Familial Aggregation of Externalizing Psychopathology

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Dedication

This thesis is dedicated to Dalia Ofrat and Penina Albilia.

Abstract

Objective Understanding familial aggregation (FA) of psychopathology in a latent variable framework allows for an understanding of shared risk for maladaptive traits and disorders in parents and their children, and improves clinical utility or risk models. Previously, FA has been investigated using bivariate approaches, providing a piecemeal understanding of risk. This study investigates 1) how externalizing disorders in parents impact risk for a broad range of internalizing and externalizing disorders in offspring, 2) if risk shared between parents and offspring is best conceptualized as general risk for a group of disorders or specific to particular disorders, and 3) how this might vary as a function of parent and offspring gender. **Methods** Data for sample one were collected as part of the National Epidemiological Survey on Alcohol and Related Conditions (NESARC) in 2001-2002 on 43,093 individuals 18 years or older living in the US. A replication sample used the Minnesota Twin and Family Study sample of twins, siblings, and their parents using parallel analyses to attempt to replicate results in an independent sample which used direct assessment of parent psychopathology. Using confirmatory factor analysis, parental externalizing disorders were investigated as a risk factor for externalizing, fear, and distress disorders in offspring, in a latent variable structural equation model. Factor analysis was used to model parent externalizing and offspring fear, distress and externalizing. DIFFTEST and regression analyses were used to consider parent and offspring gender as moderator of association between parent and offspring psychopathology. Correlations between residual variances in parent and offspring disorders were used to test specificity of risk aggregation. **Results** Externalizing in

parents was most predictive of externalizing in offspring, followed by distress and finally fear disorders. However, in female offspring, externalizing in mothers in particular was as strong a predictor of distress disorders as it was of externalizing disorders. Risk for offspring disorders associated with parent disorders was well-explained by a latent variable framework, with residual correlations for ASPD in parents associated with specific risk for offspring ASPD. **Conclusions** Results indicate that familial psychopathology aggregation follows a pattern that suggests risk is aggregated generally (transdiagnostically across similar disorders), not specifically. Additionally, externalizing in mothers is associated with increased risk for distress disorders in female offspring, and possibly also in male offspring.

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Introduction

Externalizing disorders are highly prevalent in the general population, and exact large societal and fiscal costs. Externalizing disorders are broadly described as the disinhibitory and substance use disorders, including illicit drug, prescription drug, alcohol, and nicotine use disorders; antisocial personality disorder and antisocial traits; pathological gambling; conduct disorder; and ADHD. In terms of prevalence rates, the World Health Organization estimates that there are at least 2 billion alcohol users, more than 1 billion tobacco users, and almost 185 million illicit drug users worldwide (Li and Burmeister, 2009). Additionally, these disorders have a substantial cost to society, e.g., antisocial personality disorder (ASPD) exacts a huge cost via costs of the penal system. It is estimated that half of male prisoners meet criteria for ASPD (Fazel & Danesh, 2002) and half of those people with ASPD living in the community have an arrest record (Robins & Price, 1991). For another example, a conservative estimate of the annual societal cost of ADHD in childhood and adolescence is $ 42.5 billion in the US alone (Pelham, Foster, & Robb, 2007). Overall, the high prevalence rates, and high societal and fiscal costs necessitate an understanding of risk factors associated with these externalizing disorders.

Extant research has shown strong evidence of comorbidity among common mental disorders, including externalizing disorders, in individuals (Krueger, 1999; see Krueger, Hicks, Patrick, Carlson, Iacono, & McGue, 2002, for an overview). For example, among alcohol-dependent individuals, 47% have another mental disorder and a significant proportion of this comorbidity is accounted for by drug dependence (Helzer &

Pryzbeck, 1988). The lifetime risk for substance use disorder is approximately 50% in subjects with childhood ADHD that persists into adulthood (Biederman et al. 1995). Clinical studies reveal that 23 to 70 percent of patients in alcoholism treatment also suffer from anxiety disorders, particularly anxiety neurosis and phobias (Kushner, Sher, & Beitman, 1990; Merikangas and Angst, 1995).

The costs of externalizing do not stop with one generation: an aggregation of psychopathology occurs in families, in that parent externalizing disorders are associated with offspring behavioral and social problems, as well as psychiatric disorders. The study of this aggregation of risk for psychiatric disorders in families is called familial aggregation (FA) or familial transmission of psychopathology. Understanding FA is an important step towards assessing who is at risk for developing disorders, how that risk is conferred, and what can be done to alleviate the risk burden of mentally ill parents to their offspring.

The existing literature on familial aggregation of disorders is largely bivariate in its focus, i.e., focuses on how one disorder in parents confers risk to one, or at best, several disorders in offspring. This approach ignores what is known about shared liability to groups of disorders (i.e., internalizing and externalizing disorders), and makes it more difficult to see clear patterns of risk across diagnoses. This bivariate literature provides unwieldy lists of pairwise associations between disorders in parents and offspring, yielding a literature where findings are often inconsistent across studies, and artificially siloed into diagnostic categories that do little to explain the rampant comorbidity observed in clinical contexts. Further, this fragmented literature requires

clinicians to attempt to summarize the myriad and inconsistent studies investigating disorders of interest into a coherent framework that allows for clinical applications.

Specificity or Generality of Familial Aggregation of Psychopathology

Disorders with shared liability may also share etiological variables, which are important targets for intervention. Thus, understanding the degree to which liability is shared across disorders not only improves clinical utility, but also improves our ability to search for underlying etiological factors that contribute to risk for groups of related disorders. Because of the largely bivariate methods applied to the question of familial aggregation of psychopathology, it is unclear how much variance in the association between parent psychopathology and psychiatric risk in offspring manifests as a generalized vulnerability to psychopathology, compared to risk for a specific disorder in offspring (Bornovalova, Hicks, Iacono, & McGue, 2010; McLaughlin, K. A., Gadermann, A. M., Hwang, I., Sampson, N. a, Al-Hamzawi, A., Andrade, L. H., … & Kessler, R. C., 2012; Krueger and South, 2009). Bivariate analyses remain naturally inconclusive about the relative specificity and generality of parent offspring relations in psychopathology, explicitly because they ignore patterns of covariance due to comorbidity of disease or shared etiology. As a result, it is impossible for bivariate studies to address the extent to which identified associations between disorders in parents and offspring might be explained by specific risk for specific disorders, or a generalized risk that disperses among the multiple disorders, but which cannot be simultaneously considered using bivariate methods.

The multivariate metastructure modeling approach fills in this gap in the literature by modeling relationships among multiple disorders simultaneously to uncover underlying latent variables that account for risk associations shared across multiple disorders in parents and offspring. Through existing studies, latent internalizing and externalizing variables have been well-defined using this approach, and those variables have been related to important outcomes, shown to constitute a more stable metric of psychological function than specific diagnostic categories, and are capable of explaining comorbidity patterns frequently observed in clinical work (Krueger et al., 2002; Eaton et al., 2013; Wright et al., 2013). Although multivariate methods are well-suited to answer questions regarding generality/specificity, and have been used extensively to show evidence of shared liability in individuals, there are very few multivariate studies that investigate the psychopathology metastructure and related questions in families, or how the metastructure can add to our understanding of familial aggregation.

Bivariate and multivariate findings in aggregation of parent externalizing in families. Bivariate studies do offer important insights when aggregated, and have shown that the offspring of externalizing parents have higher levels of problem behavior such as aggressiveness, delinquency, attention deficits, psychiatric treatment and poor school performance (Sher, Walitzer, Wood & Brent, 1991; Connolly, Casswell, Stewart, Silva, & O'Brien, 1993; Loukas, Fitzgerald, Zucker, & von Eye, 2001; Reich, Earls, Frankel, & Shayka, 1993; von Knorring, 1991). In addition, parental disorders related to behavioral disinhibition such as drug dependence, alcohol dependence, and antisocial personality disorder in parents are associated with greater risk for the development of offspring

externalizing disorders including drug and alcohol use disorders, antisocial personality disorder, attention deficit-hyperactivity disorder, and conduct disorder (Krueger et al., 2002; Reich et al., 1993; Chassin, Rogosch, & Barrera, 1991; Chassin, Pitts, & Prost, 2002; Gotham & Sher, 1996; Rowe & Farrington, 1997; Cadoret, Yates, Troughton, Woodworth et al., 1995; Luthar, Anton, Merikangas, Rounsaville, 1992; Kosten, Rounsaville, Kosten, and Merikangas, 1991; Luthar, Merikangas, and Rounsaville, 1993). In comparison, in the bivariate literature, externalizing disorders in parents have been less consistently associated with internalizing disorders (disorders of unipolar mood and anxiety disorders like major depressive disorder, generalized anxiety disorder, and panic disorder) in offspring: Some studies have found evidence of increased risk in the offspring of externalizing parents for anxiety (e.g., Reich et al., 1993, Merikangas et al., 1998) and depression (e.g., Merikangas et al., 1998), while others have not (e.g., Reich et al., 1993; Schuckit, Smith, Radziminski & Heyneman, 2000). As yet, it is unclear which disorders the offspring of externalizing parents are at risk for.

A small number of multivariate studies have also addressed this question. Kendler, Davis, & Kessler (1997) examined familial transmission of major depression, generalized anxiety disorder, alcohol abuse or dependence, drug abuse or dependence, and antisocial personality disorder, and in a community sample of 5385 participants using a latent multivariate framework. Before accounting for shared risk across comorbidities, risk was transmitted specifically for all disorders, in that having the disorder in parents significantly increased risk for the disorder in offspring, compared with controls. However, when controlling for the presence or absence of other disorders in both proband

and parent, there was evidence of two large, shared factors that explained much of the variance in offspring psychopathology (internalizing and externalizing). There was also some evidence of specific risk conferred by specific disorders in the cases of major depression, generalized anxiety disorder, and alcohol abuse/dependence, while for antisocial personality disorder and drug abuse/dependence, the diagnoses in parents were no longer significant predictors of diagnoses in offspring after accounting for shared variance with the other disorders. McLaughlin et al. (2012) conducted a multivariate study in an epidemiological sample of 51,507 respondents, and found little evidence that any form of parent psychopathology exerted specific risk to substance use disorders and antisocial behavior disorder in offspring. Rather, a model of general risk transmission of psychopathological risk from parents to offspring fit the data best. Additionally, controlling for comorbid parent disorders in parents uniformly attenuated the relationships between parent disorder and offspring disorder, indicating significant cross-disorder effects in risk transmission from parents to offspring. Lastly, Hicks et al. (2004) found similarity between parents and their 17-year-old twin offspring for child and adult antisocial behavior, alcohol dependence, and drug dependence could be accounted for by the transmission of a general externalizing factor (r =0.30). Taken together, these findings indicate a high degree of generality in conferred risk, and some evidence of specific risk aggregation for individual disorders. However, these studies are limited, in that one sample likely contains prevalence rates of female externalizing disorders that are too low to detect significant gender differences across parent or offspring psychopathology (Kendler et al.,1997). The other study is similarly limited in size, and further limited in

that it does not consider offspring internalizing disorders (Hicks et al., 2013). Additionally, these studies' findings need to be replicated in a larger, more diverse and generalizable sample. Lastly, the specificity findings in Kendler et al.'s (1997) study have not been independently replicated.

One disadvantage of multivariate studies that can use a metastructure approach is that they require larger samples to adequately capture sufficient prevalence rates of relevant disorders to model a broad range of psychopathology. With large sample size, and questions related to familial aggregation, direct assessment of participants and their parents quickly becomes costly. As such, many large epidemiological studies rely on retrospective and informant reporting, where offspring reported on the psychopathology of their parents. In terms of validity, offspring are among the most accurate reporters on parent psychopathology, as compared to a gold-standard interview (Thompson, Orvaschel, Prusoff, & Kidd, 1982). There is evidence that offspring reporters have good specificity but low sensitivity when compare to a gold standard, which is likely to attenuate, rather than exaggerate, associations between parent and offspring psychopathology (Kendler et al., 1997). Evidence of biased reporting has been found in internalizing offspring, whereby internalizing offspring report more internalizing in their parents, while offspring do not differ from unaffected twins in their reports of externalizing in parents, regardless of the characteristics/diagnoses of the offspring (Kendler et al., 1991). Although there is no evidence of reporting bias when offspring report on externalizing in parents, it is possible that even in externalizing disorders, offspring with psychopathology may be more accurate than offspring without

psychopathology in identifying that same disorder in their parents. This may bias results in the direction of increased associations between parent and offspring psychopathology (Chapman et al., 1994), and is a study limitation of many large epidemiological surveys.

Conclusions in Specificity/Generality

In sum, there is some evidence that risk for externalizing disorders are transmitted both generally and specifically. Twin and multivariate studies have mostly supported a generality of risk transmission model, or supported a model where the majority of risk is transmitted generally, and any evidence of specificity of transmission is relatively small in effect by comparison. The bivariate family study literature has produced strong evidence of both specificity and generality of transmission. This literature suggests strongest associations between parent externalizing disorders and offspring externalizing disorders, but also suggests a weaker, significant, but less consistent relationship between parent externalizing disorders and offspring internalizing disorders.

Gender Influences

Parent gender. Gender is an important potential moderator of risk aggregation in families. If patterns of associations differ in families dependent on gender, gender may play a moderating role in aggregation of risk for psychopathology in offspring, and may be an important piece of determining clinical risk for disorders. In the familial aggregation literature, few studies compare mothers to fathers directly, because few studies collect data on both mothers and fathers, presumably because fathers have been more difficult to include in research generally, and because mothers are lower in rates of externalizing (Connell and Goodman, 2002). As a result, the literature tends towards

psychiatric samples which have adequate rates of female externalizing, but are not generalizable, or assesses psychopathology in either mothers or fathers and do not compare associations directly. These limitations make it impossible to compare the relative associations between mothers and offspring to the associations between fathers and offspring. Research suggests that mothers and fathers with externalizing traits may be associated with different amounts of risk for offspring psychopathology, and that the risk may be received differently in male and female offspring, but the direction and magnitude of that difference is not clear. In parents, some bivariate studies have found mothers' alcohol dependence, ASPD, and drug dependence has a greater impact on offspring psychopathology (Dierker et al., 1999; Chassin, Pitts, DeLucia, & Todd, 1999; McLaughlin et al., 2012) while others have found fathers' disorders to have a greater impact (Ohannessian et al., 2005; Lieb et al., 2002; Pollock and Schneider, 1987, Luthar, Merikangas, & Rounsaville, 1993), while yet others found no difference between risk conferred by mothers and fathers with externalizing disorders (Kaij and Dock, 1975; Kendler, Neale, Heath, Kessler, & Eaves, 1994; Reich et al., 1988; Rowe, 1983; Kendler et al., 1997). Limits of this extant literature, and possible reasons for inconsistency, are bivariate methods, sample size, psychiatric samples that limit generalizability, and samples that assess risk in only one gender of parent or offspring.

