A_A$ . There was little evidence of genetic transmission ( $A_{TA} = 6\%$ , confidence interval including zero), and of phenotypic transmission ( $p = 1\%$  of the variance in adolescent offspring's symptom directionality, confidence interval does not include zero). The estimated phenotypic correlation between parents and offspring was  $r = .17$ , 32% of which was attributable to genetic transmission and 68% of which was attributable to phenotypic transmission. There was no decrement in model fit when we fixed  $d_t$ ,  $a_{ta}$ , or both to zero (see Table 3, bottom panel), but there was a decrement in model fit when we attempted to fix  $p$  to zero. Thus, the final, best-fitting model included one-third additive genetic influences ( $A_T = .39$ ,

**Table 1.** Intra-class correlations

	Twins		Children-of-twins	
	MZ	DZ	MZ	DZ
Severity	0.53	0.16	0.13	0.13
Directionality	0.40	0.15	0.09	0.04
Twin → own child	Twin → own child		Twin → niece/nephew	
	MZ	DZ	MZ	DZ
Severity	0.24	0.32	0.10	0.09
Directionality	0.16	0.17	0.08	0.08

Note. MZ = monozygotic twins (share 100% of segregating genes); DZ = dizygotic twins (share on average 50% of segregating genes).

**Table 2.** Parameter estimates

	Severity			
	Lower bound [95% CI]	Unstandardized estimate	Upper bound [95% CI]	Variance component full   final
Twin parents				
A <sub>T</sub>	-0.67	0.30	0.67	9%   9%
D <sub>T</sub>	0.27	0.67	0.79	44%   45%
E <sub>T</sub>	0.64	0.68	0.73	47%   47%
Children of twins				
A <sub>A</sub>	-0.91	0.72	0.91	52%   52%
A <sub>TA</sub>	-0.91	-0.04	0.91	<1%   0%
E <sub>A</sub>	0.31	0.63	0.84	40%   40%
P	0.18	0.29	0.40	8%   8%
	Directionality			
	Lower bound [95% CI]	Unstandardized estimate	Upper bound [95% CI]	Variance component full   final
Twin parents				
A <sub>T</sub>	-0.68	0.45	0.68	20%   39%
D <sub>T</sub>	-0.69	-0.45	0.69	20%   0%
E <sub>T</sub>	0.72	0.77	0.83	60%   61%
Children of twins				
A <sub>A</sub>	-0.76	0.46	0.76	22%   26%
A <sub>TA</sub>	-0.77	0.24	0.77	6%   0%
E <sub>A</sub>	0.60	0.84	1.00	70%   72%
P	0.01	0.11	0.22	1%   3%

Note. A<sub>T</sub> = additive genetic influences of twin parents on their own phenotype, D<sub>T</sub> = dominant genetic influences of twin parents on their own phenotype, E<sub>T</sub> = nonshared environmental influences of twin parents on their own phenotype, A<sub>A</sub> = additive genetic influences of adolescent offspring on their own phenotype, A<sub>TA</sub> = genetic transmission, E<sub>A</sub> = nonshared environmental influences of adolescent offspring on their own phenotype, P = phenotypic transmission.

95% CI [.31, .46]), and two-thirds nonshared environmental influences (E<sub>T</sub> = .61, 95% CI [.54, .69]) for twins' psychopathology symptom directionality, small additive genetic (A<sub>A</sub> = .26, 95% CI [1.9e<sup>-12</sup>, .59]) and larger nonshared environmental (E<sub>A</sub> = .72, 95% CI [.37, .98]) influences on adolescents' psychopathology symptom directionality, and 100% phenotypic transmission to offspring symptom directionality.

