# Elucidating the Link between Parent and Adolescent Psychopathology:

# A Test of Transmission Specificity and Genetic and Environmental Liabilities

by

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ABSTRACT

The tendency for psychopathology to aggregate within families is well-documented, though little is known regarding the level of specificity at which familial transmission of symptomology occurs. The current study first tested competing higher-order structures of psychopathology in adolescence, indexing general and more specific latent factors. Second, parent-offspring transmission was tested for broadband domain specificity versus transmission of a general liability for psychopathology. Lastly, genetic and environmental mechanisms underlying the familial aggregation of psychopathology were examined using nuclear twin-family models. The sample was comprised of five hundred adolescent twin pairs (mean age 13.24 years) and their parents drawn from the Wisconsin Twin Project. Twins and parents completed independent diagnostic interviews. For aim 1, correlated factors, bifactor, and general-factor models were tested using adolescent symptom count data. For aim 2, structural equation modeling was used to determine whether broadband domain-specific transmission effects were necessary to capture parent-offspring resemblance in psychopathology above and beyond a general transmission effect indexed by the latent correlation between a parental internalizing factor and offspring P-factor. For aim 3, general factor models were fitted in both generations, and factor scores were subsequently extracted and used in nuclear twin-family model testing. Results indicated that the bifactor model exhibited the best fit to the adolescent data. Familial aggregation of psychopathology was sufficiently accounted for by the transmission of a general liability. Lastly, the best fitting reduced nuclear twin-family model indicated that additive genetic, sibling-specific shared environmental, and nonshared environmental influences contributed to general psychopathology. Parent-

offspring transmission was accounted for by shared genetics only, whereas co-twin aggregation was additionally explained by sibling-specific shared environmental factors. Results provide novel insight into the specificity and etiology of the familial aggregation of psychopathology.

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The study of the impact of parental psychopathology on child development has maintained a long and storied tradition within psychological research. Our understanding of the association between parental psychopathology and child outcomes has evolved tremendously in recent decades (Zahn-Waxler, Duggal, & Gruber, 2002), yet there remain considerable gains to be made. The children of parents with psychiatric disorders are considered "high-risk," in that they are subject to both genetic and environmental vulnerabilities for adverse psychological outcomes (Stokes, 2010). The tendency for psychiatric disorders to run in families is easily observable, and this familial aggregation of psychopathology has been substantiated using both clinical and community samples (Bridge, Brent, Johnson, & Connolly, 1997), however much more remains to be answered regarding the etiological underpinnings of these associations. There is an abundance of research examining the familial aggregation of psychopathology at the disorder specific level; however, this research obfuscates the complexity with which symptoms of psychopathology actually manifest. Approximately half of individuals who meet diagnostic criteria for one psychiatric disorder simultaneously meet diagnostic criteria for another (Newman, Moffitt, Caspi, & Silva, 1998). This issue of comorbidity calls into question the specificity of the familial aggregation of psychopathology. More research is needed to determine whether this intergenerational transmission is disorder specific or whether it reflects the conferral of a general liability to psychopathology. Additionally, more research is needed to elucidate the degree of genetic and environmental influence on psychopathology at these variable levels of specificity. Addressing these questions regarding the development of psychopathology is urgently

needed and stands to greatly inform prevention and intervention research aimed at ensuring positive developmental trajectories for these vulnerable children.

**Parental Psychopathology and Child Outcomes**

The children of parents with psychiatric disorders are vulnerable to a myriad of adverse psychological outcomes. A review of longitudinal research examining the impact of parental depression on offspring revealed that these children were at a heightened risk for developing depressive symptomology themselves, exhibiting earlier onset and greater chronicity than children of non-depressed parents (Beardslee, Keller, Lavori, Staley, & Sacks, 1993). Beyond the narrow-band specific symptomology associated with depression, they are also susceptible to broad-band symptomology generally associated with internalizing problems (Connell & Goodman, 2002). Furthermore, the children of depressed parents possess a heightened risk for developing symptoms that transcend beyond the broadband domain of internalizing and into that of externalizing problems (Kim-Cohen, Moffitt, Taylor, Pawlby, & Caspi, 2005). A consideration of these variable outcomes exhibited by children of depressed parents has prompted researchers to question the specificity of transmission effects (Goodman & Gotlib, 1999).

Analogous issues of specificity emerge for the study of the transmission of other forms of psychopathology. The literature examining the impact of parental anxiety on offspring outcomes is mixed in this regard, with some studies reporting associations specific to anxiety and others reporting broader transmission effects extending to both internalizing and externalizing symptomology (Burstein, Ginsburg, & Tein, 2010). Moreover, these issues of specificity are not exclusive to the study of parental internalizing disorders. That is, the children of alcoholic parents have been found to

exhibit increased susceptibility to both externalizing and internalizing symptomology, however it has been posited that the latter association operates through disturbances in the family environment, as elimination of children's internalizing symptomology often follows parental recovery from alcoholism (Chassin, Rogosch, & Barrera, 1991). These findings allude to a need for researchers to not only determine the specificity of these intergenerational transmission effects but to also elucidate the underlying mechanisms operating at these variable levels of specificity. This task, however, is rendered tremendously complex by the fact that parents not only act as the primary architects of their children's rearing environments but also confer genetic propensities to them.

The maladaptive parenting practices of individuals exhibiting symptoms of psychopathology and associated disturbances in the family environment are considered primary mechanisms through which these intergenerational transmission effects emerge. For example, marital conflict, expressed emotion criticism, and parenting quality (composited rejection, discipline, and psychological aggression) have all been implicated as mediators of the association between parental depression and maladaptive child outcomes (Cummings, Keller, & Davies, 2005; Nelson, Hammen, Brennan, & Ullman, 2003; Riley et al., 2009). This literature is much less robust for the study of parental anxiety and child adjustment, however. There is a relative dearth of research examining the link between parental anxiety, parenting practices, and child anxiety. For the few studies that do examine these associations, findings are mixed, indicating that these parenting behaviors might be poor candidates for consideration as mediators of the familial aggregation of anxious symptomology. In fact, the mediating role of overprotection on the association between parent and child anxiety has been discounted

(van Gastel, Legerstee, & Ferdinand, 2009). The pattern reemerges when considering the association between parental alcoholism and offspring adjustment, as marital aggression, parental discipline, and family harmony have all been implicated as mediating mechanisms (Eiden, Molnar, Colder, Edwards, & Leonard, 2009; King & Chassin, 2004; Zhou, King, & Chassin, 2006).

The aforementioned parenting practices and associated disturbances in the family environment have been traditionally conceptualized as underlying mechanisms operating through the environment, accounting for intergenerational transmission effects. In actuality, the conduits for these underlying mechanisms are far more complex than typically depicted. For example, Harold et al. (2011) report evidence for mediation of the association between maternal and child depression through hostility and warmth for genetically related mothers and children conceived through in vitro fertilization but not for genetically unrelated dyads. A significant direct association between maternal and child depression was maintained for the genetically unrelated dyads, with the researchers subsequently stating that other unmeasured environmental mediators must account for transmission in this group. They summarize their findings by asserting that this research bolsters the extant literature indicating that "non-inherited factors contribute to the intergenerational transmission of depressive symptoms," however this cursory generalization unduly discounts the entangled manifestation of genetic and environmental influences on these transmission effects. The researchers briefly discuss the potential for genetic confounding of this environmental mediation via passive gene-environment correlation, but this issue warrants more attention than they and other researchers have traditionally prescribed.

Gene-environment correlation (*r*Ge) refers to the process by which likelihood of environmental exposure is influenced by an individual's genotype (Plomin, DeFries, & Loehlin, 1977). There are three categories of *r*Ge: passive, evocative, and active. Passive *r*Ge refers to the process by which associations between environmental exposures and individual traits are explained by the parental genotype, which underlies both parental provision of the environmental exposure and inheritance of the trait. Evocative *r*Ge refers to the process by which a heritable trait evokes certain reactions from an individual's environment. Lastly, active *r*Ge refers to the process by which an individual's genotype influences his/her tendency to seek out certain environments. A failure to duly consider the role of *r*Ge in the study of parent-offspring psychopathology functions to distort the degree to which we attribute these associations to environmental mechanisms of transmission. Behavioral genetic research has presented evidence for the heritability of key dimensions of parenting like warmth, control, and negativity (Klahr & Burt, 2014), providing further evidence for the need for a more dynamic perspective when considering the mediating role of parenting as it contributes to the intergenerational transmission of psychopathology.

As formerly suggested, identifying the underlying mechanisms which contribute to the intergenerational transmission of psychopathology is a pursuit muddled by the complex interplay between genes and the environment. A tendency to diminish or entirely disregard this complex interplay in the extant literature presents a gross misrepresentation of the etiology of the familial aggregation of psychopathology. While there is a robust literature addressing the development of psychopathology from a theoretical perspective, limitations on research design and implementation often preclude

our ability to navigate the intersection of theory and empiricism. Developmental psychopathological theory is often couched in a diathesis-stress framework where diathesis, or predisposition, and exposure to stressors converge to trigger the onset of psychopathology, with genetic influences often implicated as the "diathesis" (Rende & Plomin, 1992). A more comprehensive integration of this theory into research practice is needed in order to elucidate the underlying mechanisms which contribute to the development of psychopathology. The quantitative genetic approach is one means of implementing this integration and gaining a more nuanced understanding of the mechanisms at play.

**Elucidating Etiological Underpinnings via the Quantitative Genetics Approach**

Quantitative genetic research considers the degree of phenotypic resemblance between individuals of varying genetic relatedness (such as identical and fraternal twins) in order to estimate the proportion of phenotypic variance attributable to genetic and environmental influences (Knopik, Neiderhiser, DeFries, & Plomin, 2017). Specifically, this approach utilizes structural equation modeling to organize the phenotypic variance for a specified trait into various latent factors: additive genetic influence (A, representing the sum of the average effects of individual genes across the genotype), nonadditive genetic influence (D, representing the interaction of alleles at the same or different loci), shared environmental influence (C, representing aspects of the environment common to and experienced by both co-twins which contribute to co-twin similarity), and non-shared environmental influence (E, representing aspects of the environment specific to or uniquely experienced by one co-twin, contributing to co-twin differences, as well as measurement error). Studying twins presents a unique advantage in that they are

genetically related and share many experiences in having been reared together while also possessing unique experiences of their own. Beyond this, twins can vary in their degree of genetic relatedness. Identical or monozygotic (MZ) twins share 100% of their genes. An ideal comparison group is fraternal or dizygotic (DZ) twins who share, on average, 50% of their segregating genes. If a trait is uniquely influenced by genetics, MZ twins are expected to exhibit phenotypic correlations which are twice those of DZ twins (or greater than twice the correlation of DZ twins in the case of nonadditive genetic influence). Conversely, if DZ twins exhibit phenotypic correlations which exceed half of the MZ correlations, shared environmental influences are implicated.

The information that can be gleaned from quantitative genetic research is invaluable from a developmental psychopathology perspective. This ability to parse genetic and environmental influence on the manifestation of symptoms of psychopathology reveals much more in the way of the etiological underpinnings of psychopathology than can be ascertained from non-genetically informed research. The provision of estimates of heritability for different forms of psychopathology no doubt stands to greatly inform our understanding of the contributing mechanisms, but it is our understanding of gene-environment interplay which presents insight into potential windows for prevention and intervention efforts.

The twin method has been applied to the study of both internalizing and externalizing disorders across the lifespan, however much of this work lacks a developmentally informed perspective, particularly when considering adolescent twin research. Several studies include both children and adolescents in their analyses, without considering the potential etiological distinctions that underlie the manifestation of

symptoms across this significant transition. For example, Kendler, Gardner, and Lichtenstein (2008) revealed the genetic influence on symptoms of depression and anxiety to be "developmentally dynamic," in that there was evidence for the temporal stability of genetic influences present in childhood, however the influence of these genetic effects was attenuated as new effects came "on line" in adolescence. As youth transition from middle childhood to adolescence, considerable changes occur across multiple contexts, and these changes can often present new and unfamiliar stressors. For some youth, these stressors converge with significant neurobiological and hormonal change to influence the emergence of psychopathology (Paus, Keshavan, & Giedd, 2008). Increased rates of symptomology across many different disorders during this transition render it a significant risk period (Costello, Copeland, & Angold, 2011). Fortunately, the significant neurobiological change that occurs during this transition introduces a period of plasticity that, if harnessed appropriately, can lend itself well to developmentally informed intervention practices (Cicchetti & Gunnar, 2008). As demonstrated, the study of psychopathology during this developmental period warrants a much more refined approach. As such, this review of univariate twin research considers studies specifying effects for adolescent twin samples in isolation.