Of the samples that use multivariate modeling methods, one sample found a single gender difference in risk associated with psychopathology in mothers versus fathers: the odds ratio between maternal major depressive disorder and proband major depressive disorder was significantly larger than the same odds ratio observed between

father and proband (Kendler et al., 1997). However, as major depressive disorder was the disorder with the largest prevalence in that study, it is possible that the other disorders did not show gender differences because the power to detect difference was limited by lack of adequate prevalence of female externalizing. The study found no significant moderation effects of offspring gender on the association between maternal and paternal externalizing on offspring psychopathology. Another study found a small specific genetic effect for smoking in mothers, which had a specific significant association to offspring smoking, beyond the general externalizing liability (Hicks et al., 2013).

Moderation by offspring gender. The moderating impact of offspring gender, and in particular, the interaction between offspring gender and their same-sex parent, on risk for offspring psychopathology, is equally under-studied. Externalizing is less prevalent in girls and adult female offspring, meaning most familial association studies of externalizing focus mainly on male offspring, or include female offspring but are underpowered (Connell and Goodman, 2002). Several studies have suggested that parents exert greater influence on their same-sex offspring (Deater-Deckard & Dodge, 1995; Koestner, Zuroff, & Powers, 1991; Hops, 1992; Pollock & Schneider, 1987; Crawford, Cohen, Midlarsky, & Brook, 2001; Davies & Windle, 1997; Fergusson, Lysnkey, & Horwood, 1993). Drawn from Bandura's (1977) conclusion that children are more strongly influenced by models of greater similarity to themselves, Connell and Goodman suggest that parents exert the greatest influence on same-sex children, and also that influence may be bidirectional, as parents may relate more closely to their same-gender offspring, resulting in a greater investment of time and energy in them (2002).

Furthermore, there is some evidence to suggest that females in particular are sensitive to psychopathology in their same-sex parent, perhaps because they are socialized to be more relational. As evidence, Pollock and Schneider (1987) found both male and female offspring were at higher risk if they had alcoholic mothers or fathers, but only females were at higher risk if they had alcoholic mothers only. In three studies examining adolescents and their parents (Crawford, Cohen, Midlarsky, & Brook, 2001; Davies & Windle, 1997; Fergusson, Horwood, & Lynskey, 1993), maternal depressive and anxious symptoms were associated with adolescent depressive symptoms and conduct and academic problems for girls but not for boys. Reviews on this subject have called for further investigation of gender effects in studies of familial associations of psychopathology by searching for interactions across parent and offspring gender (e.g., Connell and Goodman, 2002; Phares and Compas, 1992). Taken together, this suggests there may be an especially strong association between mothers and daughters.

Conclusions in gender moderation. The impact of parent and offspring gender on the association between parent and offspring psychopathology is not as yet well-understood, and certainly poorly understood in a metastructure framework. Many researchers have called for investigation of the effects of parent and offspring gender on risk for familial expressions of psychopathology, as gender effects would have substantial implications for our understanding of familial risk (Connell & Goodman, 2002; Phares & Compas, 1992; Lieb et al., 2002). Many previous studies have likely been underpowered, particularly in terms of female externalizing disorders, a concern that is generally acknowledged and often explicitly stated as a limitation in those studies. A critical

requirement for a well-designed study to answer unaddressed questions of specificity of aggregation, while systematically controlling for gender effects, is that samples must be large enough to capture sufficient cases of both female offspring and maternal externalizing in order to model relationships with sufficient power.

Advantages of Hierarchical Multivariate Models over Bivariate Methods

There are very few studies that assess familial aggregation in a multivariate framework, reflecting our current understanding of how groups of disorders co-occur. Although we understand a great deal about comorbidity (disorders occurring together in an individual), we understand less about risk in coaggregation (disorders occurring together in families).

Although there is evidence from multivariate studies that familial risk associations of psychopathology have a general component, bivariate family and epidemiological studies of externalizing in parents have produced conflicting evidence. For example, some results indicate specific risk associated with particular disorders in parents and offspring (e.g., Ripple and Luthar, 1996; Hill, Cloninger, and Ayre, 1977; Meller et al., 1988, Merikangas et al., 1998; Clark, Cornelius, Wood, & Vanyukov, 2004) while others have found evidence for shared liability across alcohol and drug use disorders (Chassin et al., 1999; Chassin , Flora, and King, 2004; Beirut et al., 1998; Rounsaville et al., 1991; Marmorstein, Iacono and McGue, 2009) and antisocial personality disorder (Finn et al., 1997; Nurmberger et al., 2004; Zucker, Ellis, Bingham, and Fitzgerald, 1996; Chassin, Rogosch, and Barrera, 1991). It is likely that the true nature of the familial risk association structure is best reflected by a hybrid model that allows for both specificity

and generality of risk association, organized hierarchically, which allows for both generality and specificity of risk transmission (Krueger et al., 2002).

In contrast to bivariate studies that leave the risk profile unclear and inconsistent, a metastructure modeling approach to understanding risk in families clarifies and extends the clinical risk profile for offspring of externalizing parents, which has implications for early intervention, diagnosis, and treatment intervention. In addition to greater parsimony, the metastructure approach finds additional support in genetic and environmental etiological factors, which appear similarly well-organized by the same internalizing and externalizing model (Kendler et al., 2011; Kendler, Prescott, Myers, & Neale, 2003; Lahey, van Hulle, Singh, Waldman, & Rathouz, 2011).

The Current Study

Taken together, the largely bivariate literature and the few studies using a multivariate approach suggest the need for a large, adequately powered community sample that examines gender of offspring as a moderator of the risk associated with maternal and paternal psychopathology, while applying a latent variable approach that allows for maximum parsimony and clinical utility in establishing an extended risk profile for offspring of externalizing parents. This study seeks to extend and refine the understanding of psychiatric risk in offspring of parents with externalizing behavior, to improve clinical utility of extant risk models. It does so by considering a broad range of internalizing and externalizing disorders in adult offspring, using a large, nationally representative US sample (NESARC, described below). Analyses will be applied to the first nationally representative sample large enough for a multivariate metastructure

approach to modeling the association between parent externalizing and offspring internalizing and externalizing disorders, while simultaneously being suitable to the investigation of systematic parent gender influences and further moderation effects of offspring gender for risk in offspring psychopathology. Notably, compared to previous work, the proposed sample in study one has nine times higher prevalence rates than the only other study to model both internalizing and externalizing in offspring (Kendler et al., 1997), which makes it feasible to simultaneously investigate gender within a multivariate context. The inclusion of internalizing disorders in offspring as part of this study is an additional improvement to previous research using the metastructure approach (Hicks et al., 2013), and is aimed at extending our understanding of risk to offspring of externalizing parents to other disease domains.

Like many epidemiological samples, limitations of this sample include retrospective and informant reporting, where offspring reported on the psychopathology of their biological parent, as well as on other relatives. Because of this limitation, analyses in the epidemiological sample are supplemented with a second study which will utilize twins and sibling and their parents, all of whom were directly interviewed using a structured diagnostic interview. This second sample will be used for independent replication aimed at corroborating the structure and robustness of gender and specificity findings from the NESARC dataset. This second data set has already been investigated for the structure of familial transmission of externalizing parents by Hicks et al. (2013), however this previous investigation did not include internalizing disorders in offspring,

limiting the understanding of the extended risk profile for offspring of externalizing parents.

This study clarifies and extends the understanding of familial associations of psychopathology between mothers and fathers and their offspring, using a multivariate framework and methodological techniques that consider models with both general and specific latent risk factors to create a risk model of familial aggregation of psychopathology, while accounting for gender of parent and offspring systematically. Towards that goal, the following specific aims are proposed:

Study Aims

AIM 1. To extend and clarify the model of disease associations between offspring and externalizing parent, using a large, nationally representative epidemiological data set. To model parent externalizing and offspring internalizing and externalizing using a multivariate modeling approach, in order to offer a more parsimonious model of risk aggregation in families. This model and subsequent analyses will be first conducted using a large, nationally representative epidemiological data set, and then replicated in a smaller sample utilizing direct assessment of parent psychopathology.

AIM 2. To use SEM to identify moderation effects of both parent and offspring gender on the relationship between parent externalizing and offspring psychopathology. Maternal and paternal externalizing will be modeled separately, to allow comparisons of the strengths of associations between maternal/paternal externalizing and offspring psychopathology. Offspring gender will also be investigated as a moderator of the association between parent externalizing and offspring psychopathology. It is

hypothesized that same sex parent-offspring interaction effects will be especially significant, with mother-daughter associations being most significant.

AIM 3. To investigate the extent to which having a parent with an externalizing disorder is associated with a generalized vulnerability to psychopathology, or whether particular parent disorders are associated with risk for particular offspring disorders. Hypothesized results are that most of the risk shared between externalizing parents and offspring disorders will be described by a general externalizing factor, with some residual specific effects for some disorders. Further, it is hypothesized that ASPD in parents will be associated with the greatest degree of specific risk in offspring disorders. Alcohol use disorders and drug use disorders are not hypothesized to be associated with specific risk for offspring disorders, and will be fully explained by the general externalizing liability.

AIM 4. To empirically validate the results from sample one in a second independent sample of twins, siblings and parents. In addition to replication, this study addresses limitations of the epidemiological sample, specifically direct assessment of parents and offspring in the twin sample. Because of smaller sample size, more externalizing disorders will be considered for inclusion in the model to capture additional variance, and disorders will be assessed using both dichotomous diagnostic and symptom count diagnostic variables, to develop a more robust externalizing factor with more variance to model across gender and structure.

Methods

Sample 1- NESARC

Participants. This sample utilizes data from 43,093 individuals who participated in the first wave of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC; Grant et al., 2004). NESARC is a representative sample survey of adults 18 years or older living in the United States, conducted in 2001-2002, with an oversampling of African-Americans, Hispanics, and young adults. Face-to-face interviews were conducted with 43, 093 respondents. Data are weighted to be representative of the United States civilian population based on the 2000 Census, with 70.89% Caucasian, 11.07% Black, 2.12% Native American, 4.36% Asian, and 11.56% Hispanic participants. Participants were predominantly female (52.08%), with 21.8% between ages 18-29, 30.89% between ages 30-44, 31.06% between 45 and 64, and 16.25% over age 65. Response rate was 81% of those eligible. The research protocol received full ethical review and approval from the U.S. Census Bureau and the U.S. Office of Management and Budget.

Assessment.

Offspring diagnoses. The Alcohol Use Disorder and Associated Disabilities Interview Schedule DSM-IV version IV (AUDADIS-IV) assessed lifetime DSM-IV diagnoses including major depressive disorder, dysthymic disorder, generalized anxiety disorder, panic disorder, social phobia, specific phobia, alcohol dependence, nicotine dependence, and antisocial personality disorder. The AUDADIS-IV was administered by extensively trained lay interviewers. It has shown fair to very good diagnostic reliability,

with *kappa*s ranging from 0.42 to 0.84, values comparable to those seen in other epidemiological samples using validated measures (Hasin et al., 2005, Grant et al., 2003).

Parent psychopathology. Study participants were asked to inform on their biological parents' lifetime problematic use of alcohol and drugs, as well as lifetime antisocial behavior traits. The question was coded categorically with yes signifying the presence of parental problems with drugs/alcohol/antisocial behavior, and no signifying an absence of these problems. Although this methodology has limitations discussed below, informant report is commonly used in epidemiological samples (e.g., Kendler et al., 1997; McLaughlin et al., 2012) where, because of their size and goal of national representativeness, it would be very costly or otherwise prohibitive to utilize direct assessment. The following interview questions were asked about parental problems with alcohol/drugs: Is your mother/father an alcoholic or problem drinker/drug user? By alcoholic or problem drinker/drug user, I mean a person who has physical or emotional problems because of drinking/drugs; problems with a spouse, family, or friends because of drinking/drugs; problems at work or school because of drinking/drugs; problems with the police because of drinking/drugs-like drunk driving/driving under the influence, or a person who seems to spend a lot of time drinking/using drugs or being hungover/getting over their bad aftereffects." For assessing antisocial behavior traits in parents, the following question was asked: "Does your mother/father have any history of behavior problems? By behavior problems I mean being cruel to people or animals, fighting or destroying property, trouble keeping a job or paying bills, being impulsive, reckless or not planning ahead, lying or conning people or getting arrested. These people also do not

seem to care if they hurt others and often have problems at an early age such as truancy, staying out all night, or running away.“

Parental presence. Although there is no direct assessment of parental involvement in this dataset, there are several variables that can be used to establish the presence of mothers and fathers during the offspring’s childhood. Respondents were queried about whether they lived with at least one biological parent before age 18 years(yes = 41679, no = 1198); if the biological father ever lived in the house before age 18 years (no = 4750); if they were raised by anyone but their biological parents (i.e. adoptive parents, relatives, foster parents, institution, other situations; yes=1267); if parents were divorced (yes=6914); at what age parents divorced; at what age parents stopped living together; which parent the offspring lived with after separation (mother =5219, father=1232); if they ever lived with a stepparent; what age they started living with stepparent; if biological or stepparent died before respondent was 18 and at what age. These variables were used to select for all participants that a)lived with both biological parents until age 18 or b)lived with both biological parents until a divorce/separation and then continued to live with one biological parent. Cases where offspring never lived with biological fathers, or were raised by anyone other than biological parents, were excluded from analyses. Final analyses included 36,862 participants who either lived with biological parents until 18 or lived with biological parents until a divorce and then continued to live with one biological parent.