## Discussion

The present study leveraged the Twin and Offspring Study in Sweden to examine the etiology of psychopathology symptom

severity and directionality in adults, as well as the mechanisms of intergenerational transmission of symptom severity and directionality to adolescent offspring. First, we found evidence of intergenerational transmission of both symptom severity and to a lesser extent of symptom directionality ( $r = .17$  for symptom directionality vs.  $r = .29$  for symptom severity). Findings for severity provide evidence of intergenerational transmission of comorbidities and support an underlying vulnerability to psychopathology that is reflected in prior evidence of heterotypic continuity. Our findings of intergenerational transmission of directionality provide a stronger test of homotypic intergenerational continuity than has been previously achieved. Broadly, our analysis of symptom



**Table 3.** Model-fitting results

Baseline model	Severity							
	Comparison model	Estimated parameters	-2LL	df	AIC	diffLL	diffdf	p-value
CoT	NA	9	9360.9	3394	2572.9	NA	NA	NA
CoT	D <sub>T</sub> fixed to 0	8	9366.6	3395	2576.6	5.65	1	.018
CoT	A <sub>TA</sub> fixed to 0	8	9360.9	3395	2570.9	0.01	1	.907
CoT	P fixed to 0	8	9392.0	3395	2602.0	31.10	1	<.0001
Baseline model	Directionality							
	Comparison model	Estimated parameters	-2LL	df	AIC	diffLL	diffdf	p-value
CoT	NA	9	9519.6	3394	2731.6	NA	NA	NA
CoT	D <sub>T</sub> fixed to 0	8	9520.7	3395	2730.7	1.07	1	.302
CoT	A <sub>TA</sub> fixed to 0	8	9521.0	3395	2731.0	1.34	1	.248
CoT	D <sub>T</sub> and A <sub>TA</sub> fixed to 0	7	9521.9	3396	2729.9	2.25	2	.325
CoT	P fixed to 0	8	9524.5	3395	2734.5	4.88	1	.027

Note. The best fitting model as judged by no decrement in fit, lowest AIC, fewest parameters estimated (parsimony) is bolded. CoT = Children of Twins, D<sub>T</sub> = dominant genetic influences of twin parents on their own phenotype, A<sub>TA</sub> = genetic transmission, P = phenotypic transmission.

severity and directionality confirm the presence of some homotypic continuity as well as relatively stronger evidence of intergenerational transmission of an underlying vulnerability to psychopathology that may take the form of transmission of comorbidities or heterotypic continuity.

For both symptom severity and directionality, we found no evidence of genetic transmission or extended family effects; transmission was entirely phenotypic in nature. Although this study provides evidence against genetic transmission and extended family effects, findings from a children-of-twins study showing phenotypic transmission alone are not particularly informative. This is because phenotypic transmission can reflect several mechanisms, including a causal phenotypic association from parents to children or children to parents, and/or passive or nonpassive *r*GE, which could be mediated by other phenotypes (i.e., parenting). Here, to gain more insight into the likely explanation of phenotypic transmission, we interpret findings alongside those of Marceau and Neiderhiser (2022), in a dual-sample design framework.

### Insights from the dual-sample design

As noted in detail elsewhere (e.g., Marceau et al., 2016; Neiderhiser, Reiss, Lichtenstein, et al., 2007; Neiderhiser et al., 2004), comparing findings from child-based (children are twins/siblings) and parent-based (parents are twins) twin designs can help to clarify which types of *r*GE are operating. Typically, studies taking this approach have been limited to examining parenting behaviors. A similar strategy can be employed for child behavioral outcomes when the full children-of-twins design is used with measures of the same/similar behaviors in parents and offspring as in the current report. The first rows labeled “Theory” in Table 4 describe the possible findings for child-based twin studies, parent-based twin studies, and children-of-twins analyses, and the conclusions that can be drawn. The subsequent rows describe the findings from the current report and note the conclusions that are indicated by those findings. This table is meant to be a guiding heuristic to aid in interpretation – the rows are not mutually exclusive (part of the association could be due to evocative and part passive or a more direct genetic or phenotypic mechanism), nor are they exhaustive with regard to possible mechanism (non-*r*GE explanations could

include anything that is not *r*GE – genetic transmission, genetic nurturing, parenting mediators, etc.). Further, these interpretations are not necessarily specific to the correlation – we are inferring about the correlation based on a pattern of findings by describing potential/plausible mechanisms (and ruling out some). Our results suggest that phenotypic transmission (i.e., no genetic transmission), which includes direct environmental influence and/or could be mediated by specific parenting behaviors (Jami et al., 2021), plays an important role in the intergenerational transmission of symptom severity and directionality. As demonstrated in Table 4, both passive and nonpassive *r*GE likely play a role in intergenerational transmission of severity, whereas specifically nonpassive *r*GE is likely to play a role in symptom directionality. In terms of non-*r*GE explanations, we found that intergenerational genetic transmission is not indicated for either symptom severity or directionality. This, along with only modest correlations between parent and offspring symptom severity and directionality, implies that there is substantial generationally unique (not intergenerationally transmitted) psychopathology.