Several twin studies have estimated the heritability of adolescent depression, typically reporting modest to moderate additive genetic influence, substantial nonshared environmental influence, and minimal shared environmental influence. There is, however, considerable disparity across these studies, with reports ranging from no genetic influence to 80% heritability (Ehringer, Rhee, Young, Corley, & Hewitt, 2006; Eley & Stevenson, 1999; Gjone & Stevenson, 1997; Li, McGue, & Gottesman, 2012;

O'Connor, Neiderhiser, Reiss, Hetherington, & Plomin, 1998; Rice, Harold, Thapar, 2002; Tully, Iacono, & McGue, 2010). In addition to disparate heritability estimates, there are also inconsistencies in the report of sex and age effects on these estimates. These inconsistencies may reflect distinct etiologies for the specific populations considered (community versus clinical samples) or they could be artifacts of differential methods of assessment (e.g., use of different raters and measure selection).

Within this domain of internalizing twin research, there is considerably less work examining the heritability of anxiety disorders in adolescence. These studies similarly report modest to moderate additive genetic influence, although the range in heritability estimates is again substantive, from 0-74% (Ask, Torgersen, Seglem, & Waaktaar, 2014; Ehringer et al., 2006; Eley & Stevenson, 1999; Garcia et al., 2013; Ogliari et al., 2006; Thapar & McGuffin, 1995; Topolski et al., 1997). There are also reports of substantial contributions from the nonshared environment; however, where they diverge from the findings on adolescent depression is in the detection of shared environmental effects. Whereas twin research examining adolescent depression has typically reported negligible effects of the shared environment, research with a focus on anxiety indicates that the shared environment may play a larger role in adolescent anxiety, although findings are again somewhat mixed. These studies similarly report inconsistent effects of sex and age. Beyond considering the population specific effects and differential methods of assessment, variable phenotype definition may also partially account for these mixed findings, as there is considerable heterogeneity in the manifestation of anxious symptomology across disorders.

Adolescent twin research examining genetic and environmental influence on externalizing behavior broadly and oppositional defiant disorder and conduct disorder specifically has typically reported moderate estimates of heritability, although estimates range substantially from 0% to 77% heritability (Button, Lau, Maughan, & Eley, 2008; Dick, Viken, Kaprio, Pulkkinen, & Rose, 2005; Ehringer et al., 2006; Gjone & Stevenson, 1997; Kuo, Lin, Yang, Soong, & Chen, 2004; Silberg et al., 1994; Scourfield, Van den Bree, Martin, & McGuffin, 2004; Young, Stallings, Corley, Krauter, & Hewitt, 2000). The reviewed studies consistently report substantial influence of the nonshared environment, however there is an inconsistent detection of significant shared environmental effects across the studies. Reports of externalizing behaviors are consistently higher in males than females; however, the detection of sex as well as age effects on variance estimates is variable.

There is a relative paucity of research examining the etiology of attention deficit hyperactivity disorder (ADHD) in adolescence when compared to analogous research completed with child-aged samples, however these studies do report moderate to high estimates of heritability, modest to moderate influence of the nonshared environment, and no effect of the shared environment, which is in line with child research (Dick et al., 2005; Ehringer et al., 2006; Hay, Bennett, McStephen, Rooney, & Levy, 2004; Silberg et al., 1996; Young et al., 2000). The studies consistently find age and sex effects on symptom counts but report no effects on variance estimates. Of the different forms of psychopathology reviewed, it appears as if results from adolescent twin research on ADHD are the most consistent, although more research is needed which differentiates child from adolescent findings.

As demonstrated, twin-only models present substantive information regarding the underlying mechanisms that contribute to the development of psychopathology. However, there are certain addressable limitations. First, the classical twin model assumes that there is no assortative mating on the phenotypic trait. Assortative mating refers to the tendency for individuals with certain phenotypes to select mates with similar phenotypes. This phenomenon has been well established for several phenotypic traits, including psychopathologies. Evidence of assortative mating has been substantiated for both internalizing and externalizing disorders, with the effect being most pronounced for disorders demonstrating earlier onset (e.g., Attention Deficit Hyperactivity Disorder and Autism Spectrum Disorder) and greater severity (e.g., Schizophrenia and Substance Abuse). This assortment presents both within and across psychiatric disorders (Nordsletten et al., 2016). Assortment across psychiatric disorders suggests that while parents may not be concordant for a specific psychiatric disorder, they may still exhibit assortative mating on a general liability for psychopathology. A failure to account for assortative mating can render DZ twins more similar on a phenotypic trait than would be expected in the absence of assortative mating, functioning to inflate shared environmental estimates and attenuate heritability estimates.

Additional limitations of the classical twin model include inabilities to simultaneously estimate A, C, D, and E, to account for passive *r*GE, and to parse C into twin specific versus family level influences. As mentioned previously, MZ twin correlations greater than twice those of DZ twins indicate presence of nonadditive genetic influence. When this pattern emerges, the classical twin model is limited to estimating only three latent effects. ACE or ADE models can both be estimated, however when they

fit the data equally well, researchers have no empirical means of selecting one over the other. This is problematic, given that they lead to markedly distinct interpretations. Next, a failure to account for passive *r*GE functions to inflate shared environmental estimates and attenuate heritability estimates, again limiting the acuity of the conclusions researchers can draw. Finally, an inability to distinguish shared environmental influences experienced solely by twins from those that operate at the family level provides us with limited insight as to the trait-relevant contexts.

The nuclear twin-family model (see Figure 3) is a powerful extension of the classical twin model that addresses the aforementioned limitations. It incorporates the data of parents of twin offspring, presenting additional information from which parameter estimates are derived. The classical twin model utilizes covariance between MZ and DZ twins to acquire these estimates, whereas the twin-family model is able to additionally base parameter estimates on the covariance between parents and the covariance between parents and offspring. This allows the model to account for the effect of assortative mating on the estimates, to simultaneously estimate A, C, D, and E influences, and to differentiate passive *r*GE from true shared environmental influence by modeling the covariance between genetics and the environmental factors common to all family members. This model differentiates shared environmental influence which is common to all family members from that which is specific to the twin siblings. It can also determine whether familial transmission from parents to offspring significantly accounts for the intergenerational resemblance on a phenotypic trait above and beyond the influence of shared genes. Significant familial transmission is of particular interest in that it presents a promising window for intervention. (See Zyphur, Zhang, Barsky, and Li (2013) for a

review of the advantages of the twin-family model). Despite the increased power of this twin-family model, it has been rarely applied to the study of psychopathology.

To date, there are in fact no studies utilizing the nuclear twin-family model to determine the degree of genetic and environmental influence on the internalizing forms of psychopathology in childhood and/or adolescence. Rice, Harold, and Thapar (2005) did apply a similar extension of the classical twin model to elucidate the link between depression in mothers and their offspring utilizing a sample of twins aged 8 to 17 years. However, this was not a true nuclear design, as it did not incorporate fathers' data, precluding the ability to account for the effect of assortative mating. The researchers tested models utilizing maternal-ratings of twin depressive symptomology across all ages, maternal-ratings for adolescent twins only, and adolescent self-report above and below specified severity cut offs. The researchers determined that there was evidence of familial transmission of depression above and beyond the influence of shared genes only when maternal ratings of adolescent symptomology were utilized (heritability= 48%) and when adolescent-rated symptomology was high (heritability= 14%). The latter result is particularly informative in that it suggests that the familial transmission from depressed mothers to the highest-risk adolescents is significant, presenting a promising window for intervention on these environmental transmission effects.

The nuclear twin-family model has been utilized to determine the degree of genetic and environmental influence on externalizing forms of psychopathology, but this research is still quite limited. Koopmans and Boomsma (1996) sought to elucidate the genetic and environmental transmission effects from parents to adolescent offspring for alcohol use. The researchers found that there was significant evidence of familial

transmission for alcohol use when twins were between 15 and 16 years of age, accounting for 9% of the variance. The remainder of the variance was explained by twin-specific shared environmental influence (79%), nonshared environmental influence (0.05%) and age (0.07%). However, this effect was nonsignificant in an older adolescent cohort (aged 17 years and above); additive genetic, shared environmental, and nonshared environmental influences and age explained 43%, 37%, 19%, and 0.01% of the variance, respectively. These results suggest that interventions aimed at addressing the effect of familial transmission on alcohol use should be initiated in early- to mid-adolescence rather than later in order to maximize benefits.

Maes, Silberg, Neale, and Eaves (2007) estimated a nuclear twin-family model to ascertain the degree of genetic and environmental influence on conduct disorder symptoms in a sample of twins aged 8 to 30 years. They found that additive genetic, shared environmental, and nonshared environmental influences explained 38%, 23%, and 39% of the variance in symptoms of conduct disorder for male twins, respectively, and 40%, 18%, and 42% of the variance for female twins. For both groups, only the twin-specific shared environmental influence significantly contributed to the variance. Familial transmission and assortative mating accounted for only 2% and 3% of the variance, respectively, and only the latter contribution was statistically significant. Meyer and colleagues (2000) estimated a similar model with a subsample derived from the same longitudinal twin study, where the twins ranged in age from 8 to 16 years. They found that additive genetic, shared environmental, and nonshared environmental influences explained 25%, 20%, and 51% of the variance. There was also significant evidence of assortative mating. However, there was no evidence of familial transmission, suggesting

that genetic influences explained the co-occurrence of conduct disorder symptomology in parents and offspring with distinct environmental factors influencing the two generations.

Burt and Klump (2012) utilized a nuclear twin-family model to assess the etiological distinction between aggressive and non-aggressive forms of antisocial behavior, positing that genetic and environmental influences on the different forms of antisocial behavior would be distinct. The twins ranged in age from 6 to 10 years. The researchers determined that aggressive antisocial behavior was highly heritable, with 68% of the variance accounted for by both additive and non-additive genetic factors. The remaining 32% of the variance was explained by non-shared environmental influence. Given the nonsignificant effect of the shared environment, twin-specific and broadly familial environmental influences remained undetected. The results for rule breaking behavior were markedly distinct, substantiating the previously posited etiological distinction between the two domains of antisocial behavior. Specifically, rule breaking behavior was moderately heritable, with 50% of the variance accounted for by additive genetic factors. Sibling-specific, rather than broadly familial, shared environmental influence was also significant, accounting for 24% of the variance. The remaining 26% of the variance in rule breaking behavior was explained by non-shared environmental factors. While the aggressive and non-aggressive forms of antisocial behavior were etiologically distinct, the evidence indicated that genetic influences sufficiently accounted for the familial aggregation of both.

Taylor, McGue, and Iacono (2000) estimated a nuclear twin-family model to ascertain the degree of genetic and environmental influence on delinquent behavior in a sample of twins aged 16 to 18 years. The researchers found delinquency to be largely

influenced by the environment, with only 18% of the variance attributed to additive genetic effects. Most of the variance was explained by nonshared environmental influences (56%), and the remaining shared environmental influence was primarily twin-specific (26%), with only a small proportion explained through familial transmission. Additionally, there was modest evidence for assortative mating.

As demonstrated, most of the externalizing nuclear twin-family research has focused on behavior within the antisocial sphere. Outside of this and alcohol use, only one other nuclear twin-family study with a specific focus on ADHD in child or adolescent samples was identified, pointing to a need for more research in this area. Burt, Larsson, Lichtenstein, and Klump (2012) utilized the nuclear twin-family model to determine whether a failure to detect shared environmental influence on ADHD in the extant twin literature was an artifact of suppression of these estimates by the modeling of dominant genetic effects. As previously mentioned, univariate twin models are incapable of simultaneously estimating C and D, despite the fact that both influences may be important for a given phenotype. To make this determination, the researchers conducted analyses in two twin samples, one aged 6 to 10 years and the other aged 5 years. The best fitting model for the first sample was an AE model, where 53% and 47% of the variance in ADHD symptoms was explained by additive genetic and nonshared environmental influence, respectively. The best fitting model for the second sample was an ADE model, where 55%, 19%, and 26% of the variance in ADHD symptoms was explained by additive genetic, dominant genetic, and nonshared environmental influence, respectively. They also reported evidence of modest assortative mating but no twin-specific environmental variance or significant familial transmission. These results functioned to

corroborate extant findings reporting minimal to no influence of the shared environment on ADHD. The findings also indicate that the familial aggregation of ADHD symptoms is sufficiently explained by genetic transmission.

Overall, these findings point to a need for a broader application of the nuclear twin-family model to the study of both internalizing and externalizing disorders. Research by Rice and colleagues (2005) suggests that such an application might reveal interesting familial transmission effects which stand to provide a substantively more nuanced elucidation of the underlying mechanisms contributing to the intergenerational transmission of internalizing symptomology. Within the domain of externalizing psychopathology, the reviewed nuclear twin-family models presented nuanced etiological insight (e.g., evidence for familial transmission and assortment), though effects were variable across the different disorders and even within disorders when a more refined, behavior-specific approach was taken (see Burt & Klump, 2012). The latter result points to a need for future research to examine transmission effects at variable levels of specificity. The findings from nuclear twin-family models at the disorder-specific level versus those at the level of a higher-order factor reflecting general propensity toward psychopathology might reveal markedly distinct etiologies, significantly advancing our understanding of how these transmission effects operate.