Sample 2- Twin and Sibling Sample

Participants. Participants in sample two were members of the longitudinal Minnesota Twin and Family Study (Iacono et al., 1999) or Sibling Interaction and Behavior Study (Iacono et al., 1999) both of which used a family design that included the mother, father, and 2 siblings or 2 twins. Additional details about these samples are available in Iacono et al. (1999) and Iacono and McGue (2002). The twin sample was identified from searches of Minnesota birth records for birth years spanning 1971 to 1985. More than 90% of living twin pairs were located. To be eligible for the study, twins had to reside within a day's drive of Minneapolis, live with at least one biological parent, and have no physical or intellectual limitations that could interfere with completion of a day-long, in-person assessment. Eighty-three percent of eligible twin pairs agreed to participate. Participating families did not differ from nonparticipating families in parental mental illness, but participating parents had slightly more years of education and participating mothers had a modestly higher occupational status (Iacono et al., 1999). On the whole, participating parents resembled Minnesota parents with at least one child of their own living at home (Holdcraft & Iacono, 2004). All intake and most follow-up assessments were completed in person. In a minority of cases, participants completed follow-up interviews by phone. Twins were first assessed at age 11 or 17, and then followed up at three or four year intervals, with diagnostic assessments completed at each follow up. The 11 year old cohort was followed up at age 14, 17, 20, 24, and 29. The 17 year old cohort was followed up at age 20, 23/24, and 29.

The full SIBS sample includes 409 adoptive and 208 non-adoptive families, each consisting of an adolescent sibling pair and one or both of their parents. Adoptive

families were ascertained from infant placements made by the three largest, private adoption agencies in Minnesota. Non-adoptive families were ascertained through Minnesota state birth records and selected to have a pair of siblings of comparable age and gender to the adoptive sibling pairs. In all families, both rearing parents were invited to participate. In the 617 assessed families, 613 (99.4%) of the mothers and 551 (89.3%) of the fathers were assessed. An additional 13 (2.1%) fathers completed some of the mailed self-reports but did not complete an interview and so are not included in the sample here. In total, 1,232 adolescents and 1,164 parents or (2,396 individuals) completed an intake SIBS assessment. Complete datasets with relevant variables were available for 399 biologically related siblings and their parents, and 463 adopted siblings and their parents, as shown below in the table. Siblings were first assessed at variable ages, though they were required to be no more than 5 years apart, and that both siblings be between 11 and 21 years old at age of first assessment. The mean age difference was slightly larger in adopted (mean = 2.4 years, SD = 1.0, N =407) than non-adopted (mean = 2.1 years, SD = 0.7, N = 208) sibling pairs ($t = 3.80$, 613 df, $P < 0.001$). Siblings were followed up twice, at intervals 3 and 6 years from their intake dates.

Final counts of participants that are included in the twin and sibling sample are 4137 twins, 399 biologically related siblings, 463 adopted siblings, 3990 biological mothers, 541 adoptive mothers, 3868 biological fathers and 677 adoptive fathers. These numbers includes twins and siblings with extensive missing data, who were excluded from analyses if data was missing from relevant diagnoses. However, because data was collapsed across all follow-up assessments, most participants had diagnostic data for at

least several time points, if not all follow-ups. The mean (SD) age was 44.0(6.2) years for mothers,45.4 (8.2) years for fathers, and 26.2 years (range, 16.2-32.4years) for offspring at most recent assessment. Aside from controlling for family relatedness using mplus clustering by families, twin and sibling relatedness was not modeled in the sample design. Sample composition of twins, siblings, and parents for sample two is presented in below.

Relative Contributions of Twins, Siblings, Biological and Adoptive Parents to Sample Two

	Male offspring	Female Offspring	Total
Twins	1966	2171	4137
Biological Siblings	185	214	399
Adopted Siblings	217	246	463
Biological Mothers	1946	2044	3990
Adoptive Mothers	244	297	541
Biological Fathers	1906	1962	3868
Adoptive Fathers	291	386	677

Assessment. Both parent and offspring disorders were assessed via structured interviews administered by trained staff. Symptoms of alcohol, nicotine, and illicit drug abuse and dependence were assessed using the Substance Abuse Module of the World Health Organization's Composite International Diagnostic Interview (Robins, 1987). Conduct disorder and adult antisocial behavior (the adult criteria for antisocial personality disorder) were assessed using a structured interview comparable to the

Structured Clinical Interview for DSM-III-R, Axis II, and later updated to include DSM-IV disorders. The externalizing disorders measured in parents were adult antisocial behavior, conduct disorder, alcohol abuse or dependence and drug abuse or dependence, and nicotine dependence. In offspring, the same externalizing disorders were assessed. In addition, offspring internalizing disorders including major depressive disorder, generalized anxiety disorder, panic disorder, social phobia and specific phobia were assessed using the Structured Clinical Interview for DSM-III-R (SCID-R) (Spitzer et al.1987), updated to cover DSM-IV criteria.

For intake and follow-up for offspring ages 17 and younger, most diagnoses used a consensus process in which offspring self-reported symptoms, and parents also provided an informant report. Interviewers combined information from parents and offspring to arrive at a 'best estimate' for each symptom and diagnosis. For later offspring follow-ups past age 17, offspring self-reported without parent report. All diagnoses and symptoms were assessed using DSM-III-R and DSM-IV criteria, depending on the follow-up assessment and timeline. Final analyses used two different diagnostic variables. The first was a dichotomous diagnostic variable that collapsed across all assessments to arrive at a single variable for each diagnosis which indicates the lifetime presence of the diagnosis at any assessment. In calculating this lifetime diagnostic variable, DSM-IV diagnoses were used in all assessments in which they were available, and DSM-III-R diagnoses were used in the earliest assessments. Diagnoses using either diagnostic system were allowed to count towards the overall lifetime diagnostic variable. In data collection, and in other publications using this sample, an

expanded system of diagnosis was used in which diagnoses were assigned labels of absent, possible, probable, or definite, depending on the level of consensus, as well as whether impairment and duration criteria were met. In these analyses, only diagnoses labeled as definite were allowed to count towards the lifetime diagnostic variable, meaning all symptom criteria, as well as impairment and duration, were met to receive a diagnosis.

Symptom count variables were the other diagnostic variable utilized. A symptom was considered present if an interviewer designated the symptom as definitely present. Because DSM-III-R and DSM-IV had different diagnostic criteria for most disorders assessed, symptom counts were calculated based on the percentage of total possible symptoms endorsed. For example, Alcohol Dependence in DSM-III-R had eight total possible symptoms while in DSM-IV, it had seven possible symptoms. If a participant endorsed 5 of 8 symptoms in DSM-III-R, they would have a value of .625, or 62.5%. If a participant endorsed 5 of 7 symptoms in DSM-IV, they would have a value of .714, or 71.4%. In this way, the symptom count variables can be collapsed across DSM versions, allowing for comparison. Because this may introduce some methodological variance, DSM-IV diagnostic criteria were used whenever possible. The follow-up assessment with the highest symptom count across all assessments was used as the final value for that diagnosis, to capture the most severe manifestation of psychopathology present over all follow-ups.

Symptom count variable transformation. The symptom count variable required additional transformations to be useable in analyses in mplus. The symptom count

variable was treated as categorical rather than continuous, because it is ordinal in that the increase in severity as symptoms increase is not necessarily linear. In order for mplus to recognize the variable as categorical, mplus required that the values be integers, and that there be no missing values in any categories from the lowest to the highest possible value. All symptom count variables were multiplied by 100 and rounded to the nearest integer. Then, values were grouped into quartiles, so that values representing 0-25%, 25-50%, 50-75%, and 75-100% of symptoms endorsed were grouped together. This transformation allowed the symptom count variable to capture more variance in symptom endorsement than the dichotomous diagnostic variable, while still fulfilling mplus requirements for a categorical variable.

Analytical Plan

Data Design.

Sample 1. All analyses were conducted in Mplus version 7.31 (Muthén and Muthén, 2012). Weights, stratum, and clustering variables were used in the complex data design to create a population with nationally representative characteristics. In Mplus, these features were incorporated into the model.

Sample 2. Analyses for study two mirror analyses in study one. The data was not weighted and did not use stratification features, but clustering for non-independence of observations was used to control for family relatedness in siblings and twins, such that similarities between families was controlled for. Additionally, both dichotomous diagnostic variables and symptom count variables were used in parallel analyses in sample two.

Evaluations of model fit. The modeling approaches used in this study rely on evaluations of adequate model fit. There are several methods of assessing model fit. The WLSMV estimator in Mplus yields several fit statistics, including comparative fit index (CFI), the Tucker–Lewis Index (TLI), and the root mean squared error of approximation (RMSEA). For all subsequent analyses, models with CFI/TLI values > 0.95 and RMSEA values < 0.06 suggest good model fit (Hu and Bentler, 1999). Because of the size of the dataset in sample 1, adequate model fit may be achieved even when the parameters explain only a small proportion of the variance in the model, so additional metrics of factor loadings and their standard errors will also be considered, in order to assess variance explained by the model, and therefore the model's clinical utility.

Some analyses herein rely on comparisons of models; some compare models across groups like gender, while others compare model fit when a parameter is constrained across groups versus free to vary. There are several methods of comparing similar models. The most basic method is to evaluate changes to fit statistics. Guidelines have been established for determining significant differences in model fit statistics: Simulation studies of common fit indices lead investigators to propose a CFI difference critical value of .01 be used in factorial invariance research to determine whether the addition of constraints leads to notably worse model fit (Cheung and Rensvold, 2002). When there are no differences between model parameters, and no model is clearly favored by these fit indices, the number of freely estimated parameters in the model can be used to establish the model with greatest parsimony (fewest freely estimated parameters). DIFFTEST is an mplus analysis which compares model fit in a less

constrained model to model fit in a more constrained model. When DIFFTEST is significant, the model fit is significantly worsened by the addition of constraints, meaning the model should not be constrained. DIFFTEST will also be used when appropriate, to compare nested models.

Establishing the model.

Latent factor structural modeling. Confirmatory Factor Analysis was used to confirm the presence of a latent externalizing variable in parent psychopathology, and a latent externalizing and internalizing variable, where internalizing is comprised of fear and distress sub-factors, in offspring. For confirmatory factor analysis, Mplus defaults of delta parameterization and the WLSMV estimator were used. The WLSMV estimator is the best-performing estimate for categorical observed variables, and allows for incorporation of NESARC's complex sampling design variables and to model categorical variables appropriately. As discussed above, model fit will be evaluated by the comparative fit index (CFI), the Tucker–Lewis Index (TLI), the root mean squared error of approximation (RMSEA), DIFFTEST, and the standardized loadings of observed variables on latent factors, which are standardized regression coefficients.

Modeling offspring psychopathology. Previous work in the NESARC dataset has established the presence of the internalizing-externalizing structure of common mental disorders in offspring (Eaton et al., 2012, Ofrat et al., 2014). Building off of this work, each offspring diagnosis will be parameterized to load on one of three factors previously identified, with (1) major depressive disorder, dysthymic disorder, generalized anxiety disorder loading on the distress factor of internalizing, (2) panic disorder, social phobia,

and specific phobia loading of the fear sub-factor of Internalizing, and (3) antisocial personality disorder, alcohol dependence, drug dependence, and nicotine dependence loading on the externalizing factor.

Modeling parent externalizing. In sample one, it is especially critical to establish the presence of a latent externalizing factor in parents, because the assessment method for parental psychopathology is offspring report, which may theoretically change the latent structure observed in samples where participants are directly interviewed. Maternal and paternal externalizing were modeled separately, with parental drug and alcohol use behavior, as well as parental ASPD symptoms, loading on a single externalizing latent variable.

Invariance testing. Measurement invariance tests if latent constructs are measured identical across groups. Measurement invariance is established in a stepwise fashion, where the least constrained model is the base model to which more constrained models are compared. By default, Mplus assumes invariance in a multiple groups model, where loadings and thresholds are constrained across groups. This default constrained model was compared to the less constrained model where configural invariance was established, in which the number and structure of factors is constrained across groups, but loadings and thresholds are free to vary across groups. In the default constrained model, thresholds and loadings were constrained to equality across gender, and factor means and scaling factors were fixed at 0 and 1 respectively in men, and free to vary in women. In the configural constrained models, loadings and thresholds were free across gender.

Model fit was then compared between conditions, and DIFFTEST was used to determine if there was significant decrement in model fit.

Associations of risk between parents and offspring. To model risk associated between parent externalizing and offspring diagnoses, offspring latent factors (fear, distress, and externalizing) were regressed onto the latent maternal and paternal externalizing factor, setting up the structural model shown in figure 1. Within the model, maternal and paternal psychopathology were modeled separately, to allow for later comparisons across gender. Separate models were fit for male and female offspring. Standardized loadings are reported for every regression. Model fit was evaluated as described above.

Gender moderation in risk associations between parent externalizing and offspring psychopathology. To determine if gender moderated the association between parent and offspring psychopathology, the loading of offspring latent factors onto mothers' and fathers' externalizing were compared in the SEM model. Regressions were allowed to vary across parent and offspring gender in one model, and were constrained to equality across parent and offspring gender in a second nested model. Main effects of gender were evaluated by constraining across parent and offspring gender, while interactions were evaluated by constraining across specific regression pairs. Change to model fit was evaluated using change to CFI, TLI, and RMSEA statistics. As in invariance testing, DIFFTEST was also used: if the fit of the model where regressions are constrained across parent gender is significantly worse than the fit of the model where regressions are free to vary, the regressions cannot be constrained across gender.

Additionally, for multiple group analyses such as these gender moderation analyses, non-overlapping confidence intervals across groups were also used to determine significant differences across groups, when all other metrics did not provide a clear solution.

Same-sex effects in parents and offspring. Pairs of regressions were compared across relevant groups to determine if parent psychopathology was more strongly associated with offspring of the same gender. Each regression models risk association from one parent gender to one offspring gender, within one latent factor, making it possible to detect interaction effects such as differences in same-sex risk transmission from parent to offspring, as hypothesized in study aims.

Specificity vs. generality analyses. To evaluate the significance of specific associations between observed parent and offspring diagnoses, residual correlations between parent and offspring diagnoses will be evaluated for significance in a model that includes variance explained by the latent factors in parents and offspring. For example, the correlation between maternal antisocial traits and female offspring ASPD will be evaluated for significance, above and beyond the variance in offspring externalizing explained by maternal externalizing. This is computed separately for each disorder in parents and each disorder in offspring, and separately for each combination of parent and offspring gender. Because so many models are necessary, stringent Bonferroni corrections for family wise error rate are warranted, as discussed specifically in the results.