### Severity and directionality

Our analysis of symptom severity and directionality adds to the literature on psychopathology more broadly. Predominant models concerning comorbidity and the structure of psychopathology in the literature include correlated factor models, bifactor models, and hierarchical models. In correlated factors models, two distinct internalizing factors are formed, and correlations between the factors are included in the model (Caspi & Moffitt, 2018). In bifactor models, symptoms can simultaneously load on both spectrum-specific and a general factor, and thus internalizing and externalizing phenotypes are subdomains beyond the general factor (Hartman, 2021). In hierarchical models, symptoms first load on internalizing or externalizing subdomains which then load on a general factor, and thus internalizing and externalizing phenotypes are subdomains within the general factor (Hartman, 2021).

### Severity

Symptom severity, as modeled here, reflects comorbidity of internalizing and externalizing problems in a way that most closely

**Table 4.** Summary of findings and interpretation

GE correlation	Child-based design	Parent-based design	COT paths (% of covariance)	Conclusion
Theory				
	C	A (and D)	P, C <sub>TA</sub>	Passive rGE
	A (and D)	C and/or E	P	Nonpassive rGE
	C and/or E	C and/or E	A <sub>TA</sub>	Non-rGE explanations
Results of Marceau and Neiderhiser (2020) (Child-based design) and current study (Parent-based design and COT paths)				
Severity				
Passive rGE	C (20%)	A (9%), D (45%)	P (100%)	Likely passive rGE transmission
Nonpassive rGE	A (58%)	E (40%)	P (100%)	Likely some nonpassive rGE transmission
Non-rGE explanations	E (22%)	E (40%)	None	Unlikely genetic transmission, generationally unique (not intergenerationally transmitted) psychopathology
Directionality				
Passive rGE	None	A (39%)	P (100%)	Unlikely passive rGE
Nonpassive rGE	A (65%)	E (61%)	P (100%)	Likely nonpassive rGE
Non-rGE explanations	E (35%)	E (61%)	None	Unlikely genetic transmission, generationally unique (not intergenerationally transmitted) psychopathology

Note. COT paths (% of covariance) indicate the results from the covariance between parent and child phenotypes from the COT model. A = additive genetic influences, D = dominant genetic influences, C = shared environmental influences, E = nonshared environmental influences, C<sub>TA</sub> = extended family effects, A<sub>TA</sub> = genetic transmission, P = phenotypic transmission. In the second part of the Table, the variance component results are presented. For Passive rGE, for example, the combination of evidence for C in the child-based design, A and D in the parent-based design, and P in the covariance between parent and child phenotype is consistent with passive rGE for severity, whereas passive rGE is unlikely for directionality given the lack of C in child-based design. For no evidence of rGE, for example, in the absence of A<sub>TA</sub> (which would have indicated genetic transmission rather than rGE), and in the absence of C in the parent and/or child generation (which would have indicated possible extended family effects), the presence of nonshared environmental influences on both parent and adolescent psychopathology suggests also generationally unique effects (in addition to the rGE findings).

reflects a hierarchical or second-order “*p*-factor.” However, internalizing and externalizing factors and the second-order “*p*-factor” in hierarchical models are dependent on one another which creates a statistical limitation in attempts to investigate mechanisms involved in the development of the general versus specific factors (Lahey et al., 2021). Whereas, a feature of bifactor models is that the general and specific factors are orthogonal (i.e., uncorrelated with each other), which offers advantages to exploring the etiology of the specific dimensions as well as correlates of each dimension (Lahey et al., 2021). The severity-directionality model used here has the benefit of orthogonality between the general factor (severity) and unique subdomains (captured in directionality), similar to bifactor models, while the severity score is built directly from the internalizing and externalizing subdomains conceptually akin to the hierarchical model. Critically, more complex factor structures (i.e., bifactor or hierarchical models) have not been implemented within a children-of-twins frame, and so leveraging the comorbid symptom severity score allowed a new perspective on the intergenerational transmission of psychopathology. Our findings thus provide evidence that in addition to the intergenerational transmission of forms of psychopathology previously found in the literature, there is also intergenerational transmission of specifically comorbidity of psychopathology. Further, our findings suggest that direct phenotypic, passive rGE, and nonpassive rGE – but not genetic transmission – are all plausible mechanisms supporting the intergenerational transmission of comorbid internalizing and externalizing problems.