**The Higher-Order Structure of Psychopathology**

The development of psychopathology is tremendously complex. Intuitively, children of depressed parents would be deemed at-risk for developing depression themselves. In actuality, they may be at-risk for a myriad of behavior problems and different forms of psychopathology. These multi-final pathways warrant careful

consideration as they stand to inform our understanding of the variable trajectories to which these high-risk children are predisposed. Thus far, we have only considered familial aggregation research at the disorder specific level. However, this approach assumes a specificity for these intergenerational transmission effects that does not reflect the complexity with which symptoms of psychopathology actually manifest. This glaring disregard for variable trajectories in the development of psychopathology must be addressed.

Within the field of psychopathological nosology, there has been considerable debate surrounding the utility of parsing symptomology into broad dimensions versus disorder-specific categories. It has been suggested that the assumption of a dimensional approach for the study and treatment of psychopathology stands to enrich both research and clinical practice, however more evidence is needed to bolster such a dramatic restructuring of the way in which we conceptualize psychopathology and to bridge the divide between "lumper" and "splitter" perspectives (Cuthbert, 2005). The categorization of symptomologies into internalizing and externalizing dimensions has been largely embraced, but an even broader, higher-order approach may be needed. This study will contribute to the rich and emerging literature supporting such an approach.

Genetically informed research stands to elucidate the underlying mechanisms which drive development of psychopathology at variable levels of specificity. For example, a review of twin research examining the comorbidity within and between anxiety disorders and depression concluded that overlapping genetic factors account for their co-occurrence (Middeldorp, Cath, Van Dyck, & Boomsma, 2005). Within the domain of externalizing symptomology, covariation among impulsivity, inattention,

conduct problems, and oppositional defiant behavior has been found to be similarly mediated by overlapping genetic factors (Knopik, Heath, Bucholz, Madden, & Waldron, 2009; Knopik et al., 2014). These findings suggest the existence of heritable, common latent factors. In fact, behavioral genetic research has employed the common factor model to extract internalizing and externalizing latent factors and found them to be highly heritable, with modest to moderate residual disorder-specific genetic effects (Kendler, Myers, & Keyes, 2011; Kendler, Myers, Maes, & Keyes, 2011).

The degree of heritability underlying these latent factors prompts the question: how do these broader internalizing and externalizing phenotypes aggregate within families and can they potentially provide greater insight into the intergenerational transmission of psychopathology? Hicks, Krueger, Iacono, McGue, and Patrick (2004) partially addressed this question utilizing data on externalizing disorders in a sample of 542 adolescent twin pairs and their parents. Their aim was to elucidate mechanisms of familial transmission for externalizing disorders and to determine the specificity of these transmission effects. They acquired symptom counts for conduct disorder, antisocial personality disorder, alcohol dependence, and drug dependence in both parent and offspring generations and utilized structural equation modeling to extract a latent externalizing phenotype (EXT) which captured the covariance across all disorders. They then modeled the latent parent-offspring EXT correlations and conducted separate 1 *df* tests which allowed disorder-specific residual variance for mothers or fathers to covary with the residual variance for twins. The best fitting model allowed for general transmission between parents and offspring only, suggesting that a general liability to

externalizing sufficiently explained familial resemblance for psychopathology. This general vulnerability to externalizing was highly heritable ($h^2$=.80).

Bornovalova, Hicks, Iacono, and McGue (2010) utilized the same analytic approach to elucidate whether the link between parental externalizing disorders and childhood disruptive disorders was mediated by the transmission of general or disorder-specific liabilities in a sample of 1069 11-year-old twin pairs and their parents. They acquired symptom counts for parental conduct disorder, antisocial personality disorder, alcohol dependence, and drug dependence and offspring ADHD, conduct disorder, and oppositional defiant disorder. Their results, once again, indicated that a general liability to externalizing sufficiently explained the association between parental externalizing and childhood disruptive disorders. The researchers fit a common factor model to determine the degree of genetic and environmental influence on the offspring EXT phenotype as well as disorder-specific effects. The general vulnerability to childhood disruptive disorders was highly heritable ($h^2$=.81), indicating that the covariation among childhood disruptive disorders is largely mediated by overlapping genetic factors. Disorder-specific genetic effects were also detected, particularly for ADHD ($h^2$=.65).

These findings suggest that the familial aggregation of externalizing psychopathology is mediated by the transmission of a general liability rather than disorder-specific effects. There is analogous evidence for the nonspecificity of the intergenerational transmission of internalizing disorders as well. Starr, Conway, Hammen, and Brennan (2014) utilized the data of 815 mother-offspring dyads to fit several factor structures in order to determine the higher-order structure of internalizing psychopathology. They found that a one-factor model extracting a single latent

internalizing (INT) factor fit the data best in both generations. They then determined whether the INT factor sufficiently accounted for the familial aggregation of internalizing diagnoses by regressing the offspring INT factor onto the maternal INT factor and then allowing individual, disorder-specific residual variances in the two generations to covary. The only significant residual association between mothers and offspring was that of PTSD, however model fit indices provided mixed results as to whether the addition of this residual association improved model fit. Overall, these findings provide tentative evidence for non-specific intergenerational transmission of internalizing psychopathology.

This review has thus far provided substantive evidence for the transmission of a general liability to externalizing psychopathology and tentative evidence for the transmission of a general liability to internalizing psychopathology. However, recent evidence indicating the presence of an even broader general factor underlying psychopathology across the two broad-band domains suggests that these approaches to elucidating the intergenerational transmission of psychopathology may, in fact, have been too specific. Lahey and colleagues (2012) utilized diagnostic data from a nationally representative sample of adults in the United States to test several factor structures in an attempt to elucidate the higher-order structure of psychopathology. They tested a two-factor (INT and EXT) oblique model, a 3-factor (fears, distress, and EXT) oblique model, and a bifactor model extracting the lower order fear, distress, and EXT factors and a higher-order bifactor. In this model, the bifactor accounted for all of the shared variance across disorders while the fear, distress, and EXT factors accounted for the common variance among the respective disorders, after controlling for the variance accounted for

by the bifactor. The bifactor model fit the data best, and tests of external validity demonstrated that the bifactor was significantly associated with history of parental psychopathology, suggesting that intergenerational transmission effects may even operate at a more general level than considered thus far.

Caspi and colleagues (2014) found similar evidence for a factor encompassing general liability to psychopathology and coined the term "P-factor". In their sample, the best fitting model was a bifactor model extracting the P-factor and lower order INT, EXT, and thought disorder factors. They, too, found that the P-factor demonstrated stronger associations with family history of psychopathology than did the lower order dimensions. These findings point to a need for an even broader approach to elucidating the familial aggregation of psychopathology. Martel and colleagues (2016) also found that a bifactor model extracting the P-factor and lower order fear, distress, and EXT factors best represented diagnostic data for a sample of parents and their children. They also tested associations between the parent and child factors and, overall, found significant P-factor level associations and nonsignificant lower order associations. These results lend further support for a need to rigorously test whether the transmission of specific or more general liabilities explains the familial aggregation of psychopathology. If the latter, elucidating the mechanisms which underlie these general transmission effects is an important next step. Emerging molecular genetic research reports a single nucleotide polymorphism heritability of 38% for the P-factor in a sample of children (Neumann et al., 2016), and twin research has found the P-factor to be moderately heritable in childhood and adolescence ($h^2$ = .43; Waldman, Poore, van Hulle, Rathouz, & Lahey, 2016). If effectively pursued, the proposed research stands to expand upon

these findings, providing substantive insight into the specificity and etiology of the familial aggregation of psychopathology- an insight, which, if harnessed appropriately, could meaningfully inform efforts to ensure positive developmental trajectories for vulnerable children.

**Current Study**

Broadly, the current study aims to elucidate: 1) the higher-order structure of psychopathology in adolescence, 2) the specificity of transmission effects for psychopathology from parents to their adolescent offspring, and 3) the genetic and environmental mechanisms underlying the familial aggregation of psychopathology.

We first used confirmatory factor analyses (CFA) to test three alternative models of the higher-order structure of adolescent psychopathology: 1) a correlated factors model, 2) a bifactor model, and 3) a general-factor model. We hypothesized that the bifactor model would demonstrate the best fit to the data, given the corroboration of this hierarchical structure in child, adolescent, and adult samples (Caspi et al., 2014; Martel et al., 2016; Waldman et al., 2016).

We then examined whether the intergenerational transmission of internalizing symptomology from parents to their adolescent offspring was broadband internalizing and externalizing domain-specific or whether parental internalizing was associated with a more general index of offspring psychopathology encompassing co-occurring symptomology across both the internalizing and externalizing domains. Based on the readily observed association between parental psychopathology and multifinal pathways to offspring outcomes as well as studies corroborating nonspecificity of transmission (Bornovalova et al., 2010; Goodman & Gotlib, 1999; Hicks et al., 2005; Starr et a.,

2014), we hypothesized that a model specifying only general transmission of symptomology from parent internalizing to the adolescent P-factor would demonstrate the best fit to the data.

Lastly, the degree of genetic and environmental influence on the familial aggregation of general psychopathology was examined using the nuclear twin-family design. Considering evidence of pleiotropic genetic effects on multiple mental disorders and results from twin studies pointing to highly heritable common factors of psychopathology (Kendler, 2005; Kendler et al., 2011a; Kendler et al., 2011b), we hypothesized that a general factor of psychopathology would be genetically influenced. However, a developmental, family systems perspective compels the additional consideration of environmental influences that might contribute to the familial aggregation of psychopathology. Based on known associations between parent mental health and disturbances in the family environment (Cummings et al., 2005; Eiden et al., 2009; King & Chassin, 2004; Nelson et al., 2003; Riley et al., 2009; Zhou et al., 2006), we hypothesized that family level environmental influences would significantly contribute to parent-offspring covariance in general psychopathology as well. Though, as adolescents increasingly assert their autonomy, important sibling-specific and nonshared environmental influences are likely to come into play. As such, we hypothesized that a model estimating additive genetic, family level-, sibling specific-, and nonshared environmental influences would best explain the familial aggregation of general psychopathology in our adolescent sample.

## Methods

### Participants

The sample consisted of 500 twin pairs (52.6% female) and their parents drawn from the longitudinal Wisconsin Twin Project, a population-based study of child and adolescent emotion, temperament, and psychopathology (Goldsmith, Lemery-Chalfant, Schmidt, Arneson, & Schmidt, 2007). Twin births between 1989 and 2004 were identified through state records, and families were invited to participate via recruitment letters when the twins were 6 to 12 months of age. Families participated in an adolescent follow-up study when the twins were between the ages of 11 and 18 years old ($M$ = 13.24 years, $SD$ = 1.52). The sample consisted of 37% monozygotic (MZ), 34% same-sex dizygotic (DZ), and 29% opposite-sex DZ twin pairs. Approximately 83% of the sample were categorized as White (8% Black; 2% Native American; 3.8% multiracial; 2% other; less than 1% Filipino, Hmong, or Other Pacific Islander categories combined). Mothers had an average education of 15.28 years ($SD$=2.35), and fathers had an average education of 14.64 years ($SD$=2.52). The median income bracket ranged from $60,001 to $70,000 with approximately 19% of the sample reporting a family income of $40,000 or less and approximately 40% of the sample reporting a family income of $80,000 or more.

### Procedure

Adolescent twins were interviewed separately during home visits to acquire independent reports of psychiatric symptomology using structured clinical interviews administered on laptop computers by a trained staff member. Parents were interviewed separately over the telephone using similar methods.

## Measures

### *Zygosity Questionnaire for Young Twins*

The Zygosity Questionnaire for Young Twins (Goldsmith, 1991) is a 32-item measure designed to assess the zygosity of twin pairs. Caregivers responded to questions regarding their pregnancy, the physical appearance of each twin, and the presence of observable differences between the twins. The agreement of this particular questionnaire with genotyping has been estimated at 96% (Forget-Dubois et al., 2003), rendering it a less burdensome and more cost effective alternative.

### *Composite International Diagnostic Interview*

The Composite International Diagnostic Interview (CIDI; Robins et al., 1988) was administered to both mothers and fathers. The CIDI is a fully structured comprehensive lifetime interview designed to obtain information on various DSM-IV based psychiatric disorders. Symptoms of alcohol dependence, alcohol abuse, major depressive disorder, obsessive-compulsive disorder, panic disorder, social and specific phobias, and generalized anxiety disorder were assessed. The CIDI is appropriate for administration by trained lay interviewers. CIDI diagnoses are significantly related to independent clinical diagnoses, and test-retest reliability is high (Kessler & Üstün, 2004). For the purposes of this study, parent major depressive disorder diagnoses across the single/recurrent and mild/moderate/severe categories, panic disorder diagnoses with and without agoraphobia, specific phobia diagnoses across the animal/natural/blood/situation categories, and alcohol dependence and abuse were collapsed and recoded into Any Major Depression Diagnosis, Any Panic Disorder Diagnosis, and Any Specific Phobia Diagnosis, and Any Alcohol Disorder Diagnosis categories, respectively. Confirmatory

factor analysis was used to form parental internalizing factors in the parent-offspring transmission specificity models, indicated by Any Major Depression, Any Panic Disorder, Any Specific Phobia, obsessive-compulsive, generalized anxiety, and social phobia diagnoses. General psychopathology factors were additionally indicated by Any Alcohol Disorder, and extracted factor scores were used in nuclear twin-family modeling.