Power considerations.

Study 1: Power in large samples. A sample as large as NESARC allows for a unique design which accommodates multiple group analyses in a latent variable framework. Traditional concerns about power are less germane when working with a large sample, because even very small effects are sufficiently powered to be detected. An interesting problem develops, however, in that clinically insignificant relationships between variables may become significant in samples as large as NESARC. As a consequence, it is necessary to be cognizant of this power, and consider a priori how regression coefficients and standard errors will be considered for clinical significant. One method is to use Cohen's (1988) characterization of effect sizes, where .10 is a small effect, .30 is a medium effect and .50 is a large effect, and these values can also be applied to standardized regression coefficients to evaluate clinical significance of the regression, above and beyond statistical significance.

Study 2: Sample size considerations. Because study two has a small sample relative to NESARC, symptom count variables were used in analyses, to capture and model more variance in psychopathology. Additionally, twins as well as adopted and biological siblings are included in the sample to maximize sample size.

Results

Prevalence Rates

Prevalence rates for diagnoses in sample one and two are shown in table 1, for males and females separately, as well as for the total samples. Because of differences in assessment measures used, diagnoses are not identical in the two samples, but are similar as described in methods section under diagnostic assessment for both samples. In table 2, symptom count variable prevalence rates are provided for the twin and sibling sample's symptom count variables.

Does the Latent Model in Parents Externalizing Disorders and Offspring Internalizing and Externalizing Disorders Conform to Previous Findings?

Building off of previous work establishing the existence of latent internalizing and externalizing factors that account for much of the variance in common mental disorders (Krueger et al., 1998; Eaton et al., 2012, Eaton et al., 2013), models in the offspring were organized such that disorders loaded on latent externalizing and internalizing (made up of fear and distress) factors. As shown in figure 1, Structural Equation Model of Parent Externalizing and Offspring Diagnoses, each diagnosis was parameterized to load on one of three factors previously identified, with (1) major depressive disorder, dysthymic disorder, and generalized anxiety disorder loading on the distress factor of internalizing, (2) panic disorder, social phobia, and specific phobia loading on the fear sub-factor of internalizing, and (3) antisocial personality disorder, alcohol dependence, drug dependence, and nicotine dependence loading on the externalizing factor. In parents, the presence of an externalizing latent factor was established, in which antisocial traits, drug dependence traits, and alcohol dependence

traits loaded on the externalizing factor, which was modeled separately in mothers and fathers to allow for comparison across parent genders.

As shown in table 3, the model has adequate model fit in the NESARC sample in both male and female offspring (In male offspring RMSEA=0.015; CFI= 0.977; TLI=0.970, 42 free parameters; In female offspring, RMSEA=0.015; CFI=0.980, TLI=0.975, 42 free parameters). Parameter estimates for the full models are provided separately in male and female offspring in figures 2 and 3 respectively. All observed variables (in rectangular figures) load significantly on latent variables in parents and offspring (in circular figures). Regression coefficients are also presented between parent and offspring latent factors. Loadings and regression coefficients are all standardized, and can be squared to derive variance explained in the observed variables by the latent variables.

Model Fit in Twin and Sibling Sample

In the twin sample, the performance of two models was compared, in which one model replicated the model used in NESARC analyses (table 4), and the second model provided an extension of the NESARC variables by including more diagnoses that load on the externalizing factors (the extended model; table 5). In the first model, the NESARC replication diagnoses were used (Parent externalizing defined by parent ASPD, Alcohol Dependence, and Drug Dependence; Offspring externalizing defined by offspring ASPD, drug dependence, alcohol dependence, and nicotine dependence; offspring fear defined by panic disorder, social phobia, specific phobia; offspring distress defined by major depressive disorder and generalized anxiety disorder). In the extended

model (table 5), all disorders from the replication model were included, in addition to several other diagnoses (Parent externalizing additionally defined by drug abuse traits, alcohol abuse traits, nicotine dependence and conduct disorder, and offspring externalizing additionally defined by conduct disorder, drug abuse traits, and alcohol abuse traits). These models were compared using both dichotomous diagnostic variables, which more closely replicates the approach in the NESARC sample, and also utilized symptom count variables, intended to capture more variance in fear, distress, and externalizing. Model fit statistics for the replication model and extended model using symptom count variables are provided in tables 6 and 7 respectively.

All four models (tables 4-7) in the twin sample had adequate fit, as described by criteria from the research literature (CFI value of .95 or higher is presently accepted as an indicator of good fit, RMSEA ranges from 0 to 1, with smaller values indicating better model fit; A value of .06 or less is indicative of acceptable model fit; Hu & Bentler, 1999). For both the dichotomous diagnostic and the symptom count variable models, the NESARC replication model with fewer diagnoses defining the latent variables had significantly better fit (CFI difference of .01 or more; Cheung and Resnvold, 2002), and fewer freely estimated parameters for a more parsimonious model. Diagnoses added in the extended model were intended to extend the model to additional constructs, but decreased model fit significantly. Although the overall measurement model has adequate fit in both replication and extended models, the models where NESARC diagnoses were more closely replicated had better model fit, so will be utilized for subsequent analyses.

Measurement Invariance

Measurement invariance is established in a stepwise fashion, where the least constrained model is the base model to which more constrained models are compared. By default, Mplus assumes invariance in a multiple groups model, where loadings and thresholds are constrained across groups. This model was compared to the less constrained model where configural variance was established, in which the number and structure of factors is constrained across groups, but loadings and thresholds are free to vary across groups. In the default constrained model, thresholds and loadings were constrained to equality across gender, and factor means and scaling factors were fixed at 0 and 1 respectively in men, and free to vary in women. In the configural constrained models, loadings and thresholds were free across gender. Model fit was then compared between conditions.

Table 8 shows the model comparing the mplus default constrained to the configural constrained model for NESARC, and table 9 and 10 show the comparison for the twin sample's dichotomous diagnostic and symptom count models, respectively. DIFFTEST was used to compare model fit, and when significant, indicates the model produced poorer fit when more constrained. For all models, DIFFTEST was significant, meaning the model fit was significantly worsened when loadings and thresholds were constrained in male and female offspring. In the NESARC model, while DIFFTEST favors the configural constrained model, the model fit statistics are not significantly different, using the CFI difference critical value of .01 (Cheung and Rensvold, 2002), In contrast, both twin study models did favor the configural constrained model, according to both DIFFTEST and model fit statistics. Favoring the configural constrained model

(bolded) means that the number of factors and the structure of those factors is the same in male and female offspring, but the degree to which every observed variable loads on the latent factors is different in males and females. As a result, subsequent analyses will treat male and female offspring as two separate groups, so that differences in measurement of the latent factor across groups is allowed to contribute to group differences. In each model, although measurement invariance was not established for factor loadings and thresholds, differences between loadings are not large (NESARC mean loading difference = .026, range= .001-.07; twin and sibling sample using dichotomous diagnostic variable mean loading difference = .09, range = .014-.178; twin and sibling sample using symptom count diagnostic variable mean loading difference = .045, range = .013-.105).

Main Analyses

How does gender impact the association between externalizing in parents and disorders in offspring, in a large epidemiological sample (NESARC)? To understand the impact of parent and offspring gender on associations between latent variables, offspring fear, distress, and externalizing factors were regressed on parent externalizing, separately in mothers and fathers, and male and female offspring. Risk associated with maternal externalizing was compared to the risk associated with paternal externalizing, for offspring disorders. Male and female offspring's fear, distress and externalizing latent factors were regressed separately on maternal and paternal externalizing factors. In order to test main effects of either parent or offspring gender, regression coefficients were first constrained across parent and offspring gender, and model fit and DIFFTEST were used to compare the models. As shown in table 11, in the NESARC sample, when the

regression of offspring externalizing was constrained across parent and offspring gender, DIFFTEST was not significant, meaning that there was no significant effect of gender on the strength of association between parent and offspring externalizing. Results are shown in the first model in table 11. Similarly, there was no effect of gender in the regression of offspring fear on parent externalizing, as shown in model two of table 11. For the latent distress factor in offspring, DIFFTEST was significant when the model was constrained across parent and offspring gender, meaning that model fit was significantly worsened when constrained across gender, and indicating significant differences in the regressions of offspring distress on parent externalizing across gender (model 4 under main effects in table 11).

Next, in order to test parent and offspring gender as a moderator of risk association (to locate the difference in associations within distress disorders across gender) gender interaction effects in distress disorders were tested by comparing individual regression coefficients in male and female offspring separately, and in mothers and fathers separately. DIFFTEST was significant when female offspring distress was constrained with male offspring distress and regressed onto paternal externalizing (model 1 under interactions in table 11). DIFFTEST was also significant when female offspring distress regressed onto maternal externalizing was constrained with female offspring distress regressed onto paternal externalizing (model 4 under interactions in table 11). This indicates that distress disorders in female offspring were more strongly associated with maternal externalizing traits than paternal externalizing traits (Beta for unconstrained maternal externalizing traits = .394, SE= .081, $p<.001$; Beta for

unconstrained paternal externalizing traits = .122, SE=.077, *p*=.155; DIFFTEST= 8.919, df=3, *p*=.0304). Additionally, the association between maternal externalizing and offspring distress was stronger for female offspring than for male offspring (Beta for unconstrained male offspring = .116, SE= .120, *p*=.336; Beta for unconstrained female offspring = .394, SE=.081, *p*<.001; DIFFTEST= 4.454, df=1, *p*=.0348). These standardized regression coefficients are shown in table 12. However, these are those presented in the unbolded unconstrained model for offspring distress on parent externalizing, as these coefficients do not represent associations between factors for the final model. The final model for distress was identified after all interaction effects were tested, and is bolded in table 11.

Comparing strength of associations between parent externalizing and offspring fear, distress, and externalizing in NESARC. In the final model (bolded in table 11), offspring fear and externalizing are regressed on parent externalizing, with regressions constrained across parent and offspring gender. The regression of offspring distress on parent externalizing is constrained in male offspring across parent gender, and in female offspring in fathers, with female offspring distress free to vary. As shown in table 12, in terms of strengths of associations, maternal and paternal externalizing were both associated with greatest risk for offspring externalizing disorders. Parental externalizing explains 11% of the variance in offspring externalizing disorders. In female offspring, the association between maternal externalizing and female offspring distress is more similar in strength to the association between parent externalizing and offspring externalizing disorders. So, for female offspring, maternal externalizing is as strongly

associated with distress disorders as is it with externalizing disorders. For mothers and fathers of male offspring, parental externalizing accounts for 5% of the variance in offspring distress disorders. For fathers of female offspring, paternal externalizing also accounts for 5% of the variance in female offspring distress. For mothers of female offspring, maternal externalizing accounts for 9% of the variance in female offspring distress. Parental externalizing explains 5% of the variance in offspring fear disorders. Full models for male and female offspring are presented in figure 2 and 3, and regression coefficients for male and female models are presented together for comparison in figure 4.

How does gender impact the association between externalizing in parents and disorders in offspring, in a sample of twins, siblings, and parents assessed directly? Parallel analyses were replicated in a twin sample with direct assessment of both parents and offspring. An identical procedure was utilized in this sample, where offspring fear, distress, and externalizing factors were regressed on parent externalizing. Risk associated with maternal externalizing was compared to the risk associated with paternal externalizing, for offspring disorders. Male and female offspring's fear, distress and externalizing latent factors were regressed separately on maternal and paternal externalizing factors. As in the NESARC sample, in the twin sample, when the regression of offspring externalizing was constrained across parent and offspring gender, DIFFTEST was not significant, meaning that there was no effect of gender on the strength of association between parent and offspring externalizing (DIFFTEST=4.429, df=3, p=.2187). Results are shown in the first model in table 13. Similarly, there was no

effect of gender in the regression of offspring fear on parent externalizing, as shown in model two of table 13 (DIFFTEST=6.100, df=3, p=.1068). For the latent distress factor in offspring, DIFFTEST was significant when the model was constrained across parent and offspring gender, meaning that model fit was significantly worsened when constrained across gender, and indicating significant differences in the regressions of offspring distress on parent externalizing across gender (DIFFTEST=9.418, df=3, p=.0242; model 4 under main effects in table 13).

Next, in order to test offspring gender as a moderator of risk association (to locate the source of difference in associations within distress disorders across gender) gender interaction effects in distress disorders were tested by comparing individual regression coefficients in male and female offspring separately, and in mothers and fathers separately. The first four models in table 13, under the interaction heading, test interactions effects across gender in the regression of offspring distress on parent externalizing. DIFFTEST was not significant in any of the individual interactions, so although there is a significant effect of gender in the association between parent externalizing and offspring distress, this effect could not be located within a specific regression path using DIFFTEST.

Table 14 compares the regression coefficients for all regressions of offspring latent factors on parent externalizing, both constrained across gender and free to vary. In offspring externalizing and fear, DIFFTEST favored the constrained model, bolded in table 14. For offspring distress regressed onto parent externalizing, although significant differences were not located in any specific interaction, regression coefficients were most

similar within parent gender. In paternal externalizing, male and female offspring had relatively similar regression coefficients (male offspring Beta = .101, SE= .122, p=.408; female offspring Beta = -.136, SE=.123, p=.269) and within maternal externalizing, male and female offspring had similar regression coefficients (male offspring Beta = .291, SE= .126, p=.021; female offspring Beta = .300, SE=.146, p=.041). Since there is a significant interaction effect which could not be specifically located, the regression for distress was constrained across most similar regression coefficients, as shown in the constrained distress model in bold. DIFFTEST allowed this constraint (DIFFTEST=4.327, df=2, p=.1149; bolded in table 13).

In this sample, regression coefficients for offspring distress regressed onto maternal vs paternal externalizing have non-overlapping 90% Confidence intervals, but overlapping 95% confidence intervals (Maternal regression 95% CI = $0.10668 \leq \beta \leq 0.47132$, 90%CI = $0.13600 \leq \beta \leq 0.44200$; paternal regression 95% CI = $-0.20380 \leq \beta \leq 0.11380$, 90% CI= $-0.17826 \leq \beta \leq 0.08826$). If interpreted as significantly different, this would mean that offspring distress disorders are significantly more strongly associated with maternal externalizing, as compared to paternal externalizing. Although these findings are marginally significantly, they are in line with findings in the much larger NESARC sample, which showed significant differences the association between offspring distress disorders and parent externalizing disorders cross gender.