Interestingly, much of the variance in adult twins’ symptom severity was attributable to dominant and to a lesser extent additive genetic effects. This is somewhat inconsistent with recent findings that the heritability index for the *p*-factor was estimated as 48% for

adults from two different parameterizations, though it is unclear whether dominant effects were tested (Rosenström et al., 2019). In the current study, dropping dominance effects produced a decrement in model fit, but yielded a heritability estimate more similar to Rosenström et al. (2019). Our findings, considered alongside the similar analysis of adolescent twins (Marceau & Neiderhiser, 2022) could indicate a developmental effect whereby the etiology of comorbidity changes from adolescence – where symptom severity reflects primarily familial variance – mainly additive genetics but also the shared environment – to adulthood – where symptom severity reflects primarily nonshared environmental influences and dominant genetic influences. Or, these findings could reflect measurement differences in terms of the specific scales included between the two studies.

#### Directionality

Symptom directionality is an interesting measure because it directly measures differentiation, which contributes to the work needed to better understand the “splitting” side of psychopathology at least at the spectra level (Hartman, 2021). This analysis does not examine the etiology of internalizing problems either within or beyond a general “*p*-factor,” as other hierarchical models of psychopathology do (Hartman, 2021; Lahey et al., 2021). Instead, the intergenerational transmission of directionality can be conceptualized as a specific test of homotypic continuity after controlling for comorbidity. That is, the positive association (though small) between parents’ and adolescents’ directionality scores is evidence of weak but still important homotypic continuity, and we further show that homotypic intergenerational continuity is primarily attributable to either direct phenotypic or nonpassive rGE processes. This latter explanation underscores

the critical limitation that our analysis is of a cross-sectional correlation between parents and offspring, and it is entirely possible that youths' genetically influenced, relatively pure externalizing problems (high scores on directionality) evoke their parents' relatively specific externalizing problems and/or that youths' genetically influenced and/or relatively pure internalizing problems (more negative scores on directionality) evoke their parents' relatively specific internalizing symptoms. Directionality scores may be more likely to contain random measurement error, so that we were able to recover intergenerational transmission at all – that was not all attributable to nonshared environmental influences (which also hosts the measurement error) – indicates that symptom directionality scores do contain a signal worth examining.

#### *Additional insights from the univariate decomposition of severity and directionality*

Although not a central conceptual focus of this study, the univariate decomposition on symptom severity and directionality in adults inform on the generalist genes – specialist environments hypothesis, which posits that genetic influences are more likely to contribute to commonalities in types of psychopathology exhibited – or comorbidity, whereas environmental influences are more likely to push individuals toward one form of psychopathology versus another (Kovas & Plomin, 2007; Marceau & Neiderhiser, 2022; Rhee et al., 2015). Surprisingly, dominant genetic and nonshared environmental influences were primarily implicated in twin parents' symptom severity, which was quite different than the etiology in adolescence (Marceau & Neiderhiser, 2022), where shared environmental influences also contributed to symptom severity. In contrast, differentiation of problem type (i.e., symptom directionality) in twin parents was attributable to additive genetic and nonshared environmental influence, mirroring that found in adolescence (Marceau & Neiderhiser, 2022).

Genetic influences on symptom severity support the notion of “generalist genes.” Although in general the contribution of generalist genes was similar in adolescence (58% additive genetic variance) and adulthood (54% dominant + additive genetic variance), findings on the etiology of symptom severity to date confirm the importance of generalist genes, although in a tempered way, since half of the variance of comorbidity in the current study and in Marceau and Neiderhiser (2022) was attributable to environmental influences. Further, although we find some support for specialist environments, in that there were substantial nonshared environmental influences on symptom directionality, the presence of genetic influences weakens the overall support for the generalist genes specialist environments hypothesis.