*Diagnostic Interview Schedule for Children*

The National Institute of Health's computer-assisted Diagnostic Interview Schedule for Children, version IV (C-DISC-IV; Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000), was administered to each twin. The C-DISC-IV is a structured diagnostic instrument based on the DSM-IV designed for nonclinician assessment of 30 childhood and adolescent diagnoses occurring over the past 12 months and the past 4 weeks. Symptoms of major depressive disorder, obsessive-compulsive disorder, panic disorder, social and specific phobias, generalized anxiety disorder, separation anxiety, attention deficit hyperactivity disorder, conduct disorder, and oppositional defiant disorder were assessed. Reliability and validity of the C-DISC are acceptable and represent the gold standard in the field (Shaffer et al., 2000). Confirmatory factor analysis was used to test competing higher-order structures of adolescent psychopathology: 1) a correlated factors model, 2) a bifactor model, and 3) a general-factor model. P-, general psychopathology, internalizing, and externalizing factors were formed. The P-and general psychopathology factors were formed in the bifactor and general-factor models, respectively, and indicated by symptom counts on major depressive disorder, obsessive-compulsive disorder, panic disorder, social and specific phobias, generalized anxiety disorder, separation anxiety, attention deficit hyperactivity disorder, conduct disorder,

and oppositional defiant disorder. The internalizing factor in the correlated factors model was indicated by major depressive disorder, obsessive-compulsive disorder, panic disorder, social and specific phobias, generalized anxiety disorder, and separation anxiety symptom counts, whereas the internalizing factor in the bifactor model was indicated by residual variance in symptom counts unaccounted for by P. The externalizing factor in the correlated factors model was indicated by attention deficit hyperactivity disorder, conduct disorder, and oppositional defiant disorder symptom counts, whereas the externalizing factor in the bifactor model was indicated by residual variance in symptom counts unaccounted for by P. The bifactor structure was used to model the higher-order structure of adolescent psychopathology in the parent-offspring transmission specificity models. Finally, general psychopathology factor scores were extracted from the general-factor model and utilized in nuclear twin-family modeling.

**Covariates**

Sex and age were included as covariates in both phenotypic and genetic analyses. Covariate effects were regressed out of adolescent symptom counts and residual scores were utilized in subsequent confirmatory factor analyses.

**Statistical Approach**

Correlations and descriptive statistics for twin symptom counts and parent diagnoses were conducted in MPlus version 7.4 (Muthén & Muthén, 2012). Twin intraclass correlations on general psychopathology factor scores were computed in OpenMX (Neale, et al., 2016).

Confirmatory factor analysis was conducted in MPlus version 7.4 (Muthén & Muthén, 2012) using the MLR estimator to test three alternative models of the higher-

order structure of adolescent psychopathology: 1) a correlated factors model, 2) a bifactor model, and 3) a general-factor model (Figure 1). Twin symptom counts were normally distributed and not zero-inflated, qualifying MLR estimation as appropriate. The MLR estimator produces maximum likelihood parameter estimates and standard errors which are robust to non-normality and non-independence of observations when used with the "type = complex" command. First, a two-factor model extracting the latent internalizing (INT) and externalizing (EXT) factors and allowing them to correlate was tested (i.e., the correlated factors model). The INT factor was defined by generalized anxiety, obsessive-compulsive, panic, separation anxiety, social phobia, specific phobia, and depressive symptoms, and the EXT factor was defined by oppositional-defiant, conduct, and attention deficit hyperactivity disorder symptoms. Second, a bifactor model extracting the lower order INT and EXT factors and a higher-order bifactor representing general psychopathology (P-factor) was tested. In this model, the P-factor accounts for the shared variance across all disorders while the INT and EXT factors account for the residual variance specific to the broadband-domains. Lastly, a general-factor model extracting only a single general factor of psychopathology was tested. Model fit was verified using multiple indices, including the Tucker-Lewis Index (TLI: Tucker & Lewis, 1973), the Root Mean Square Error of Approximation (RMSEA; Browne & Cudeck, 1992), the Standardized Root Mean Square Residual (SRMR; Bentler, 1995), and the Bayesian Information Criteria (BIC; Raftery, 1995).

Next, structural equation modeling was conducted in MPlus version 7.4 (Muthén & Muthén, 2012) using the weighted least squares means and variances adjusted (WLSMV) estimator to test transmission effects from parent internalizing diagnoses to

twin psychopathology at varying levels of specificity (Figure 2). The WLSMV estimator is appropriate for use with categorical data (i.e., parental diagnoses) and robust to non-normality and non-independence of observations when used with the "type = complex" command. First, an initial model that allowed only for general transmission of psychopathology from the latent parent INT factor to the offspring P-factor was tested, against which all subsequent models were compared. Parental INT rather than a general factor of psychopathology was selected to allow for the testing of broadband domain-specific transmission (e.g., parental INT to offspring INT significantly accounting for transmission above and beyond general transmission to just the offspring P-factor); a bifactor measurement model could not be specified for the parents due to insufficient externalizing indicators. The general transmission effect was operationalized as the latent correlation between parent INT and offspring P phenotypes. Next, to test for broadband domain-specific transmission effects, separate tests allowing maternal and paternal INT phenotypes to covary with offspring residual INT and EXT phenotypes were conducted. The DIFFTEST option in Mplus (along with the Comparative Fit Index (CFI; Bentler, 1990) and RMSEA fit indices) was used to determine change in model fit and whether broadband domain-specific transmission effects were necessary to account for parent-offspring resemblance in psychopathology above and beyond only the general transmission effect.

Finally, structural equation modeling was conducted in the statistical program OpenMx (Neale et al., 2016) to fit a nuclear twin-family model of general psychopathology (Figure 3). Factor scores were extracted from confirmatory factor analyses modeling latent general psychopathology factors in mothers, fathers, and twins

independently and subsequently used for the nuclear twin-family modeling. Selection of the general psychopathology factor score as the phenotype of interest was informed by the hypothesis that general transmission of psychopathology would sufficiently explain familial aggregation of psychopathology. As mentioned, the bifactor model could not be fit with parental data; as such, the general psychopathology factor was the closest approximation of P. Offspring P- and general psychopathology factor scores were highly correlated ($r = 0.97$, $p < .01$), substantiating use of the latter for nuclear twin-family modeling. The model utilizes observed covariances between mothers, fathers, and twins (both MZ and DZ) and their degree of genetic relatedness (MZ twins share 100% of their segregating genes with each other and 50% with each parent where DZ twins share 50% of their segregating genes with each other and with each parent) in order to estimate the proportion of phenotypic variance attributable to genetic and environmental influences. The covariance between parents and between parents and offspring provides additional information above and beyond the classical twin model, allowing for the simultaneous estimation of A (additive genetic influence representing the sum of the average effects of individual genes across the genotype), D (nonadditive genetic influence representing the interaction of alleles at the same or different loci), C (shared environmental influence representing aspects of the environment contributing to familial similarity), and E (nonshared environmental influence representing aspects of the environment contributing to co-twin differences). The model has the additional capacity to parse C into twin-specific shared environmental influence (S) and that which operates through familial transmission from parents to offspring (F). However, a single model is only able to estimate 3 out of the 4 A, D, S, and F components, requiring one of the estimates to be

fixed at zero. The model is also able to account for assortative mating, or the covariance between mothers and fathers, as it impacts the estimation of A and F. Passive *r*GE is represented by the covariance between the two. An assumption of the nuclear twin-family design is that genetic variance components are equal in the parent and offspring generations (See Keller et al. (2009) for nuclear twin-family model review).

First, all possible full models with variances, covariances, and means freely estimated were tested (i.e., ADSE, ADFE, and ASFE). The best-fitting full model was selected as the base model against which the fits of reduced, nested models were compared (i.e., ADE, ASE, AFE, and AE). D, S, and F parameters were systematically dropped and models were evaluated for fit. The Akaike's Information Criterion (AIC; Akaike, 1987), the Bayesian Information Criteria (BIC; Raftery, 1995), and the sample-size adjusted Bayesian Information Criterion (SABIC; Sclove, 1987) fit indices were used to determine the most parsimonious fit to the data. A significant change in fit after dropping a parameter indicates that the reduced model fits significantly worse than the full model. In this case, the parameter should be retained, as the pathway contributes significantly to the phenotypic variance. These fit indices do not consistently agree; as such, best fitting model criteria required lower or more negative values for at least two of the three fit indices.

## Results

### Preliminary Analyses

Correlations and descriptive statistics for twin symptom counts, parent diagnoses, and latent factor scores of psychopathology are presented in Tables 1, 2, and 3. Prevalence estimates for adolescent twins in the current sample were as follows: major

depressive disorder, 2%; obsessive-compulsive disorder, 2%; panic disorder, 1%; social phobia, 2%; specific phobia, 8%; generalized anxiety disorder, 1%; separation anxiety disorder, 2%; attention deficit hyperactivity disorder, <1%; conduct disorder, 2%; oppositional defiant disorder, 1%. For comparison, national lifetime prevalence rates for adolescents aged 13-14 years are as follows: major depressive disorder, 8.4%; panic disorder, 1.8%; social phobia, 7.7%; specific phobia, 21.6%; generalized anxiety disorder, 1%; separation anxiety disorder, 7.8%; attention deficit hyperactivity disorder, 8.8%; conduct disorder, 4.4%; oppositional defiant disorder, 12% (Merikangas et al., 2010). Generally, adolescent rates in the current sample were lower than national rates. Lifetime prevalence estimates for mothers in the current sample were as follows: major depressive disorder, 21%; obsessive-compulsive disorder, 3%; panic disorder, 4%; social phobia, 7%; specific phobia, 13%; generalized anxiety disorder, 4%; alcohol disorder, 24%. For fathers, estimates were as follows: major depressive disorder, 11%; obsessive-compulsive disorder, 1%; panic disorder, 1%; social phobia, 3%; specific phobia, 6%; generalized anxiety disorder, 3%; alcohol disorder, 46%. For comparison, national rates of lifetime prevalence for adults aged 30-44 years are as follows: major depressive disorder, 19.8%; obsessive-compulsive disorder, 2.3%; panic disorder, 5.7%; social phobia, 14.3%; specific phobia, 13.9%; generalized anxiety disorder, 6.8%; alcohol abuse, 16.3%; alcohol dependence, 6.4% (Kessler, Berglund, Demler, Jin, Merikangas, & Walters, 2005). Generally, maternal rates in the sample were comparable to those derived from nationally representative samples. Paternal rates were consistently lower with the exception of alcohol disorder which was considerably higher than the national rate.

All but one of the adolescent symptom count variables were beneath the recommended cutoffs for skew (+/-2.00) and kurtosis (+/-7.00; Muthén & Kaplan, 1985); the adolescent conduct disorder symptom count was square root transformed to approximate normality. Symptom counts across all of the adolescent diagnoses were significantly and positively correlated (Table 1). The lowest correlation was between conduct disorder and social phobia symptom counts ($r = 0.16$, $p < .01$), and the highest was between major depressive and attention deficit hyperactivity disorder symptom counts ($r = 0.62$, $p < .01$).

There was much less co-occurrence in the parental diagnoses (Table 2). For mothers, the lowest correlation was between alcohol disorder and obsessive compulsive disorder ($r = 0.03$, ns), and the highest was between generalized anxiety disorder and obsessive compulsive disorder ($r = 0.26$, $p < .01$). For fathers, the lowest correlation was between alcohol disorder and obsessive compulsive disorder ($r = -0.08$, ns) and the highest was between major depressive disorder and generalized anxiety disorder ($r = 0.40$, $p < .01$). The only significant disorder specific mother-father correlations were those of major depressive disorder ($r = 0.17$, $p < .01$) and alcohol disorder ($r = 0.19$, $p < .01$). Otherwise, correlations between maternal and paternal diagnoses were broadband domain-specific, including correlations between paternal major depressive disorder and maternal panic disorder, social phobia, and specific phobia ($r = 0.12$, $p < .05$; $r = 0.16$, $p < .01$; $r = 0.23$, $p < .01$, respectively), maternal panic disorder and paternal obsessive compulsive disorder and social phobia ($r = 0.23$, $p < .01$; $r = 0.21$, respectively), maternal specific phobia and paternal generalized anxiety disorder ($r = 0.21$, $p < .01$), and maternal

generalized anxiety disorder and paternal panic disorder ($r = 0.14$, $p < .05$). There were no significant cross-broadband domain mother-father correlations.

All of the maternal and paternal latent factor scores of psychopathology were positively and significantly correlated (Table 3). Offspring P and general factor scores of psychopathology were positively and significantly correlated with both maternal and paternal INT and general psychopathology factor scores. The maternal general factor score was positively and significantly correlated with the offspring residual INT and EXT factor scores ($r = 0.10$, $p < .01$; $r = 0.10$, $p < .01$, respectively). Maternal INT factor scores were positively and significantly correlated with offspring residual INT and EXT factor scores ($r = 0.11$, $p < .01$ & $r = 0.08$, $p < .05$, respectively). Paternal general psychopathology and INT factor scores were not significantly correlated with offspring residual INT and EXT factor scores.