Final model of parent externalizing and offspring latent factors in twin sample, using dichotomous diagnostic variables. In the final model, shown separately in male and female offspring below in figure 5 and 6, offspring fear and externalizing are

regressed on parent externalizing, with regressions constrained across parent and offspring gender. The regression of offspring distress on parent externalizing is constrained in male offspring across maternal and paternal externalizing, and separately in female offspring across maternal and paternal externalizing. In terms of strengths of associations, the strongest association was between maternal externalizing and male/female offspring distress disorders (beta = .289, SE=.093, p=.002). Male and female offspring externalizing disorders were also associated with parent externalizing (beta=.170, SE=.021, p<.001). There were no significant associations between parental externalizing and offspring fear (beta=.055, SE= .033, p=.099) or between paternal externalizing and offspring distress disorders (beta=-.045, SE=.081, p= .580). Full models for male and female offspring are presented in figure 5 and 6, with regressions for male and female offspring highlighted in figure 7. For this sample, all regressions were constrained across offspring gender, meaning all associations between offspring latent variables and parent externalizing could be constrained to equality across male and female offspring. As a result, there is a single value for each regression presented in figure 7.

Gender analyses within the twin and sibling study using symptom count variables

As described above in the model fit analyses, in the twin sample, the model fit using symptom count variables was adequate but significantly worse than model fit using dichotomous variables. Analyses were replicated in this sample using these symptom count variables to capture greater variance in parent and offspring psychopathology. As shown in table 15, externalizing and distress regressions were constrainable across

gender, while fear regressions were not constrainable (models 1-4 under main effects). However, within the regressions of fear onto parent externalizing, no individual interaction effects were significant, meaning that although the regression of fear onto parent externalizing could not be constrained across gender of parent and offspring, when regressions were free to vary across gender, there were no significant associations between offspring fear and parent externalizing, perhaps due to large standard errors and small effects. Because the significant difference could not be located by DIFFTEST in a specific set of constraints, two methods of applying constraints were considered- one where the regressions were constrained across parent gender in male and female offspring separately, and one in which regressions were constrained across offspring gender in maternal and paternal externalizing separately. The model in which fear was constrained across male and female offspring for maternal externalizing and separately, male and female offspring for paternal externalizing yielded a significant DIFFTEST (DIFFTEST= 7.560, df=2, p=.0228), so the regression was constrained across paternal gender and was allowed to vary across offspring gender. As shown in table 16, when regression coefficients were constrained to equality across parent gender (constrained beta for male offspring fear =-0.035, SE=.036, p=.341; constrained beta for female offspring fear =.086, SE=.028, p=.002), a small but significant association between female offspring fear and parent externalizing emerged that explained less than 1% of the variance in female offspring fear. This tiny effect was likely detected because constraining regressions pools samples across gender, increasing the power to detect differences and

reducing standard error, meaning the model can better detect even very small differences. The association between male offspring fear and externalizing remained non-significant.

Final model of associations between latent externalizing in parents and latent variables in offspring in twin and sibling sample, using symptom count variables. The final model is presented in table 16. Overall, the association between parent externalizing and offspring externalizing was strongest (beta= .167, se= .017, p<.001) followed by the association between parent externalizing and offspring distress (beta= .104, SE=.020, p<.001), and most weakly, the association between parent externalizing and female offspring fear (beta = .086, se=.028, p=.002). Male offspring fear was not significantly associated with parental externalizing. Overall parameter estimates and regressions for male and female offspring are shown in figures 8 and 9, respectively.

Discrepancy in gender effects in offspring distress using symptom count variables. In the NESARC sample, as well as in the twin sample using dichotomous diagnoses, there was a significant effect of gender on the association between parent externalizing and offspring distress. This difference was notably absent in the twin sample using the symptom count variable. Taking a closer look at distress in offspring, although DIFFTEST is not significant in the models which constrain the regression of offspring distress across parent and offspring gender, the regression coefficients in offspring distress show large differences across parent gender. In the unconstrained regression of distress on paternal externalizing, distress was not significantly associated with offspring distress (male offspring beta=.039, SE=.090, p=.667; female offspring beta= -.064, SE=.079, p=.424), while in the regression of distress on maternal

externalizing, DIFFTEST was significantly associated with offspring distress (male offspring beta = .213, SE=.097, p=.028; female offspring beta= .274, SE=.093, p=.003). This difference did not produce a significant DIFFTEST, which is perhaps due to the use of the symptom count variable, which partials variance into four distinct groups. This difference may account for a lack of significance in gender analyses, which are detectable using the dichotomous diagnostic variables. There is evidence to support the hypothesis that methodological differences account for the failure to find significant differences across gender in this sample using symptom count variables. First, the model using dichotomous variables in this same sample did detect significant differences. Second, same-sex analyses did produce some significant gender associations in the distress factor in offspring, as described below.

Is offspring psychopathology more strongly associated with same-sex parent psychopathology in NESARC? The hypothesis that parent externalizing would be more strongly associated with offspring psychopathology for offspring of the same sex was tested by constraining pairs of regressions. Although there were no significant main effects of gender in fear and externalizing latent factors in offspring, same-sex interactions were still evaluated, since main effects can suppress significant gender interactions. Pairs of regressions were compared in all possible combinations that would indicate stronger same-sex associations between parent and offspring psychopathology. For example, this hypothesis would be supported in female offspring distress was more strongly associated than male offspring distress with maternal externalizing, and the hypothesis would also be supported if male offspring distress was more strongly

associated with paternal externalizing than female offspring distress. The more offspring psychopathology is associated with same-sex parent psychopathology, the more this hypothesis is supported. In the latent fear and externalizing factors, there were no significant same-sex interactions, as shown by non-significant DIFFTEST results in all pairs of regressions in tables 17 and 18. Table 19 shows latent distress in offspring, where one regression showed significant same-sex effects: Female offspring distress was more strongly associated with maternal externalizing than male offspring distress. Male offspring distress was not more strongly associated with paternal externalizing as compared to maternal externalizing, nor was it more strongly associated with paternal externalizing than female offspring. Because only a single same-sex association showed significant differences as compared to opposite-sex association, the hypothesis that same-sex parent externalizing is associated with greater risk for offspring psychopathology is not generally supported in this sample.

Same sex associations in twin study: Dichotomous diagnostic variables

As in NESARC, the hypothesis that parent externalizing would be more strongly associated with offspring psychopathology for offspring of the same sex was tested by constraining pairs of regressions across same-sex and opposite-sex parent-offspring relationships. Table 20 shows same-sex association interactions for the externalizing offspring factor. In this sample, male offspring externalizing was more strongly associated with paternal externalizing, as compared to the association between female offspring externalizing and paternal externalizing (bolded; beta in males=.305, SE= .078, p<.001, beta in females= .043, SE=.110, p=.692, DIFFTEST=4.035, df=1, p=.0446). This

significant difference does support the hypothesis that offspring externalizing is more strongly associated with externalizing in the same-sex parent. However, this is the only same-sex interaction that was significant, and may be an incidental sample specific finding, as it is not replicated in the NESARC sample.

In the offspring fear latent factor, there were two pairs of same-sex interactions that were significantly different, according to DIFFTEST, as shown bolded in table 21. In offspring latent fear, male offspring latent fear was more strongly associated with latent paternal externalizing, as compared to the association between female offspring fear with paternal externalizing (beta in males = .110, SE=.127, p=.385, beta in females = -.326, SE=.174, p=.062, DIFFTEST=4.644, DF=1, p=.0312). However, neither of these regression coefficients is significant, so although the regressions are significantly different according to DIFFTEST, they are not meaningful in that parent externalizing does not explain significant variance in either male or female offspring fear. Female offspring fear was also more strongly associated with maternal externalizing than paternal externalizing (Maternal externalizing beta= .492, SE=.204, p=.016, paternal externalizing beta =-.326, SE=-.174, p=.062, DIFFTEST= 7.013, df=1, p=.0081). Betas are significantly different in these two regressions, in that maternal externalizing does explain significant variance in female offspring, while paternal externalizing does not explain significant variance in female offspring, and the 90% and 95% confidence intervals of the regressions are non-overlapping (maternal externalizing 95% CI = $0.09207 \leq \beta \leq 0.89193$, 90% CI = $0.15639 \leq \beta \leq 0.82761$; paternal externalizing 95% CI= $-0.66719 \leq \beta \leq 0.01519$, 90% CI = $-0.61231 \leq \beta \leq -0.03969$). This finding does support

the hypothesis that offspring psychopathology is more strongly associated with psychopathology in the same-sex parent. However, this is the only regression pair that showed a meaningful significant same-sex interaction effect, and the finding is not replicated in the NESARC sample, increasing risk that it is a sample-specific finding. If this finding does represent true difference, maternal externalizing explains 9.3% of the variance in female offspring externalizing, paternal externalizing does not significantly predict female offspring externalizing. For distress disorders, as shown in table 22, pairs of regressions were compared in all possible combinations that would indicate stronger same-sex associations between parent and offspring psychopathology. No regressions showed stronger same-sex associations, so the hypothesis that same-sex parent externalizing is associated with greater risk for offspring distress is not supported in this sample. Overall, there is some evidence for stronger associations between psychopathology in same-sex parents and offspring in this sample, but because findings did not replicate across studies and effect sizes are small, the effects are not robust.

Same-sex effects in twin study using symptom count variables. Table 23 shows the regressions of female offspring distress onto maternal and paternal externalizing. Female offspring distress was more strongly associated with maternal externalizing (beta=.274, SE=.093, p=.003), as compared to paternal externalizing (beta=-.064, SE=.079, p=.424; DIFFTEST=4.731, df=1, p=.0296). This is in line with findings in the NESARC sample, and in the twin sample using dichotomous diagnostic variables. Although it provides only weak support for the hypothesis that same-sex parents confer greater risk to their same-sex offspring, it does provide additional support

that parent externalizing impacts offspring of differently depending on gender. There were no significant same sex effects in the association between parent externalizing and offspring fear, as shown by non-significant DIFFTEST values in all same-sex analyses in table 24. Table 25 shows the regression of offspring externalizing on paternal externalizing, in which male offspring externalizing (beta=.270, SE=.067, p<.001) was more strongly associated with paternal externalizing than female offspring (beta=-.067, SE=.073, p=.353; DIFFTEST=4.158, df=1, p=.0414). This finding replicates a similar finding in the same sample using a dichotomous diagnostic variable, which is not surprising given that these analyses utilize the same dataset, albeit with different methods of measuring diagnostic variance. Given that the finding is not replicated in NESARC, and is the only same-sex interaction to be significant, it is only weak evidence for a same-sex effect in externalizing.

Specificity in Familial Aggregation of Risk in Parents and Offspring

Specificity analyses were used to test the association between residual variance in observed variables unexplained by latent factors in parents and offspring. Residual variances in offspring diagnoses were correlated with residual variances in parent diagnoses, using mplus. It was hypothesized the latent externalizing variable in parents would explain a majority of the variance in diagnoses in the offspring, and that any cases where residual variances were correlated were more likely to occur in when correlating residuals for the same diagnoses in parents and offspring. For example, residual variance in maternal antisocial traits should be most correlated with residual variance in antisocial traits in offspring. However, there might also be significant correlations between

residuals in maternal antisocial traits and offspring Major Depressive Disorder, but these correlations would be expected to be smaller than those for more similar diagnoses in parents and offspring. In any analyses where no residual correlations were significant, the latent externalizing variable in parents is explaining all variance in offspring psychopathology, as measured by this model.

Specificity in NESARC, a large epidemiological study. As shown in table 26, parent antisocial traits were correlated with offspring antisocial personality disorder to determine if additional variance in offspring ASPD was explained by residual variance in parent antisocial traits, above and beyond the latent externalizing factor. Because multiple tests were run for these analyses, required p-value was corrected using a Bonferroni correction (.05/12=.004). Residual variances in maternal antisocial traits were correlated with male (r=.416, SE=.097, p<.001) and female (r=.304, SE=.045, p<.001) offspring ASPD. Similarly, residual variances in paternal antisocial traits were correlated with male (r=.401, SE=.075, p<.001) and female (r=.434, SE=.117, p<.001) offspring ASPD. Identical analyses were conducted to test if residual variance in maternal and paternal alcohol use disorder traits and drug use disorder traits were correlated with residual variances in those same offspring disorders, but there were no significant residual correlations. In this model, all the variance explained in offspring alcohol and drug use disorders by parent alcohol and drug use disorder traits was explained by the latent externalizing factor, with no incremental variance explained by the specific diagnoses. Variance in offspring ASPD attributable to associations with parent antisocial traits was not completely explained by the latent externalizing variable in parents, as

maternal and paternal antisocial traits still explained additional variance in offspring disorders. Maternal ASPD explains an additional 17% of the variance in male offspring ASPD and an additional 9% of the variance in female offspring ASPD; paternal ASPD explains an additional 16% of variance in male offspring ASPD and an additional 19% of the variance in female offspring ASPD.

Cross-diagnostic specific residual associations. Next, all parent traits were cross-correlated with all offspring diagnoses, to determine whether any parent traits provided incremental associations with offspring diagnoses, above and beyond the latent externalizing factor. Tables 27-29 show residual correlations between parent antisocial traits, drug use disorder traits, and alcohol use disorder traits, respectively, with offspring diagnoses. Because multiple models were run for each diagnosis, a conservative p-value was used to determine significance. Bonferroni correction would require a p-value of .0004 (.05/108 tests=.0004), but mplus only provides p-values to 3 significant figures, so any p-value provided by mplus as .000 (listed as <.001 in the tables) was considered significant. Table 27 shows residuals of paternal antisocial traits were significantly correlated with residuals of male offspring nicotine dependence (r=-0.254, SE= .071, p<.001). After accounting for the variance in parent antisocial traits defined by the externalizing factor, the unique variance attributable to antisocial traits in fathers was actually correlated with reduced prevalence of offspring nicotine dependence. Residuals of the observed variable maternal antisocial traits were correlated with residuals of dysthymia in female offspring (r=0.331, SE= .093, p<.001). After accounting for the variance in parent antisocial traits defined by the externalizing factor, the unique variance

attributable to antisocial traits in mothers was correlated with increased prevalence of female offspring dysthymia, and explained an additional 10.9% of the variance in female offspring dysthmia.