#### *Limitations*

Several limitations should be considered before generalizing these findings. First, the sample was drawn from Sweden and was reflective of the demographics of that country at the time of data collection – nearly all White individuals of European ancestry. Future children-of-twins studies that include a wider array of diversity in terms of country of origin, ancestry, and social context are critical for moving this work forward. Second, the measures used in the present study and Marceau and Neiderhiser (2022) differed, which may limit the validity of the dual-sample design comparisons. Specifically, externalizing in NEAD primarily reflected antisocial behavior, whereas in TOSS externalizing reflected aggression; the NEAD internalizing measure was mostly depressive symptoms, whereas in TOSS it was more balanced for depression and anxiety

and also included phobias. Thus, the severity and directionality scores contain slightly different information across studies. Past behavioral genetics work has established that patterns of genetic and environmental correlations of conduct/antisocial and depressive phenotypes are reasonably consistent with the broader externalizing and internalizing phenotypes (Cosgrove et al., 2011; Subbarao et al., 2008). Nonetheless, the interpretations regarding possible *r*GE will be important to follow-up in studies using parent- and child-based twin studies with better matched phenotypes.

As noted above, we were limited in our ability to identify specific mechanisms within the phenotypic pathway. Several more complex models can attenuate these limitations (see McAdams et al., 2018 for discussion). For example, the inclusion of spouses in more complex models could test assortative mating and specific pathways of environmental transmission (e.g., explicitly modeling passive *r*GE separate from the phenotypic pathway). Although TOSS does have data on spouses, we did not include them for the following reasons. First, there were a limited number of families and sibling types (only MZ and DZ twins, no non-twin sibling types) in this study leading to reduced power for more complex models. Second, some of the constraints necessary for those models to be identified were questionable for this application given differences in the univariate findings in TOSS and NEAD. Phenotypic correlations between twins and spouses were modest  $r = .19$  for severity and  $r = .10$  for directionality<sup>3</sup>. Unmeasured assortative mating could either inflate the measure of genetic transmission (for which we found no evidence) or could inflate the phenotypic correlation; however, we are unable to distill which of these may be occurring in this study.

Finally, two critical future directions include dyadic gender differences and longitudinal extensions. A large literature has shown robust dyadic gender differences in intergenerational transmission of psychopathology (Andreas et al., 2018), which we did not have the statistical power to address here. However, phenotypic correlations did not point to large dyadic gender differences in intergenerational transmission, with parent-offspring correlations for severity ranging from  $r = .25$ – $.33$  across dyad gender constellations and  $r = .15$ – $.19$  for directionality. There was no discernable pattern of correlations by which one type of transmission (i.e., same vs. opposite gender, male vs. female twin or offspring) differentiated the magnitude of parent-offspring correlations. Nevertheless, given well-known gender differences in the prevalence of internalizing and externalizing problems in adolescence and adulthood future research should continue to examine dyadic gender differences.

Another limitation was that we lacked longitudinal data and could not test longitudinal associations, despite transmission being a process that likely unfolds over time. For example, recent evidence from a within-family design suggested that correlations of mother and adolescent internalizing and externalizing problems was a between-family phenomenon (Schulz et al., 2021). This study also found evidence of an evocative effect on the order of years: earlier child internalizing symptoms predicted later mother internalizing symptoms, whereas father and adolescent internalizing and externalizing symptoms were uncorrelated (Schulz et al., 2021). Replicating and extending this work in larger studies that can leverage longitudinal data with increased power to detect dyadic gender differences are critical future directions.

<sup>3</sup>Please see the files including ‘revision’ in the filename on <https://osf.io/ure8z/> for these correlations and additional information gathered via responding to initial reviews of the present manuscript.

## Conclusions

The present study leveraged a children-of-twins design and the severity-directionality model of psychopathology to examine the intergenerational transmission of comorbid internalizing and externalizing symptoms as well as the differentiation of internalizing and externalizing symptoms (i.e., homotypic intergenerational continuity). We found evidence that comorbid problems and preponderance of symptoms of a particular – internalizing versus externalizing – spectrum are each correlated across parent and child generations, although associations were modest especially for homotypic continuity. We further demonstrated that the intergenerational transmission of comorbid symptom severity and symptom directionality are both unlikely to be attributable to genetic transmission, and are both likely to be influenced by direct phenotypic transmission and/or nonpassive *rGE*, and for symptom severity, also passive *rGE*.

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**Conflicts of interest.** None.

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