Twin intraclass correlations for the latent factor scores of psychopathology are also presented in Table 3. MZ twins were more similar than DZ twins on all latent factor scores, suggesting additive genetic influences. For the P and general factors of psychopathology, DZ correlations were greater than half the MZ correlations, suggesting an additional influence of shared environmental factors. For the residual INT and EXT factors, MZ correlations were higher than twice DZ correlations, suggesting nonadditive genetic influence. Finally, MZ correlations were less than 1.00 across all latent factor scores, suggesting nonshared environmental influences as well.

*Parent Internalizing and General Factors of Psychopathology*

The INT factor representing the parental measurement model for parent-offspring transmission specificity testing was run independently for descriptive purposes. The

maternal INT factor model demonstrated good fit ($\chi^2$ (9) = 15.986, TLI = 0.947, RMSEA = 0.031). The standardized loadings for Any Major Depression, Any Panic Disorder, Any Specific Phobia, obsessive-compulsive, generalized anxiety, and social phobia diagnoses were 0.524, 0.724, 0.727, 0.751, 0.562, and 0.506, respectively. The paternal INT factor model demonstrated good fit as well ($\chi^2$ (9) = 6.260, TLI = 1.049, RMSEA = 0.000). The standardized loadings for Any Major Depression, Any Panic Disorder, Any Specific Phobia, obsessive-compulsive, generalized anxiety, and social phobia diagnoses were 0.906, 0.608, 0.181, 0.583, 0.776, and 0.369, respectively. Parental general psychopathology factor scores were extracted and used in nuclear twin-family modeling. The maternal general-factor model demonstrated good fit ($\chi^2$ (14) = 21.446, TLI = 0.956, RMSEA = 0.026). The standardized loadings for Any Major Depression, Any Panic Disorder, Any Specific Phobia, obsessive-compulsive, generalized anxiety, social phobia, and Any Alcohol Disorder diagnoses were 0.539, 0.760, 0.709, 0.729, 0.545, 0.503, and 0.341, respectively. The paternal general-factor model demonstrated acceptable fit ($\chi^2$ (14) = 27.313, TLI = 0.839, RMSEA = 0.042). The standardized loadings for Any Major Depression, Any Panic Disorder, Any Specific Phobia, obsessive-compulsive, generalized anxiety, social phobia, and Any Alcohol Disorder diagnoses were 0.853, 0.682, 0.356, 0.529, 0.728, 0.431, and 0.393, respectively.

*Adolescent Higher-Order Structure of Psychopathology*

Confirmatory factor analysis was used to address the first aim of the study, testing competing models of the higher-order structure of adolescent psychopathology. Fit statistics and standardized factor loadings for the correlated factors, bifactor, and general-factor models are presented in Table 4. The correlated factors model, arguably the most

frequently modeled higher-order structure of psychopathology in the extant literature, demonstrated inconsistently acceptable fit: $\chi^2$ (34) = 285.969, TLI = 0.878, RMSEA = 0.087, SRMR = 0.051, BIC = 37568.843. Loadings for the internalizing and externalizing factors were all positive and high, ranging from 0.501 to .770 for the internalizing factor and from 0.647 to 0.799 for the externalizing factor. The factors were highly correlated at 0.751. In contrast, the bifactor model consistently met criteria for good fit: $\chi^2$ (25) = 88.947, TLI = 0.958, RMSEA = 0.051, SRMR = 0.023, BIC = 37374.245. Loadings for the P-factor were all significant and moderate to high, ranging from 0.396 to 0.878. Loadings for the externalizing factor were all significant and moderate, ranging from 0.266 to 0.521. All but one loading for the internalizing factor were significant and moderate. The internalizing factor loading onto major depressive symptoms was near zero and nonsignificant, as most of the variance was subsumed by the P-factor. Finally, the general-factor model was tested to determine whether the lower order internalizing and externalizing factors were necessary when modeling a general factor of psychopathology. This model demonstrated the worst fit of the three: $\chi^2$ (35) = 461.011, TLI = 0.800, RMSEA = 0.111, SRMR = 0.067, BIC = 37785.233. The best-fitting bifactor model is depicted in Figure 4.

*Parent-Offspring Transmission Specificity Models*

Structural equation modeling was used to address the second aim of the study, testing parent-offspring transmission specificity. Results of the model fitting are presented in Table 5. A base model allowing only for general transmission of psychopathology from parent INT to offspring P demonstrated an acceptable fit to the data ($\chi^2$ (442) = 648.170, CFI = 0.932, RMSEA = 0.023) and served as the comparison

model against which models allowing for more specific transmission effects were tested. One degree of freedom tests were conducted, allowing maternal and paternal INT phenotypes to covary with offspring residual INT and EXT phenotypes individually (i.e., mother INT with offspring INT, father INT with offspring INT, mother INT with offspring EXT, and father INT with offspring EXT). Improvements in model fit were subsequently ascertained. None of the specific transmission effects resulted in a significant change in chi-square or the alternative fit indices, suggesting that the general transmission only model sufficiently accounts for parent-offspring resemblance in psychopathology. Latent correlations from maternal INT to offspring P in the general transmission only model were moderate and significant ($p < .001$), where those from paternal INT were nonsignificant. The final, general transmission only model is depicted in Figure 5.

*Nuclear Twin-Family Model*

Finally, nuclear twin-family modeling was used to address the third aim of the study, determining the degree of genetic and environmental influence on the familial aggregation of general psychopathology. Model fitting results for a series of nested nuclear twin-family models of general psychopathology are presented in Table 6. The best fitting full model was the ADSE model, indicating that environmental influences rendering twins more similar to one another on general psychopathology were specific to the siblings and not shared with parents (family-level environmental influences could be constrained to zero). The best fitting reduced model was the ASE model, depicted with raw and standardized variance components in Figure 6. Genetic influences on general psychopathology were modest in magnitude (8%) and additive in nature (dominant

genetic influences could be constrained to zero). Sibling-specific shared environmental influences were also modest (25%), where nonshared environmental influences were moderate (67%). Parent-offspring transmission of psychopathology was accounted for by shared genetics. Lastly, there was modest evidence of assortative mating on general psychopathology.

## Discussion

The current study aimed to elucidate the phenotypic structural and genetic architecture of psychopathology in adolescence, utilizing twin-family data to examine the specificity and etiology of familial transmission and aggregation. Specifically, the study aims were to test: 1) the higher-order structure of psychopathology in adolescence, 2) the specificity of transmission effects for psychopathology from parents to their adolescent offspring, and 3) the genetic and environmental mechanisms underlying the familial aggregation of psychopathology. In contrast to the correlated factors and general-factor models, the bifactor structure exhibited the best fit to the adolescent symptom count data, evidencing important co-occurrence across internalizing and externalizing symptomology while substantiating a need to still capture the residual variance specific to the broadband domains. Next, familial aggregation of psychopathology was sufficiently accounted for by the transmission of a general liability from parental internalizing to the offspring P-factor, with no evidence for broadband domain-specific transmission (e.g., parental internalizing to offspring internalizing) emerging. Lastly, the best fitting reduced nuclear twin-family model was an ASE model, where parent-offspring transmission of general psychopathology was uniquely accounted for by shared genetics, and sibling-specific shared environmental factors accounted for additional symptom aggregation in the twins

only. Results are placed within the context of the broader literature, and strengths, limitations, and future directions are discussed.

**Adolescent Higher-Order Structure of Psychopathology**

The bifactor structure exhibited the best fit to the adolescent symptom count data, replicating previous findings from studies testing the bifactor model with lower-order internalizing and externalizing factors in similarly aged samples (Castellanos-Ryan et al., 2016; Lahey, Rathouz, Keenan, Stepp, Loeber, & Hipwell, 2015; Snyder, Young, & Hankin, 2017; Tackett, Lahey, van Hulle, Waldman, Krueger, & Rathouz, 2013; Waldman et al., 2016). Depression and ADHD exhibited the highest loadings on the P-factor which is generally consistent with the reviewed literature and likely reflective of transdiagnostic features underlying the disorders and accounting for co-occurrence with others. The model inherently captures the important co-occurrence across internalizing and externalizing symptomology that the correlated factors model, arguably the most frequently modeled higher-order structure of psychopathology in the extant literature, inadequately addresses. This is not to say that there is not important broadband domain-specific variance to consider; in fact, the bifactor structure indicates that there is significant residual variance unaccounted for by the P-factor which must be modeled. These findings compel nosological tradition to consider that which is *in common* across presumably distinct domains as clinically meaningful rather than treating it as nuisance. For the current study, these findings bolster the rationale for examining familial transmission effects at a broader level of psychopathology.

The recent proliferation of bifactor modeling of psychopathology has garnered criticism (Bonifay, Lane, & Reise, 2016). The first contention is interpretability;

specifically, what do these latent factors mean? Critics warn against the premature misattribution of the P-factor as emerging from some speculative, unitary cause and validly so. Various hypotheses have been posited, including that the P-factor captures "disordered form and content of thought" (Caspit & Moffit, 2018), however more research is needed before such an interpretation can be responsibly extended for clinical use. However, this does not discount other valid applications of the bifactor model, including testing questions of specificity such as in the current study. Despite these unknowns, measured gene research has compared genetic correlations across major psychiatric disorders and found support for a genetic P-factor, indicating that the P-factor is not simply a statistical artifact; rather, there is some meaningful, genetically influenced mechanism underlying symptom co-occurrence (Selzam, Coleman, Caspi, Moffitt, & Plomin, 2018). An additional concern is that the bifactor model has a tendency to over-fit data, with critics warning against the blind selection of models as a function of best fit (Murray & Johnson, 2013). Rather, a theoretical approach should always inform model selection and, for the current study, the bifactor model provides the ideal structure to test questions of specificity. Finally, concerns regarding the validity of the P-factor have been brought forward. This is a burgeoning area of research, and these concerns are likely to be quelled as new associations emerge in the literature. For example, the current study provides external validation of the adolescent bifactor structure by demonstrating associations with parental psychopathology.

**Parent-Offspring Transmission Specificity**

In the examination of parent-offspring transmission specificity, specification of the bifactor measurement model in the parental generation was not possible due to

insufficient externalizing indicators. Instead, a general internalizing factor was specified and broadband domain-specific transmission effects above and beyond general transmission to the offspring P-factor were tested. Phenotypic tests of parent-offspring transmission specificity revealed that transmission of a general liability from parental internalizing to the offspring P-factor was sufficient in explaining familial aggregation of psychopathology; model comparisons produced no evidence for broadband domain-specific transmission effects. Results parallel those of research examining the familial aggregation of internalizing and externalizing psychopathology independently which also evidence transmission of a general liability rather than disorder-specific effects (Bornovalova et al., 2010; Hicks et al., 2005; Starr et a., 2014). Further corroboration of this nonspecific aggregation of psychopathology within families has important implications for outcome measurement in high-risk, family history studies of psychopathology and for clinical practice regarding assessment and treatment of children whose parents experience mental health issues. Results bolster a need for broader, transdiagnostic assessment and the implementation of prevention and intervention efforts that are less targeted towards disorder-specific symptomology and more broadly applicable to potential mechanisms accounting for symptom co-occurrence.

Interestingly, results indicate that mother but not father internalizing symptomology was significantly associated with offspring symptomology across both the internalizing and externalizing domains. There is a relative dearth of research examining the effects of paternal internalizing symptomology on offspring relative to maternal effects and for studies examining both, evidence of parental differential effects has been mixed. For example, studies examining both maternal and paternal transmission of

depression to offspring consistently find maternal effects whereas evidence for paternal associations is mixed. These studies have both confirmed and discounted paternal effects, with one study indicating that paternal associations emerge only when offspring depressive symptomology is moderate to severe (Brennan, Hammen, Katz, & Le Brocque, 2002; Klein, Lewinsohn, Rohde, Seeley, & Olino, 2005; Lieb, Isensee, Hofler, Pfister, & Wittchen, 2002). Reviewed findings indicate that more research is needed to examine the impact of both maternal and paternal psychopathologies on offspring before generalizations can be made regarding whether there is a parent that acts as "primary transmitter" or not. Furthermore, this research should give due consideration to maternal and paternal caregiving roles, particularly as norms regarding parental involvement become increasingly egalitarian.

**Genetic and Environmental Transmission of Psychopathology**

The nuclear twin-family design is a powerful extension of the classical twin model in that it accounts for the effect of assortative mating, estimates A, C, D, and E influences simultaneously, differentiates passive *r*GE from true shared environmental influence, and distinguishes familial environmental transmission (F) from that which is specific to siblings (S). Despite these strengths, it is severely underutilized. In fact, this is the first nuclear twin-family study to examine genetic and environmental influences on the familial aggregation of general psychopathology. Existing nuclear twin-family studies have exclusively examined the etiology of externalizing disorders. In this study, the best fitting reduced model was an ASE model. Results indicated that there was no evidence of familial environmental transmission; as such, parent-offspring resemblance in general psychopathology was entirely accounted for by shared genetics. There was also no

evidence for passive *r*GE. Genetic influences on general psychopathology were modest in magnitude and additive in nature. There was modest sibling-specific shared environmental influence, accounting for co-twin only resemblance in general psychopathology. Lastly, there was modest evidence of positive assortative mating.