Table 28 shows residual correlations for drug use traits in parents with offspring diagnoses. Residual variance in paternal drug use traits was correlated with residual variance in male offspring ASPD (r=0.339, SE= .095, p<.001), and also with residual variance in female offspring GAD (r=-0.254, SE= .071, p<.001). After accounting for the variance in parent drug use traits accounted for by the externalizing factor, specific residual variance in paternal drug use traits was associated with increased risk for offspring ASPD, explaining an additional 11% of the variance in male offspring ASPD. After accounting for the shared variance between parent externalizing and offspring distress latent factors, paternal antisocial traits accounted for an additional 16% of unique variance (r= -0.405, SE=.096, p<.001), in that the female offspring of fathers with drug use traits were less likely to have GAD. Table 29 shows residual variances for parental alcohol use traits correlated with residual variance in offspring disorders. There were no significant residual correlations between alcohol use traits in parents and disorders in offspring, meaning all variance in offspring disorders in this model is explained by the association between latent externalizing in parents and latent fear, distress, and externalizing in offspring.

Specificity in the twin and sibling sample: replication. Analyses in the large epidemiological survey were compared to those where direct assessment was utilized for parent assessment, in the twin and sibling sample. When using the dichotomous

diagnostic criteria, and looking at similar disorders in parents and offspring (i.e. antisocial traits in parents and ASPD in offspring), there were no significant residual correlations, when applying the more stringent p-value correction for multiple tests ($p<.001$ required for significance). Results are shown in table 30. As shown in table 31, when analyses were rerun using symptom count variables in the twin study, there was a significant residual correlation between paternal antisocial traits and male offspring ASPD ($r=.347$, $SE=.094$, $p<.001$). Above and beyond the variance attributable to latent externalizing in parents and offspring, antisocial traits in fathers explained 12% of the variance in male offspring in this model. This significant residual association was also found in the NESARC study, making this finding robust across samples. No other findings were replicated across samples, for specificity analyses.

Cross-diagnostic residual correlations: replication in a twin and sibling sample. In an identical analyses to NESARC, all parent traits were also cross-correlated with all offspring diagnoses, to determine whether any parent traits provided incremental associations with offspring diagnoses, above and beyond the latent externalizing factor. Tables 32-37 below show residual correlations between parent antisocial traits, drug use disorder traits, and alcohol use disorder traits, respectively using dichotomous and symptom count diagnostic variables, with offspring diagnoses. Because multiple models were run for each diagnosis, a conservative p-value was used to determine significance. Bonferroni correction would require a p-value of .0004, but mplus only provides p-values to 3 significant figures, so any p-value provided by mplus as .000 (listed as <.001 in the tables) was considered significant. Using this stringent correction, no residual

correlations were significant, meaning that in these models, latent externalizing in parents and latent distress, fear, and externalizing in offspring, explained all of the variance in familial aggregation of psychopathology. There was no incremental gain in explained variance when allowing for residual correlations in observed variables.

Discussion

Main Findings

First aim: Modeling psychopathology in parents and offspring using a metastructure approach. The first aim of this study was to extend and clarify the model of disease associations between offspring psychopathology and parent externalizing using a multivariate modeling approach, in a large, nationally representative epidemiological data set. This approach offers a more parsimonious understanding of comorbidity and risk aggregation in families, and has greater clinical utility than bivariate approaches. A model where externalizing disorders loaded on an externalizing factor in parents, and internalizing and externalizing disorders loaded on offspring latent externalizing, fear, and distress factors, had adequate model fit in both samples, and using both diagnostic variables in the twin and sibling sample. This study is the first to model externalizing in parents and a full range of both internalizing and externalizing psychopathology in offspring, while using SEM to model associations between parent and offspring latent variables. This study fills a gap in the extant literature, by providing a parsimonious model of familial risk aggregation of parent externalizing.

Measurement across groups. Invariance across offspring gender was established for the configural model, meaning the number of factors, and pattern of disorders that load on each factor, was invariant across offspring gender. A more constrained model where loadings and thresholds were constrained across gender was variant across groups, according to DIFFTEST. Thus, strong measurement invariance was not established across gender in any of the samples, meaning the factor loadings and thresholds are left

free to vary across groups. Although DIFFTEST favored the less constrained configural model, the model fit statistics in the more and less constrained models are identical and the loadings of the manifest variables onto the latent factors in male and female offspring are very similar, and as such do not significantly impact interpretability of later analyses (NESARC mean loading difference = .026, range= .001-.07; twin and sibling sample using dichotomous diagnostic variable mean loading difference = .09, range = .014-.178; twin and sibling sample using symptom count diagnostic variable mean loading difference = .045, range = .013-.105).

Second aim: Strengths of association between parent externalizing and offspring psychopathology, and gender moderation. A second aim of this study was to compare strengths of associations between parent externalizing and offspring latent fear, distress, and externalizing factors, while modeling moderation effects of both parent and offspring gender on the relationship between parent externalizing and offspring psychopathology. In terms of strengths of associations, analyses in the NESARC sample found parent externalizing was most strongly and consistently associated with offspring externalizing disorders, explaining 11% of the variance in offspring externalizing disorders. However, in the case of distress in female offspring, female offspring distress and maternal externalizing was nearly as strongly associated as offspring and parent externalizing, explaining 9% of the variance in female offspring distress. Associations between male offspring distress and maternal and paternal externalizing, as well as female offspring distress and paternal externalizing, were less strongly but still significantly associated with parent externalizing. Associations between parent

externalizing and offspring fear were similar in strength to latent distress associations and were least associated, though still significant predictors.

In the twin and sibling study, using dichotomous diagnostic variables, the association between maternal externalizing and male and female offspring distress was strongest, explaining 8.3% of the variance in offspring distress. Association between parent externalizing and offspring externalizing is next strongest, explaining 2.9% of the variance in offspring externalizing. The association between parent externalizing and offspring fear was non-significant, and the association between paternal externalizing and offspring distress was non-significant. In the twin and sibling study using symptom count diagnostic variables, the associations were attenuated, perhaps due to variable transformations required for analyses which may have interfered with the ability of the modeling approach to locate significant differences. Associations between parent externalizing and offspring externalizing were strongest, explaining 2.8% of the variance in offspring externalizing. Parent externalizing's association with offspring distress was slightly weaker, explaining 1% of the variance in offspring distress, and parental externalizing was non-significantly associated with male offspring fear, and very weakly associated with female offspring fear, explaining less than 1% of the variance in female offspring fear. Because this variable should theoretically be measuring the same construct as the dichotomous diagnostic variable, but yields different conclusions, it is likely that the method of transforming the variable to make it usable in a modeling approach attenuated relationships between latent factors. In looking more closely at the results for distress disorders regressed onto parent externalizing in table 16, although DIFFTEST

allowed for constraint of regressions across gender, distress disorders in offspring are more strongly associated with maternal externalizing, as compared to paternal externalizing, following the pattern seen in the twin study using dichotomous diagnostic variables, and more closely resembling the findings in the NESARC sample. And indeed, in later analyses that compared pairs of regressions in same-sex parent-offspring dyads, female offspring distress was more strongly associated with maternal externalizing than with paternal externalizing, supporting the hypothesis that distress disorders in female offspring respond differently to maternal vs paternal externalizing, with a stronger association between maternal externalizing and female offspring distress.

Conclusion: Strength of association and gender. In conclusion, it appears that parent externalizing is associated most strongly and consistently with offspring externalizing disorders, but there is also a significant and relatively sizable association between maternal externalizing and offspring distress disorders. This is particularly true for female offspring, but may also extend to male offspring. This effect in female offspring was replicated in both samples, while the effect in male offspring was only observed in the twin and sibling sample using dichotomous diagnostic variables. Regardless, it can be concluded that female offspring of externalizing mothers are equally likely to develop distress and externalizing disorders, and less likely to develop fear disorders. For male offspring of externalizing mothers, the evidence across samples is mixed, so a more conservative interpretation would conclude that male offspring of externalizing mothers are most at risk for externalizing disorders, either at less or equal risk for distress disorders, and least at risk for fear disorders. Additionally, a clear picture

has emerged for offspring of externalizing fathers, who are more likely to develop externalizing disorders than distress disorders, and are least likely to develop fear disorders, regardless of offspring gender. There is a significantly greater aggregated risk conferred to distress in offspring by externalizing mothers, as compared to fathers.

Fit with previous findings on strengths of associations and gender as a moderator of those associations. These findings clarify a confusing bivariate literature that finds clear evidence of increased risk for externalizing in the offspring of externalizing parents, but finds inconsistent evidence for internalizing disorders in the offspring of externalizing parents. A review of existing literature provides a confusing depiction of risk for internalizing in the offspring of externalizing parents. Schuckit, Smith, Radziminski and Heyneman (2000) found children of alcoholics are not at increased risk for major depression or anxiety disorders, whereas Merikangas et al. (1998) found significant associations between family histories of alcoholism and anxiety. Reich et al. (1993) found increased risk for anxiety, but not for depression, in children of alcoholics. Other authors have found that those with drug use disorders and their relatives show increased prevalence of depression (Mirin, Weiss, Griffin, & Michael, 1991; Rounsaville et al., 1991).

This study organizes parent externalizing disorders into a latent externalizing liability, which is associated most strongly with externalizing disorders in offspring, but also significantly with distress disorders and fear disorders. Additionally, this study provides a possible explanation for the highly variable and inconsistent literature on internalizing disorders in offspring of externalizing parents: Most of these studies ignore

the moderating effect of parent and offspring gender. If it is indeed the case that externalizing mothers confer the risk for internalizing disorders in offspring, or that the risk is conferred more strongly to daughters as compared to sons, this is one possible reason for the inconsistencies in the literature. Studies investigating externalizing disorders in fathers are likely to find no association between parent externalizing and offspring internalizing disorders, while studies investigating externalizing disorders in mothers, if properly powered, will detect associations with internalizing disorders, but perhaps only if studying female offspring. Additionally, if the association between parent externalizing and offspring distress is more pronounced in mothers and daughters, and externalizing is less common in women in general, larger samples would be needed to detect a significant effect, and collapsing across parent gender would attenuate this effect, as paternal externalizing does not seem to confer strong risk for offspring distress.

This study also clarifies the literature on externalizing in offspring of externalizing parents. Rather than understanding aggregation of risk through bivariate associations, where studies have questioned if one externalizing disorder in parents is associated with risk for that same disorder, or another single externalizing disorder in offspring, a multivariate modeling approach allows for a more parsimonious understanding of risk. When understood through a latent variable framework, these results have shown that risk in externalizing parents is passed to offspring as risk for a group of related disorders, rather than risk for one disorder in particular. These results suggest that general latent externalizing liability is what is shared between parents and offspring, and the specifics of which disorder manifests in offspring may be more a

function of environmental or other characteristics that shape the manifestation of the specific disorder (Krueger and South, 2009). Understanding that the offspring of externalizing parents are at risk for the broad range of disorders, traits, and behaviors that make up the broad externalizing dimension also explains other findings from the literature, that show offspring of externalizing parents are at greater risk for other problems related to externalizing behavior, such as aggressiveness, delinquency, attention deficits, psychiatric treatment and poor school performance (Sher, Walitzer, Wood & Brent, 1991; Connolly, Casswell, Stewart, Silva, & O'Brien, 1993; Loukas, Fitzgerald, Zucker, & von Eye, 2001; Reich, Earls, Frankel, & Shayka, 1993; von Knorring, 1991).

Magnitudes of association compared to previous findings. In comparison to other samples that used multivariate modeling methods, strength of association found between parent and offspring latent factors in this study were in line with the literature. Regression coefficients in this study in the NESARC sample ranged from .331 (externalizing in parents and offspring) to .214 (externalizing in parents and distress in offspring). In the twin and sibling study using dichotomous diagnostic variables, associations range .289 (distress in offspring and externalizing in mothers) to .170 (externalizing in parents and offspring). In the twin and sibling study using symptom count variables, significant regression coefficients ranged from .167 (externalizing in parents and offspring) to .086 (fear in female offspring and parental externalizing). Kendler et al. (1997) reported odds ratios for risk for specific offspring disorders, but they also provided the structural equation model, showing a regression coefficient of .21 for the association between parent externalizing and offspring externalizing, and a

coefficient of .12 between parent externalizing and offspring internalizing. These associations are similar to those found in the present study, between offspring and parent externalizing. In the present sample, associations between parent externalizing and offspring internalizing (in the present study, divided into fear and distress) are higher than those found in the Kendler et al. (1997) study. This is likely because that study collapses across distress and fear sub-factors of internalizing, which have different magnitudes of risk association, effectively averaging the magnitude across sub-factors. This could also be because that study modeled parent internalizing and externalizing, and may have separated shared variance between internalizing and externalizing in parents, which the present study cannot parse because it does not model internalizing in parents (a future direction for study described below).

McLaughlin also reported odds ratios for individual offspring disorders, given the presence of parental disorders, which could not be converted to equivalence with the analyses in the present study, but they also reported that parent disorders were associated with 7.1-19.9% of the variance in offspring disorders, though more specific metrics were not provided. This amount of variance explained is not dissimilar from the analyses herein. Taken together, these two studies provide reasonable confidence that the magnitude of associations between parent and offspring psychopathology found in this study are reasonable measures of the constructs of interest.

Associations between latent factors and gender: Comparison to previous findings. The finding that parent externalizing is most consistently and strongly associated with offspring externalizing needs no explanation. It is well supported in the

literature that the offspring of externalizing parents are at risk for the same disinhibitory behavioral disorders as their parents (Young et al. 2000; Krueger et al. 2002; Kendler et al. 2003). It is also perhaps not surprising that parent externalizing appears to be less strongly correlated with offspring fear. Externalizing disorders are characterized by low constraint and high excitement seeking (Krueger and South, 2009), while fear disorders are characterized by high constraint, low sensation or novelty seeking, and avoidance behavioral patterns. So while internalizing and externalizing disorders are correlated, the traits associated with externalizing and fear disorders do seem at face value to be quite different. The finding most worthy of scrutiny and explication is that maternal externalizing appears to be associated with distress disorders as strongly as to externalizing disorders. This finding appears to be specific to maternal externalizing and does not extend to paternal externalizing. As previously described, the bivariate literature provides mixed evidence for the differential impact of maternal versus paternal externalizing on offspring disorders. Findings in the present study are in line with the bivariate studies that have found mothers' alcohol dependence, ASPD, and drug dependence has a greater impact on offspring psychopathology (Dierker et al., 1999; Chassin, Pitts, DeLucia, & Todd, 1999; McLaughlin et al., 2012), but are contrary to findings from the same literature that find fathers' disorders to have a greater impact (Ohannessian et al., 2005; Lieb et al., 2002; Pollock and Schneider, 1987, Luthar, Merikangas, & Rounsaville, 1993), and studies that find no difference between risk conferred by mothers and fathers with externalizing disorders (Kaij and Dock, 1975;

Kendler, Neale, Heath, Kessler, & Eaves, 1994; Reich et al., 1988; Rowe, 1983; Kendler et al., 1997).