Though the current study examined the etiology of familial aggregation on co-occurring symptomology across the internalizing and externalizing domains, the failure to detect familial environmental transmission is consistent with nuclear twin-family models considering externalizing psychopathology only. Overall, nuclear twin-family studies indicate that parent-offspring resemblance in psychopathology is explained by shared genetics (Burt & Klump, 2012; Burt et al., 2012; Koopmans & Boomsma, 1996; Maes et al., 2007; Taylor et al., 2000). However, the additive genetic influence on general psychopathology in the current study was modest which stands in contrast to existing twin-only studies that report common factors of psychopathology to be highly heritable (Kendler et al., 2011a; Kendler et al., 2011b). To date, there is not a means of estimating common factors within a nuclear twin-family framework; as such, scores were extracted from independently conducted general-factor models and subsequently used in nuclear twin-family analyses. These methodological differences may account for the divergent findings. Additionally, the aforementioned common factor twin models were conducted with participants ranging in age from 25 to 74 years. Participants of the current study were adolescent twins averaging 13 years in age. There are likely important developmental considerations operating in adolescence which may render the environment a more potent influence on co-occurring symptomology at this time.

Indeed, the current study found modest evidence of sibling-specific shared environmental influence on general psychopathology and moderate effects of the nonshared environment. Assertions of autonomy are a hallmark of this developmental period (Steinberg & Silverberg, 1986), and research has demonstrated that sibling companionship decreases as children enter into adolescence (Cole & Kerns, 2001). However, findings from the current study indicate that there are still important sibling-specific environmental effects despite nonsignificant familial environmental transmission which may indicate that individuation from parents is more potent than that from siblings at this time. This individuation may account for the robust estimates of nonshared environmental influence, as twins explore new, independent experiences which may render them dissimilar to their parents and siblings on symptoms of psychopathology.

The current study also found modest evidence of assortative mating on general psychopathology ($r$ =.18). The ability to account for the effect of assortative mating in nuclear twin-family models is an advantage in that a failure to do so functions to inflate estimates of shared environmental influence and attenuate heritability. This is the first study to examine phenotypic assortment on general psychopathology indexing co-occurring symptomology across internalizing and externalizing domains. In focusing on general psychopathology, the current study addresses limitations of existing nuclear twin-family studies which consider disorder-specific assortment only. Assortment (and familial resemblance more broadly, for that matter) presents both within and across psychiatric disorders (Nordsletten et al., 2016). In fact, some cross-disorder partner correlations are higher than within disorder correlations. For example, correlations between alcoholism in male partners and depression in female partners have been found

to be higher than either within disorder correlations (Maes et al., 1998). Additionally, studies examining disorder-specific assortative mating on affective disorders have produced mixed results (Mathews & Reus, 2001), however findings from the parent-offspring transmission specificity models indicate moderate evidence of assortative mating on a general factor indexing co-occurring internalizing symptomology ($r$ = .57). A consideration of co-occurring symptomology more accurately represents the nonspecific aggregation of psychopathology across partners and within families, providing novel insight into the etiology of familial resemblance.

A univariate twin model of general psychopathology was tested so that findings from the nuclear twin-family model could be contrasted with the classical approach. Full model results indicated that general psychopathology was moderately heritable at 42%, with an additional 15% and 43% of the variance accounted for by shared and nonshared environmental influence, respectively. Reduced model comparisons were conducted, and the shared environmental influence could be dropped without producing a significant decrement in model fit. These findings stand in contrast to results from nuclear twin-family model fitting which indicated that heritability was modest and that sibling-specific shared environmental influence significantly contributed to variance in general psychopathology. This is an important consideration in that the univariate model's dampening of the shared environmental effect could be masking important contextual influences on general psychopathology in adolescence. The nuclear twin-family model is stricter but more powerful in its approach to estimating genetic influence than the classical twin model. One important assumption of the nuclear twin-family model is that genetic influences are assumed to be equal in the two generations. The model does not

allow A-by-age interaction effects which is not a concern when samples are comprised of adult twin offspring. However, there may be important etiological developmental changes in psychopathology which would potentially function to attenuate genetic covariation between parents and adolescent offspring under this assumption. Accordingly, more research is needed to ascertain the degree of genetic continuity in psychopathology across the transition from adolescence to adulthood.

**Strengths, Limitations, and Future Directions**

The current study utilized novel and rigorous statistical methods to elucidate the phenotypic structural and genetic architecture of psychopathology in adolescence, addressing questions of intergenerational transmission specificity and etiology. Strengths of the study include a consideration of both maternal and paternal data within both phenotypic and genetic frameworks, as research has tended to neglect the role of fathers in the development of children's psychopathology (Cassano, Adrian, Veits, & Zeman, 2006). Additionally, gold-standard diagnostic assessment of psychopathology is a formidable strength of this study, particularly within the genetic literature where rich phenotypic measurement is not the standard.

Limitations of the current study should also be acknowledged. Generalizability of the findings is a primary concern. First, the sample is predominantly Caucasian, limiting our understanding of whether these findings generalize to other populations. This is also a community sample and transmission effects may operate differentially as a function of symptom severity. However, this does not negate the importance of examining these intergenerational associations at sub-clinical levels. Notably, lifetime prevalence rates of paternal alcohol disorder in the sample (46%) were considerably higher than national

lifetime prevalence rates of alcohol use disorder for adult males at 36%. Maternal rates of 24% were comparable to national rates for adult females at 22.7% (Grant et al., 2015). These findings likely reflect the drinking culture in Wisconsin, where binge drinking is more normative than in the United States broadly (CDC, 2017). Lastly, the generalizability of twin study results of psychopathology to singleton populations has been challenged, with studies examining disorder-specific rates in twins and singletons producing mixed results; though overall, rates appears to be generally equitable (Kendler, Martin, Heath, & Eaves, 1995). However, more research is needed to ascertain whether rates of co-occurrence in symptomology are different in twin and singleton samples.

Final limitations concern measurement in the parental and offspring generations. Diagnoses, rather than symptom counts, were ascertained in the parent generation. This entailed reduced variability and precluded the ability to test for disorder-specific transmission effects in the phenotypic transmission specificity models. However, these diagnoses capture a level of clinical significance that is not necessarily reflected in symptom counts. Additionally, assessment of externalizing symptomology in the parents was limited to alcohol dependence and abuse disorders. This precluded the ability to specify a parental bifactor measurement model, pointing to an important future direction. Next steps entail utilizing symptom counts in both generations and testing transmission of a general liability to psychopathology, indexed by latent parent and offspring P-factor correlations. This approach would allow for tests of broadband domain- *and* disorder-specific transmission effects, providing an even more nuanced examination of transmission specificity. Future research in the nuclear twin-family framework and

beyond should consider co-occurrence of psychopathology, examining assortative mating and familial aggregation on general rather than disorder-specific psychopathology.

Overall, this study makes a significant contribution to the literature examining intergenerational transmission of psychopathology, providing novel insight into the specificity of transmission effects and the etiological mechanisms underlying symptom co-occurrence. Findings illuminate how and why symptoms of psychopathology aggregate within families, informing future approaches to the assessment of phenotypic familial associations and genetic and environmental influences on psychopathology.

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Table 1. *Partial Correlations Controlling for Age and Sex and Descriptive Statistics for Twin Symptoms Counts*

| | 1. | 2. | 3. | 4. | 5. | 6. | 7. | 8. | 9. | 10. |
|---|---|---|---|---|---|---|---|---|---|---|
| 1. MDD | - | | | | | | | | | |
| 2. OCD | .54** | - | | | | | | | | |
| 3. PD | .37** | .39** | - | | | | | | | |
| 4. Soc Phob | .35** | .34** | .22** | - | | | | | | |
| 5. Spec Phob | .35** | .35** | .28** | .36** | - | | | | | |
| 6. GAD | .59** | .50** | .38** | .50** | .40** | - | | | | |
| 7. Sep Anx | .49** | .50** | .38** | .44** | .51** | .54** | - | | | |
| 8. ADHD | .62** | .47** | .30** | .27** | .33** | .46** | .40** | - | | |
| 9. CD | .44** | .30** | .20** | .16** | .22** | .27** | .26** | .49** | - | |
| 10. ODD | .53** | .30** | .26** | .24** | .23** | .39** | .26** | .56** | .56** | - |
| Mean | 4.06 | .82 | .40 | 3.53 | 1.14 | 2.87 | 1.87 | 3.55 | 1.37 | 3.11 |
| SD | 4.03 | 1.14 | .61 | 3.71 | 1.39 | 2.44 | 2.13 | 3.99 | 2.38 | 2.81 |
| Minimum | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Maximum | 20 | 6 | 4 | 13 | 8 | 11 | 11 | 20 | 20 | 12 |
| Skewness | 1.14 | 1.63 | 1.88 | .61 | 1.49 | .69 | 1.41 | 1.46 | 2.89 | .86 |
| Kurtosis | .73 | 2.77 | 5.45 | -1.02 | 2.28 | -.35 | 1.67 | 1.93 | 11.20 | -.01 |
| N Dx | 16 | 16 | 9 | 19 | 81 | 7 | 20 | 4 | 18 | 11 |
| N Total | 1000 | 1000 | 1000 | 1000 | 1000 | 1000 | 1000 | 1000 | 1000 | 1000 |

*Note.* MDD = major depressive disorder; OCD = obsessive compulsive disorder; PD = panic disorder; Soc Phob = social phobia; Spec Phob = specific phobia; GAD = generalized anxiety disorder; Sep Anx = separation anxiety; ADHD = attention deficit hyperactivity disorder; CD = conduct disorder; ODD = oppositional defiant disorder; SD = standard deviation; N Dx = number of diagnoses in sample; N Total= number of participants with diagnostic data; ** Correlation is significant at the 0.01 level (2-tailed).

Table 2. *Zero-Order Correlations and Counts for Parent Diagnoses*

| | 1. | 2. | 3. | 4. | 5. | 6. | 7. | 8. | 9. | 10. | 11. | 12. | 13. | 14. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. $MDD_M$ | - | | | | | | | | | | | | | |
| 2. $OCD_M$ | .11* | - | | | | | | | | | | | | |
| 3. $PD_M$ | .20** | .18** | - | | | | | | | | | | | |
| 4. $SocPhob_M$ | .05 | .17** | .15** | - | | | | | | | | | | |
| 5. $SpecPhob_M$ | .13** | .22** | .22** | .21** | - | | | | | | | | | |
| 6. $GAD_M$ | .15** | .26** | .09 | .15** | .15** | - | | | | | | | | |
| 7. $AlcDis_M$ | .15** | .03 | .12* | .12* | .15** | .06 | - | | | | | | | |
| 8. $MDD_F$ | .17** | .08 | .12* | .16** | .23** | -.01 | -.02 | - | | | | | | |
| 9. $OCD_F$ | .06 | -.01 | .23** | -.02 | .09 | -.02 | -.05 | .10 | - | | | | | |
| 10. $PD_F$ | .02 | -.02 | -.02 | -.03 | .04 | .14* | .00 | .05 | -.01 | - | | | | |
| 11. $SocPhob_F$ | .07 | .11 | .21** | -.05 | .06 | -.03 | .00 | .07 | -.01 | .16** | - | | | |
| 12. $SpecPhob_F$ | -.09 | .06 | -.05 | -.07 | -.05 | .03 | .00 | .04 | -.02 | -.03 | .05 | - | | |
| 13. $GAD_F$ | .05 | -.03 | .07 | -.05 | .21** | -.04 | -.02 | .40** | .21** | .14* | .08 | -.05 | - | |
| 14. $AlcDis_F$ | -.01 | .04 | .00 | .06 | .06 | .02 | .19** | .12* | -.08 | .07 | .10 | .16** | -.02 | - |
| N Dx | 87 | 13 | 16 | 28 | 54 | 16 | 100 | 34 | 2 | 4 | 8 | 18 | 10 | 135 |
| N Total | 409 | 409 | 409 | 409 | 409 | 403 | 409 | 296 | 296 | 296 | 296 | 296 | 296 | 296 |

*Note.* MDD = major depressive disorder; OCD = obsessive compulsive disorder; PD = panic disorder; Soc Phob = social phobia; Spec Phob = specific phobia; GAD = generalized anxiety disorder; Alc Dis = alcohol disorder; M subscript = mother; F subscript = father; N Dx = number of diagnoses in sample; N Total= number of participants with diagnostic data; ** Correlation is significant at the 0.01 level (2-tailed); * Correlation is significant at the 0.05 level (2-tailed).