In terms of multivariate studies and gender effects, one sample found a single gender difference in risk associated with psychopathology in mothers versus fathers: the odds ratio between maternal major depressive disorder and proband major depressive disorder was significantly larger than the same odds ratio observed between father and proband (Kendler et al., 1997). The present study did not investigate internalizing (major depressive disorder) in parents, so this finding is not comparable. The other study to use a metastructure approach found a small specific genetic effect for smoking in mothers, which had a specific significant association to offspring smoking, beyond the general externalizing liability (Hicks et al., 2013). Findings from the present study are inconsistent with findings from the Hicks et al. (2013) study, as this study found no significant differences in the association between parent externalizing and offspring externalizing by gender (findings in the current study differed by gender only within the internalizing factor in offspring, which was not assessed as part of the Hicks et al., 2013 study). Given the inconclusive nature of the extant literature on differential associations between maternal and paternal externalizing and offspring psychopathology, the present study provides a novel and parsimonious framework for understanding the nature of risk aggregation in families.

Possible explanations for the differential impact of maternal externalizing on offspring distress. Intuitively, it may seem likely that because women in general have higher rates of internalizing disorders, maternal externalizing should be more strongly

associated with female offspring internalizing. However, this explanation does not explain gender findings in this study for two reasons. First, the correlation between male internalizing and externalizing is equivalent to the correlation between female internalizing and externalizing (Eaton et al., 2012, Kendler et al. 1997), meaning that mothers and fathers at equivalent levels of externalizing should also have equivalent levels of internalizing. Although females have higher trait internalizing, this would not account for the difference in association between maternal and paternal externalizing on female offspring distress. Rather, this suggests that offspring are more likely to receive maternal externalizing risk and manifest that risk as either externalizing disorder or distress disorder, as compared to paternal externalizing, which confers risk primarily for externalizing disorders. A question remains if this is only true for female offspring, or also true for male offspring, as the results of this study are mixed across samples. As further evidence that this finding is not explainable by higher internalizing rates in women in general, in the twin and sibling study, male offspring showed the same pattern of stronger association between offspring distress and maternal externalizing, as compared with paternal externalizing. This finding obviously cannot be explained by generally higher levels of female internalizing, as the effect was found in male offspring.

One possible explanation for the increased influence of maternal externalizing on offspring distress may be assortative mating. There may be a tendency for persons affected with psychiatric disorders to partner with other affected persons, thereby increasing risk of psychopathology in their spouses. Dierker et al. (1999) found that mothers with externalizing are more likely to display assortative mating, where a person

with a characteristic seeks out a partner with the same or similar traits. This is one potential explanation for why mothers with externalizing disorders may exert more influence on offspring (Merikangas, Weissman, Prusoff, and John, 1988). Perhaps father who externalize are not as likely to select externalizing mothers as partners, so there still may be one parent who provides a nurturing environment, even though the father displays externalizing that may negatively impact child rearing. In this way, the family system is able to compensate better for an externalizing father. When mothers are externalizing, the impact of assortative mating may be stronger, leaving the child with two externalizing parents and less warmth and nurturing, leading to risk for more psychopathology because of a more dysfunctional environment. There is some evidence for this explanation. In another study using a subset of the twin and sibling sample, Hicks et al. (2004) discovered evidence of assortative mating in that mothers and fathers high in latent externalizing tended to be married to each other (r=0.51; 95% CI, 0.41-0.61). In this case, the impact of higher assortative mating in externalizing females means that children of externalizing mothers are more likely to have two externalizing parents than children of externalizing fathers, thereby increasing overall externalizing risk load to children of externalizing mothers.

Associations between parents and their same-sex offspring. It was hypothesized that offspring psychopathology would be more strongly associated with externalizing in the offspring's same-sex parent. In sample one, this hypothesis was overwhelmingly unsupported, with only one of fifteen regression pairs that would indicate a stronger same-sex effect showing a significant difference using DIFFTEST. In

sample two using dichotomous diagnostic variables, the hypothesis was supported in three of 15 regression pairs. In one pair of regressions, neither association was significant, but the trend was in the expected direction, where male offspring fear disorders were significantly more strongly associated with paternal externalizing than female offspring fear disorders. Additionally, female offspring's fear disorders were more strongly associated with mothers' than with fathers' externalizing. Because of relatively low prevalence rates of fear disorders in this sample, and relatively large standard errors, it is possible that these findings are highly variable and sample specific, especially as this effect was not found in the much larger NESARC sample. Taking a closer look at NESARC results for fear in offspring, there do not appear to be significant differences in regression coefficients across gender, further supporting the conclusion that these results may be due to low prevalence rates or sample-specific findings. In the twin and sibling sample using dichotomous diagnostic scoring, male offspring's externalizing was more strongly associated with fathers' externalizing than with mothers', which was also supported in study two using symptom count variables. Taking a closer look at the lack of significant findings in NESARC, the regression coefficients are similar across gender, suggesting this finding may again be sample-specific.

In both NESARC and the twin and sibling sample using symptom count variables, female offspring distress was more strongly associated with maternal externalizing than with paternal externalizing. Although this finding in isolation does not provide strong support for the hypothesis that same-sex parent offspring dyads have more strongly associated risk for psychopathology, it does further support the finding that distress

disorders in female offspring respond differently to maternal vs paternal externalizing, with a stronger association between maternal externalizing and female offspring distress. This begs the question of why the model in sample two using dichotomous scoring did not find the same effect. Taking a closer look at those results, there is indeed a sizeable difference in regression coefficients in the expected direction, with female offspring distress being significantly associated with maternal externalizing, but not paternal externalizing, though DIFFTEST did not detect a significant difference in model fit.

To conclude, there is little evidence for consistently stronger same-sex associations between parent externalizing and offspring psychopathology in these two samples. Although there are gender differences, as described above, those differences are mostly specific to the associations between offspring distress and parent externalizing, or failed to replicate across samples. There do not appear to be systematic same-sex effects in the aggregation of psychopathology in parents and offspring. And because the literature on same-sex parent offspring aggregation of psychopathology is inconsistent, it is not surprising that there was no strong evidence to support this hypothesis in the current study. Although it is true that externalizing mothers are more strongly associated with female offspring distress disorders in these samples, there does not appear to be a pervasive pattern wherein parent psychopathology is more strongly associated with psychopathology in offspring of the same sex. Examining the studies that support this same-sex effect, a majority have found the effect when examining internalizing disorders in parents, which is beyond the scope of this study. To illustrate this point, three of the four studies examining this question found evidence that maternal depressive and anxious

symptoms were associated with adolescent depressive symptoms and conduct and academic problems for girls but not for boys (Crawford, Cohen, Midlarsky, & Brook, 2001; Davies & Windle, 1997; Fergusson, Horwood, & Lynskey, 1993). It is possible that same-sex effects are uniquely present when investigating parental internalizing, which is a direction for future study using the present study's methods.

Third aim: Specificity or generality of risk aggregation? A third aim of this study was to investigate if aggregation occurring in families was best understood as a general liability to a group of comorbid disorders, or to specific disorder associations between parents and offspring. Results show that aggregation is mainly general, in that parent externalizing explains most of risk conferred to offspring latent externalizing, fear and distress, with patterns of general risk described above. However, there were some significant associations between specific disorders in parents and offspring. As hypothesized, most of these specific associations were found between ASPD or antisocial traits in parents and disorders in offspring. ASPD or antisocial traits in mothers and fathers were associated with specific risk for antisocial behavior or ASPD in male and female offspring. In NESARC, variance in offspring ASPD attributable to associations with parent antisocial traits was not completely explained by the latent externalizing variable in parents, as maternal and paternal antisocial traits still explained additional variance in offspring disorders. Maternal ASPD explains an additional 17% of the variance in male offspring ASPD and an additional 9% of the variance in female offspring ASPD; paternal ASPD explained an additional 16% of variance in male offspring ASPD and an additional 19% of the variance in female offspring ASPD. This

result was partially replicated in the twin and sibling sample using the symptom count variable, in that there was a significant residual correlation between paternal antisocial traits and male offspring ASPD. Interestingly, the finding was not replicated in the twin and sibling sample using dichotomous diagnostic variables. Still, at least for the specific association of male offspring ASPD and paternal ASPD, the finding is robust across samples. Above and beyond the variance attributable to latent externalizing in parents and offspring, antisocial traits in fathers were specifically associated with male offspring ASPD. Because the twin and sibling study is much smaller than NESARC, the lack of significant findings may be due to limited power to detect female externalizing.

For parent alcohol and drug use disorder traits in NESARC, all the variance explained in offspring alcohol and drug use disorders was explained by the latent externalizing factor, with no incremental variance explained by the residuals of specific diagnoses. This same pattern of results was found using both diagnostic variables in the twin and sibling study.

Cross-diagnostic residual correlations. In NESARC, there were two significant cross-diagnostic residual correlations that survived the Bonferroni correction. After accounting for the variance in parent antisocial traits defined by the externalizing factor, the unique variance attributable to antisocial traits in fathers was actually correlated with reduced prevalence of offspring nicotine dependence. Also, after accounting for the variance in parent antisocial traits defined by the externalizing factor, the unique variance attributable to antisocial traits in mothers was correlated with increased prevalence of female offspring dysthymia, and explained an additional 10.9% of the variance in female

offspring dysthmia. Neither of these specific effects were replicated in the twin and sibling sample, indicating these findings may be sample specific. There were no significant residual cross-diagnostic correlations in the twin and sibling study.

Conclusions from specificity analyses. Taken together, these results suggest that the majority of variance in offspring psychopathology explained in this model by parent externalizing is explained by the latent psychopathology structure. This large general risk factor partially explains the pattern of contradictory evidence in bivariate analysis, in which studies find different associations between specific externalizing diseases, but these findings fail to replicate consistently, presumably because the association is not specific to a particular disease, but a class of diseases among which the effect can be distributed in different data sets. However, as hypothesized, ASPD in parents is uniquely and consistently associated with offspring ASPD, above and beyond the variance explained by the externalizing factor in parents and offspring.

Fit with previous literature for generality/specificity findings. Findings from this study suggest that the risk between alcohol and drug use disorders aggregated in families is shared, and well-accounted for by a latent externalizing liability. This finding is supported by most bivariate studies in the literature, as well as by multivariate studies (Marmorstein, Iacono and McGue, 2009; Rounsaville et al., 1991; Chassin, Flora, and King 2004). Bivariate studies show clearly that alcohol and drug use disorders seem to share risk across families, but the literature on shared risk across substances use disorders and ASPD in families is more mixed. Reich et al. found little difference between children of alcoholics and children of parents with ASPD: In parents with ASPD plus alcohol

dependence, there was no difference in psychopathology or externalizing behaviors in the offspring, when compared with parents with just alcohol dependence (Reich et al., 1993). Hill and Hruska (1992) examined the rates of psychopathology in 53 children from families with multigenerational alcoholism and compared them with rates in 42 children who had no first-degree relatives with a DSM-III diagnosis and found the 2 groups did not differ in the rates of specific DSM-III diagnoses. Zucker, Ellis, Bingham, and Fitzgerald (1996) compared children from families where parents had only alcoholism, or had alcoholism with comorbid ASPD, and found the relatives of the comorbid families had greater prevalence of alcoholism and more severe alcoholism, indicating that the presence of ASPD in addition to alcoholism may indicate an increase in severity of risk, rather than a change in the type of risk. Finn et al. (1997) compared parents with alcoholism, alcoholism plus depression, and alcoholism plus ASPD, and found increased rates of alcoholism and antisocial behavior in all three groups as compared to controls. In the first-degree relatives of alcoholics, Nurmberger et al. (2004) found increased rates of other forms of substance dependence, ASPD, several anxiety disorders, major depression, and dysthymia, suggesting shared risk even beyond externalizing disorders. Diagnoses that were not increased in relatives were anorexia, bulimia, mania, and several forms of substance abuse, including DSM-IV alcohol abuse. On the other hand, Kuperman et al. (1999) investigated transmission of ASPD and alcoholism through direct clinical interview in parents and offspring. They found that among offspring, parental alcoholism was related to ADHD, conduct disorder, and overanxious disorder, while parental alcoholism plus ASPD was related to Oppositional Defiant Disorder in offspring.

However, this study has several important limitations, including small sample sizes (the alcohol and ASPD parent group was only 79 children). Additionally, the study did not find higher rates of alcoholism in children of alcoholics, or higher rates of conduct disorder in children of parents with ASPD, which are well-replicated finding, and may be due to the young average age of the offspring included in the study (12.1 ± 3.3 years). In a well-designed and adequately powered sample, Chassin, Rogosch, and Barrera (1991) found evidence that parent ASPD contributes specific risk to adolescent offspring externalizing problems, above and beyond the effect of parental alcoholism. This finding most closely aligns with findings from the current study.

Multivariate studies have found evidence mostly of generalized aggregation of psychopathology in families. Of the three studies that address this question using a multivariate metastructure approach, two found no evidence of specific residual associations (Hicks et al. 2013; McLaughlin et al., 2012). Kendler et al. (1997) utilized methodology most similar to the present study, but in a sample that was likely underpowered to detect female externalizing. They found major depression, generalized anxiety disorder, and alcohol abuse/dependence were associated with specific residual associations, while for antisocial personality disorder and drug abuse/dependence, there were no specific residual associations. However, as previously discussed, the sample in Kendler et al.'s study (1997) likely contains prevalence rates of female externalizing disorders that are too low to detect significant gender differences across parent or offspring psychopathology. Additionally, most findings related to specificity were found in internalizing disorders in parents (major depressive disorder and generalized anxiety

disorder), which were not investigated in the present study. Lastly, the only specificity finding in externalizing disorders was in alcohol abuse/dependence, which, because it includes alcohol abuse, captures a mild form of externalizing liability. Alcohol abuse was not included in these analyses, because its inclusion worsened model fit significantly. It is possible that in Kendler et al.'s sample (1997), alcohol abuse is specifically related to less severe manifestations of externalizing in offspring, leading to residual correlations unexplained by the latent liability, which captures more severe externalizing.