Table 3. *Parent-Offspring Zero-order correlations, Twin Intraclass Correlations, and Descriptive Statistics for Latent Factor Scores of Psychopathology*

| | 1. | 2. | 3. | 4. | 5. | 6. | 7. | 8. |
|---|---|---|---|---|---|---|---|---|
| 1. Offspring General Psychopathology Factor Score | - | | | | | | | |
| 2. Offspring P Factor Score | .97** | - | | | | | | |
| 3. Offspring INT Factor Score | .39** | .17** | - | | | | | |
| 4. Offspring EXT Factor Score | .21** | .16** | -.20** | - | | | | |
| 5. Mother General Psychopathology Factor Score | .18** | .16** | .10** | .10** | - | | | |
| 6. Mother INT Factor Score | .19** | .17** | .11** | .08* | .97** | - | | |
| 7. Father General Psychopathology Factor Score | .13** | .13** | .05 | -.02 | .16** | .15** | - | |
| 8. Father INT Factor Score | .10* | .10* | .04 | -.06 | .17** | .17** | .91** | - |
| MZ ICC | .48** | .47** | .43** | .54** | | | | |
| DZ ICC | .38** | .34** | .16** | .22** | | | | |
| Mean | .00 | .00 | .00 | .00 | .08 | .09 | .12 | .16 |
| Standard Deviation | 3.00 | 3.23 | .67 | 1.02 | .62 | .59 | .58 | .52 |
| Minimum | -4.33 | -4.76 | -2.41 | -3.24 | -.39 | -.30 | -.33 | -.07 |
| Maximum | 11.42 | 12.96 | 3.02 | 3.84 | 2.67 | 2.77 | 2.02 | 2.26 |
| Skewness | .86 | .97 | .84 | .58 | 1.28 | 1.48 | 1.44 | 2.26 |
| Kurtosis | .24 | .44 | 1.49 | .77 | 1.08 | 1.64 | 1.37 | 3.68 |

*Note.* INT = internalizing; EXT = externalizing; MZ ICC = monozygotic twin intraclass correlation; DZ ICC = dizygotic twin intraclass correlation; Offspring P, INT, and EXT factor scores extracted from bifactor model; ** Correlation is significant at the 0.01 level (2-tailed).

Table 4. *Higher-Order Structure of Adolescent Psychopathology: Model Fit Statistics, Standardized Factor Loadings, and Factor Correlations*

| | Correlated factors model | | | Bifactor model | | | | 1-Factor model | |
|---|---|---|---|---|---|---|---|---|---|
| Statistics, loadings, and correlations | Model fit | INT | EXT | Model fit | P | INT | EXT | Model fit | GEN |
| Statistic | | | | | | | | | |
| Chi-square | 285.969 | | | 88.947 | | | | 461.011 | |
| df | 34 | | | 25 | | | | 35 | |
| TLI | .878 | | | .958 | | | | .800 | |
| SRMR | .051 | | | .023 | | | | .067 | |
| BIC | 37568.843 | | | 37374.245 | | | | 37785.233 | |
| RMSEA[90% CI] | .087 | | | .051 | | | | .111 | |
| | [.077, .096] | | | [.040, .063] | | | | [.102, .120] | |
| Standardized Factor loading | | | | | | | | | |
| Generalized Anxiety | | .761 | | | .657 | .367 | | | .731 |
| Obsessive Compulsive | | .684 | | | .614 | .277 | | | .670 |
| Panic | | .501 | | | .431 | .242 | | | .486 |
| Separation Anxiety | | .700 | | | .538 | .560 | | | .658 |
| Social Phobia | | .544 | | | .396 | .444 | | | .509 |
| Specific Phobia | | .545 | | | .399 | .464 | | | .519 |
| Major Depressive | | .770 | | | .878 | .014 | | | .801 |
| Attention Deficit Hyperactivity | | | .799 | | .713 | | .266 | | .716 |
| Conduct | | | .647 | | .492 | | .521 | | .521 |
| Oppositional Defiant | | | .727 | | .588 | | .516 | | .599 |
| Factor correlation | | .751 | | | | | | | |

*Note.* INT = internalizing factor; EXT = externalizing factor; P = P-factor; GEN = general factor; df= degrees of freedom; TLI = Tucker-Lewis index; SRMR = standardized root mean square residual; BIC = Bayesian information criterion; RMSEA = root-mean-square error of approximation; CI = confidence interval.

Table 5. *Indices of Fit for Alternate Parent-Offspring Transmission of Psychopathology Models*

| Model | $\chi^2$ | df | RMSEA | CFI | $\Delta\chi^2$ | df |
|---|---|---|---|---|---|---|
| **General Transmission** | 648.170 | 442 | .023 | .932 | | |
| Father INT | | | | | | |
| Offspring INT | 648.501 | 441 | .023 | .932 | $.816^{ns}$ | 1 |
| Offspring EXT | 647.281 | 441 | .023 | .932 | $1.513^{ns}$ | 1 |
| Mother INT | | | | | | |
| Offspring INT | 648.411 | 441 | .023 | .932 | $.565^{ns}$ | 1 |
| Offspring EXT | 646.399 | 441 | .023 | .933 | $3.244^{ns}$ | 1 |

*Note.* $\chi^2$ = chi-square; df = degrees of freedom; RMSEA = root-mean-square error of approximation; CFI = comparative fit index; $\Delta\chi^2$ = chi-square difference statistic via DIFFTEST option in MPlus for use with weighted least squares means and variances adjusted (WLSMV) estimator; ns = nonsignificant; INT = internalizing factor; EXT = externalizing factor.

Table 6. *Nuclear Twin-Family Model Fit Statistics*

| Model | -2Lnl | df | AIC | BIC | SABIC |
|---|---|---|---|---|---|
| ADSE | 8888.811 | 2256 | 4376.811 | -7834.385 | 8926.934 |
| ASFE | 8892.215 | 2256 | 4380.215 | -7830.980 | 8930.339 |
| ADFE | 8904.893 | 2256 | 4392.893 | -7818.303 | 8943.016 |
| **ASE** | 8892.215 | 2257 | 4378.215 | -7838.393 | 8926.103 |
| ADE | 8904.893 | 2257 | 4390.893 | -7825.716 | 8938.78 |
| AFE | 8944.304 | 2257 | 4430.304 | -7786.305 | 8978.191 |
| AE | 8944.304 | 2258 | 4428.304 | -7793.717 | 8973.955 |

*Note*. Best fitting model in bold type. -2Lnl = negative two log likelihood; df = degrees of freedom; AIC = Akaike's information criterion; BIC = Bayesian information criterion; SABIC = sample-size adjusted Bayesian information criterion; A= additive genetic variance; D= dominant genetic variance; S= sibling-specific environmental variance; F= family-level environmental variance; E= unique (nonshared) environmental variance

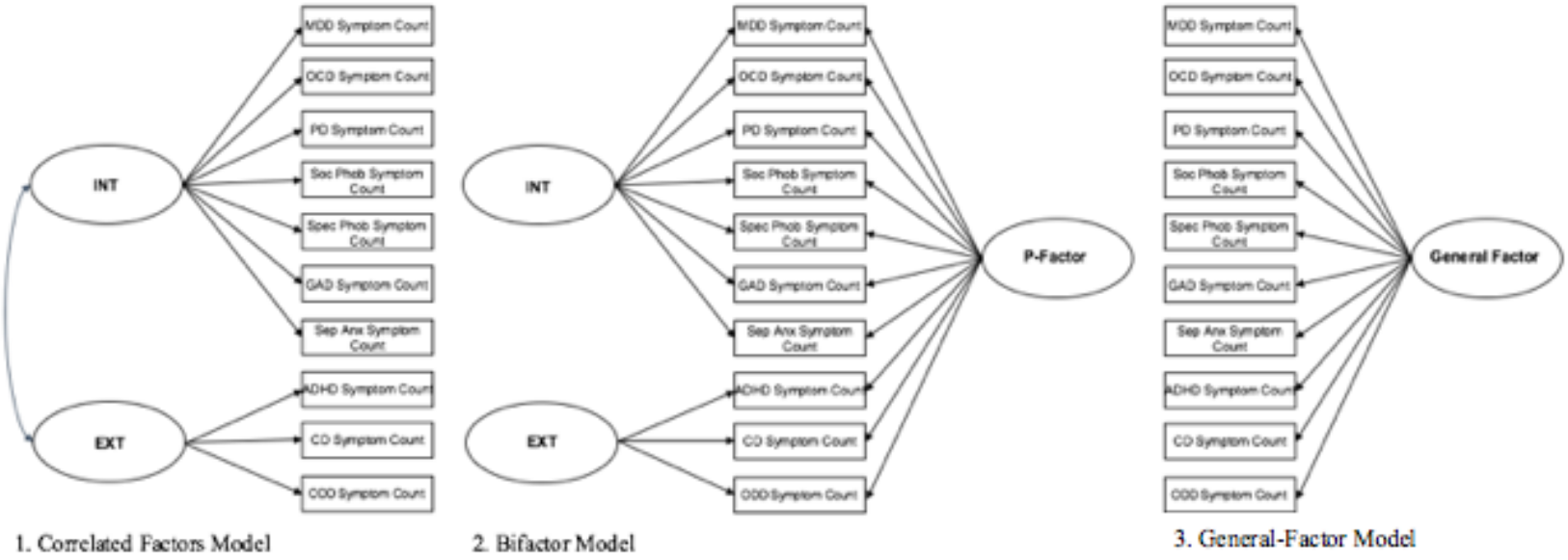


*Figure 1.* Alternative models of the higher-order structure of adolescent psychopathology. Three models were tested using confirmatory factor analysis: 1) a correlated factors models, 2) a bifactor model, and 3) a general-factor model. Ovals represent latent (unobserved) factors and boxes represent observed symptoms counts. Note: MDD = major depressive disorder; OCD = obsessive compulsive disorder; PD = panic disorder; Soc Phob = social phobia; Spec Phob = specific phobia; GAD = generalized anxiety disorder; Sep Anx = separation anxiety; ADHD = attention deficit hyperactivity disorder; CD = conduct disorder; ODD = oppositional defiant disorder.

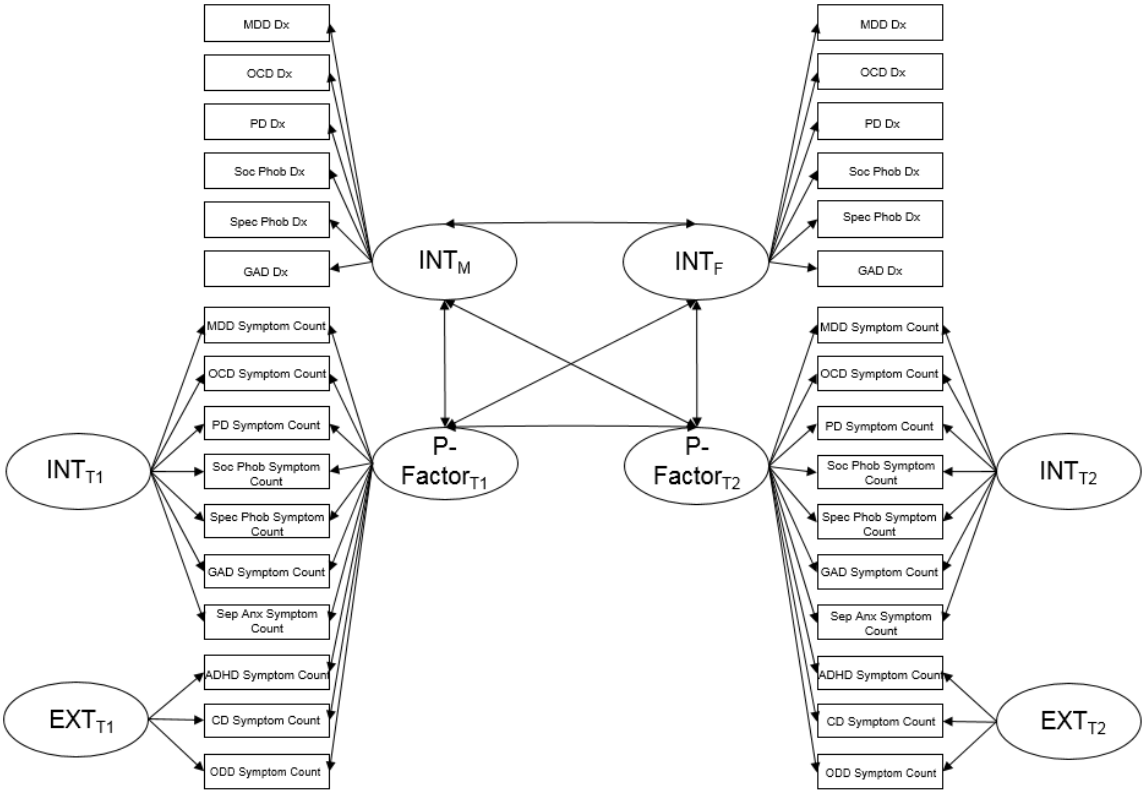


*Figure 2.* Parent-offspring general transmission model. The fits of additional models testing broadband domain-specific transmission from mother and father INT to twin INT and EXT were compared to the model specifying only general transmission to the twin P-factor. Ovals represent latent (unobserved) factors and boxes represent observed diagnoses in the parent generation and symptom counts in the offspring generation. Double headed arrows connecting mother and father INT to twin P-factors represent the general transmission effect. Note: INT = internalizing; EXT = externalizing; M subscript = mother; F subscript = father; T1 subscript = twin 1; T2 subscript = twin 2; Dx = diagnosis; MDD = major depressive disorder; OCD = obsessive compulsive disorder; PD = panic disorder; Soc Phob = social phobia; Spec Phob = specific phobia; GAD = generalized anxiety disorder; Sep Anx = separation anxiety; ADHD = attention deficit hyperactivity disorder; CD = conduct disorder; ODD = oppositional defiant disorder.

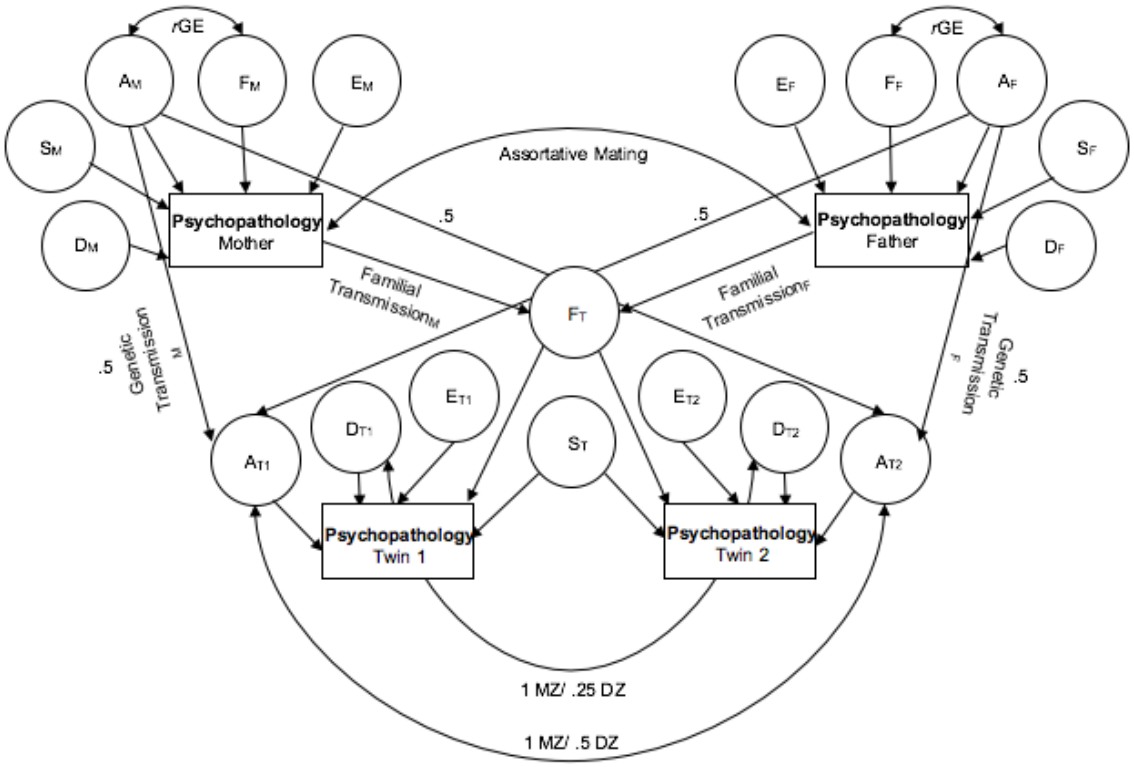


*Figure 3.* Nuclear twin-family model. The variance in general psychopathology is parsed into that which is due to additive genetic influence, dominant genetic influence, sibling-specific environmental influence, family-level environmental influence, and nonshared environmental influence. D, S, and F cannot be estimated simultaneously, requiring one of the three to be dropped. Note: A= additive genetic variance; D= dominant genetic variance; S= sibling-specific environmental variance; F= family-level environmental variance; E= unique (nonshared) environmental variance.

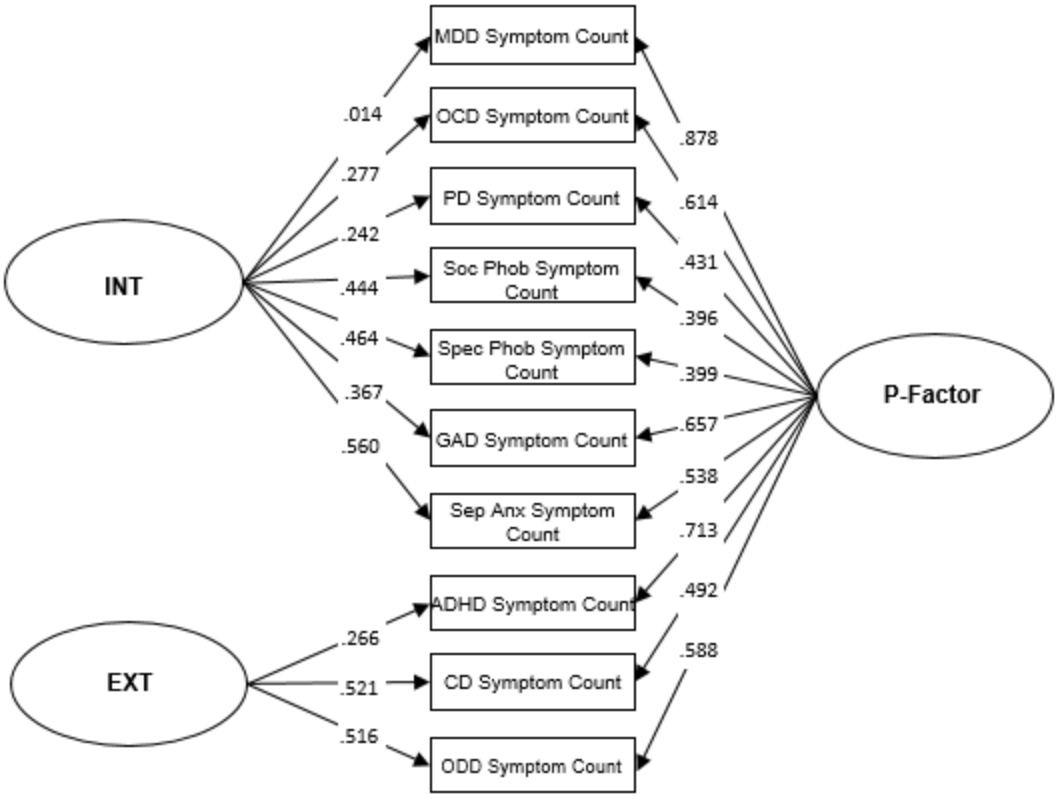


*Figure 4.* Best-fitting bifactor model of adolescent psychopathology with standardized factor loadings. Note: INT = internalizing factor; EXT = externalizing factor.

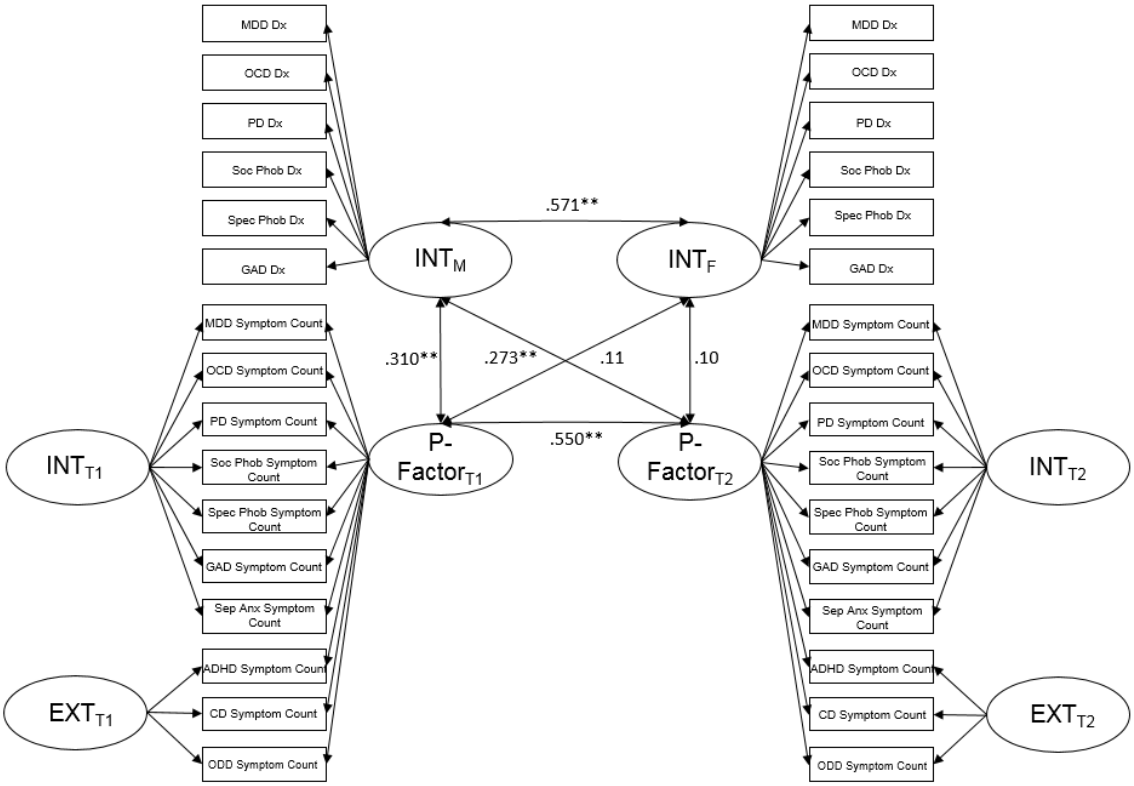


*Figure 5.* Best-fitting parent-offspring general transmission model. Ovals represent latent (unobserved) factors and boxes represent observed diagnoses in the parent generation and symptom counts in the offspring generation. Double-headed arrows connecting mother and father INT to twin P-factors represent the general transmission effect. Note: INT = internalizing; EXT = externalizing; M subscript = mother; F subscript = father; T1 subscript = twin 1; T2 subscript = twin 2; Dx = diagnosis; MDD = major depressive disorder; OCD = obsessive compulsive disorder; PD = panic disorder; Soc Phob = social phobia; Spec Phob = specific phobia; GAD = generalized anxiety disorder; Sep Anx = separation anxiety; ADHD = attention deficit hyperactivity disorder; CD = conduct disorder; ODD = oppositional defiant disorder; ** Latent correlation is significant at the 0.01 level (2-tailed).

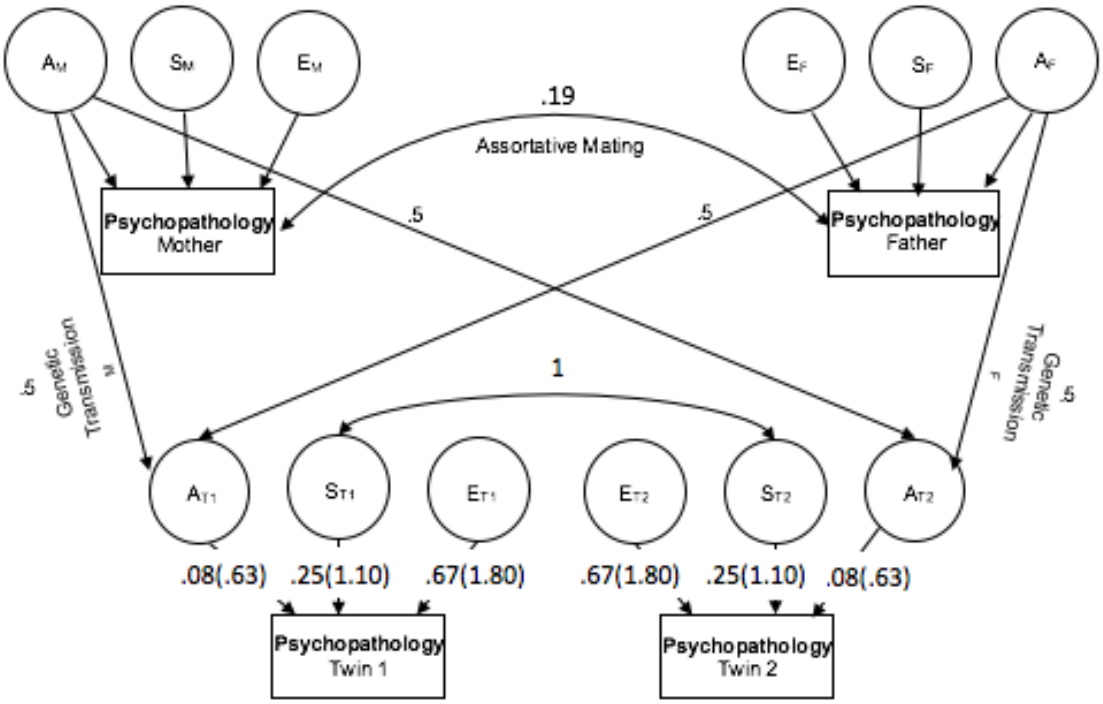


*Figure 6.* Best-fitting nuclear twin-family model. The variance in general psychopathology is parsed into that which is due to additive genetic influence (A), sibling-specific environmental influence (S), and nonshared environmental influence (E). Standardized variance components are presented with raw variance components provided in parentheses.