Why is most of the risk in association between parents and offspring psychopathology general? The literature has suggested several possible shared etiological correlates of externalizing disorders, and to a lesser extent, of internalizing disorders as well. Personality likely plays a role in shared liability to internalizing and externalizing disorders. Two broad domains within the empirical structure of personality are especially relevant to latent externalizing: negative emotionality/neuroticism (N/NE) and disinhibition (DIS: Costa & Widiger, 2002; Markon et al. 2005). Substance dependence syndromes, conduct disorder and antisocial personality disorder are all linked with traits from both the N/NE and DIS domains (Krueger & South, 2009), suggesting because externalizing and to a lesser extent, internalizing, are associated with these same traits, they are likely to co-occur and may share etiology. Indeed, there is considerable and mounting evidence of shared genetic etiological factors across externalizing disorders, as well as shared specific environmental risk factors, and shared neural substrates, biomarkers, and cognitive and emotional processing abnormalities in externalizing disorders (Krueger and South, 2009 for a review). Further, environmental

variables likely contribute general risk to groups of disorders, and genetic and environmental risks can interact to confer additional risk. For example, Repetti, Taylor, and Seeman, (2002) describe 'risky families', characterized by conflict and aggression and by relationships that are cold, unsupportive, and neglectful. They report these family characteristics can create vulnerabilities and/or interact with genetically based vulnerabilities in offspring that produce disruptions in psychosocial functioning (specifically emotion processing and social competence), disruptions in stress-responsive biological regulatory systems, including sympathetic-adrenomedullary and hypothalamic–pituitary–adrenocortical functioning, and poor health behaviors, especially substance abuse. With such broad, nonspecific effects, it is no surprise that these environments would create risk for many common mental disorders, but might interact with specific genetic liabilities and thus be expressed as different disorders in people with different genetic risk factors. Zucker (2006) found that for environmental effects, identifiable influences external to the person that enhance the risk of psychopathology (e.g. maltreatment, family violence) tend to be non-specific, impacting disorders in a general way, as opposed to impacting specific syndromes in a highly specific manner. Moffitt, Caspi, Rutter and Silva (2001) found shared environmental risk factors (eg, family disruption, poor parental monitoring, or low social class of rearing may contribute to shared etiology for externalizing disorders. So there are several plausible mechanisms for shared etiology and risk for externalizing disorders that have some empirical support. Further, understanding shared risk for disorders allows researchers to search for broader

mechanisms that better reflect shared liability across disorders, without becoming artificially siloed in the search for a mechanism for a particular disorder.

Why is ASPD in parents not fully explained by latent externalizing? It is possible that the externalizing factor as measured in these samples better represents the behavioral disinhibition contribution to latent externalizing than it does other forms of externalizing behaviors, like antisocial traits. The attempted addition of conduct disorder and nicotine dependence into the model (extended model briefly considered) was intended to extend the externalizing factor and measure it more broadly, but these additions significantly worsened model fit. The addition of other externalizing disorders such as ADHD or pathological gambling or other problems of behavioral disinhibition, might have provided a more broad measure of externalizing, which might therefore explain more variance between parent and offspring ASPD, leaving a smaller residual correlation. However, the loadings of antisocial traits or ASPD in parents onto the externalizing latent factor were as strong and sometimes stronger than loadings of drug and alcohol dependence traits, so it appears that in these samples, at least one component of variance in ASPD is being well-captured by the externalizing latent variable.

Another possible explanation is that in addition to a strong loading on the general externalizing latent factor, ASPD or antisocial behavior has unique risk associated with it. If the externalizing latent factor is considered most closely related to behavioral disinhibition, there are some antisocial traits that do seem to extend beyond behavioral disinhibition. The tripartite antisocial model describes antisocial behavior consisting of three dimensions: a) callous-unemotional traits (Cleckley, 1976) also labeled as ‘deficient

affective experience' (Cooke at al., 2006) or the 'affective factor' (Hare, 1993), b) an arrogant and deceitful interpersonal style involving a narcissistic view of one's self and conning and manipulative behavior and c) an impulsive and irresponsible behavioral style involving poorly planned behavior and proneness to boredom. This last dimension is most similar to the impulse control disorders that define the rest of the externalizing trait, but it is possible that the other two dimensions are less-well described by the externalizing latent factor in this model, and so contribute to residual correlation between parent and offspring antisocial traits.

Previous studies on genetic contributions to ASPD support this explanation. Blonigen, Hicks, Krueger, Patrick and Iacono (2005) factor analyzed the traits that compose ASPD and compared their associations to latent internalizing and externalizing factors. They found ASPD was composed of two uncorrelated components: Fearless Dominance and Impulsive Antisociality. Fearless dominance was negatively correlated with a measure of internalizing, and was not correlated with externalizing, while impulsive antisociality was positively correlated with a measure of externalizing. In the present study, the component of ASPD that loaded on the externalizing factor is likely the impulsive antisociality domain, with the fearless dominance component, which in Blonigen et al.'s study did not load on externalizing, remaining as residual variance (2005). Thus, the externalizing latent factor in the present study captures the components of ASPD that relate to impulsivity and behavioral inhibition, and which overlap with other disorders of behavioral disinhibition such as substance and alcohol use disorders. The uncorrelated component included in the residual of ASPD is likely fearless

dominance, and it is this component that is likely associated with specific risk for offspring ASPD.

Overall conclusions

The overarching goal of this study was to develop a parsimonious and clinically useful model of psychopathology risk aggregation in families with externalizing parents, while accounting for moderating effects of parent and offspring gender. Secondary aims were to investigate the impact of gender moderation on disorder associations, compare associations between latent factors, characterize aggregation in terms of generality and specificity, and replicate results in an independent sample.

In terms of advancements to extant literature, the NESARC sample provides improvement in that it has a large sample size with many cases of female externalizing, which is rare and understudied relative to male externalizing. This study also uses multivariate modeling methods, and models internalizing disorders in offspring, to provide a clear and expanded understanding of the association between parent externalizing and offspring psychopathology. This is also the first study to model gender of parent and offspring and to systematically investigate the possibility that gender affects the association between parent and offspring psychopathology, using a multivariate framework. The twin and sibling sample provides a replication sample for the NESARC sample in a study that assesses parents directly, and does not rely on offspring report of psychopathology. Taken together, these studies provide more robust conclusions about the extended risk profile in the offspring of externalizing parents, the generality of that risk, and the impact of parent gender and offspring gender on that association. In

particular, structure and gender findings were tested and then replicated in two different samples with complementary strengths and limitations, each addressing a portion of the question unaddressed by the extant literature.

This study provides a clearer picture of parental externalizing, in that paternal externalizing confers strong risk for externalizing disorders, medium risk for distress disorders, and least risk for fear disorders. Maternal externalizing confers strong risk for externalizing disorders in male and female offspring, and equally strong risk for distress disorders in female offspring. It is possible that risk to male offspring distress is also increased, but results are less conclusive across studies on this point. Lastly, mothers and fathers confer approximately equal risk to offspring fear disorders, regardless of parent or offspring gender.

In terms of patterns of aggregation, most of the risk for externalizing disorders in parents is aggregated generally, in that parent externalizing is better described through a latent variable framework which groups risk for related disorders, as compared to understanding risk for one disorder in parent and one disorder in offspring. Although a majority of the risk is best characterized as generalized, parent ASPD does show residual association with offspring ASPD, above and beyond what is measured by the latent externalizing factors. This finding is robust across samples.

One implication of these results, that show externalizing is aggregated both generally and specifically in families, is that familial aggregation should be modeled hierarchically (Krueger et al., 2002), allowing for both general risk factors (latent factors) and specific risk factors for specific disorders (ASPD). Much like in the structure of

common mental disorders modeled within individuals, risk for a general externalizing liability subsumes a majority of specific risk for individual disorders, but it is also possibly to model specific risk factors above and beyond the general factor. The model can reflect both simple and complex patterns of interrelationships across disorders, and explains comorbidity and patterns of co-aggregation within families.

Strengths and Limitations

This study has several important strengths. It is among the first to take a latent variable approach in investigating familial aggregation of psychopathology, and the first to investigate gender of parent and offspring systematically. The study uses a large, nationally representative community sample which allows it to be adequately powered to investigate externalizing in mothers and female offspring. It also includes a second sample used to test replicability. Additionally it assesses impact of parental psychopathology in adult children with a broad age range, protecting against any cohort-specific or age range-specific findings, and allows for conclusions that can generalize to adult offspring in other samples. Independent replication in an unrelated sample strengthens significant findings, making results more robust.

A potential limitation in the larger of the two samples (NESARC) is that parental externalizing traits were not directly assessed by interview, but were reported on by offspring enrolled in the study. Previous work has investigated the accuracy of offspring report on parental psychopathology. Several investigators have noted differences in the accuracy of information as a function of the relationship of the informant to the relative (Thompson et al, 1982; Andreasen et al, 1986). Fortunately, offspring may be among the

best informants on parent psychopathology (Thompson et al, 1982). The concern with informant reporting is that specificity tends to be good, while sensitivity tends to be lower than a gold standard interview (i.e. offspring may not know about psychopathology that was well-hidden or occurred before they were born; Kendler et al., 1997). In terms of the impact on results, in general, low sensitivity is more likely to attenuate than exaggerate any associations between parent and offspring psychopathology, so would not be likely to bias results in the direction of expected findings.

A related literature has investigated the accuracy of offspring report on parent psychopathology as a function of the characteristics of the reporter (i.e. gender, presence of psychopathology). In cases where the offspring also have psychopathology, at least one study has shown that offspring with internalizing disorders are more likely to correctly report internalizing disorders in their parents than siblings with no internalizing disorders, when compared to a 'gold standard' assessment (Kendler et al., 1991). This study also found that offspring with alcoholism did not differ from their unaffected twin in the accuracy of their report on parental psychopathology, suggesting that this bias may be specific to reports of internalizing in parents (Kendler et al., 1991). Another study also found that individuals with alcohol dependence were able to accurately report on alcoholism in their parents and relatives (Prescott, 2002). To date, there are no findings that identify a tendency for offspring with either internalizing or externalizing psychopathology to report parent *externalizing* in a biased way in parents, and a meta-analysis concluded there was no evidence for biased reporting in substance use disorders (Hardt & Franke, 2007).

A related literature compares the reporting styles of male and female offspring as a function of gender. These findings on gender reporting bias are mixed, with many studies reporting no difference between male and female responding, and a recent meta-analysis finding no effect of gender impacting on reporting (Hardt & Franke, 2007). However, two studies have found evidence that female and male offspring may report differently. Roy et al. (1996) found females were more likely to report Schizophrenia and affective disorders in their parents, but again did not examine externalizing disorders. Another study found females were more accurate in reporting smoking in relatives, and more likely to report MDD, alcohol dependence, and conduct disorder in family members (Milne et al., 2008), which could exaggerate the association between female offspring psychopathology and parental psychopathology. However, because the interview asks respondents about objective, measurable, behavioral criteria, this study may be protected from some biased reporting. Lastly, since this work will focus on differences in risk conferred by mothers and fathers, any bias in reporting would need to differentially impact reports of maternal psychopathology, and not paternal psychopathology, or vice versa. There is no evidence in the literature of any bias which differentially impacts reporting on parents of one gender, as compared with the parent of the opposite gender. In sum, this is a methodological limitation, but not a fatal flaw. This limitation was also addressed by the addition of the twin and sibling sample, which addresses issues related to direct assessment, as parents were directly assessed by trained interviewers in that sample. This lends reasonable confidence to results that were replicated across samples, and also partially validates the methodology of indirect or informant assessment used in

NESARC, which in most cases replicated findings from the twin and sibling sample using direct assessment.

Clinical Utility

This study is the first of its kind to compare the risk conferred by a parental externalizing risk factor to groups of offspring disorders, while accounting for gender. The clinical utility of this approach organizes a confusing literature and assesses the risk associated with externalizing in parents to a wide swath of disorders in offspring, including mood and anxiety disorders, substance use disorders, and antisocial personality disorder. Taken together, these disorders account for a large proportion of psychopathology, and are responsible for substantial pain and suffering. There are no studies to date that investigate the associations between parent externalizing and offspring internalizing and externalizing disorders, while also accounting for gender, in a large, nationally representative, generalizable sample. The multivariate modeling approach is a novel extension, used by very few studies to address this question. The multivariate modeling approach allows for a clinically meaningful and parsimonious understanding of the clinical risk profile for offspring of externalizing parents.

This study has implications beyond academia: these findings allow clinicians to better predict which groups of offspring are at greatest risk in parents with externalizing disorders, while further weighing the incremental risk contribution of parent and offspring gender. This work has implications for prevention work, potentially targeting female offspring of externalizing mothers for early intervention, both for externalizing disorders, but also for distress disorders like depression and anxiety. Just as a family

history of breast cancer allows for early screening and intervention, these results better position clinicians to predict and intervene in offspring of parents with externalizing disorders. Further, clinicians can better understand what disorders the offspring of externalizing parents are at risk for. Just as patients with a family history of breast cancer are at increased risk of other forms of cancer, these results suggest that a similar extended risk profile exists for externalizing disorders, while integrating specific risk associated with particular parent disorders.

Future directions

The next step towards a more parsimonious understanding of risk aggregation in families is a full risk model that includes internalizing disorders in parents. Only a single study (Kendler et al., 1997) uses a metastructure modeling approach and includes both internalizing and externalizing disorders in parents and offspring. However, this approach could be extended further, to include a broader range of internalizing and externalizing diagnoses, and a larger sample size to capture adequate prevalence rates of all measured disorders.

An equally important extension is to attempt to parse genetic and environmental contributions to the association between parent and offspring psychopathology. This study supports early intervention to inoculate against distress disorder in female offspring of externalizing mothers, but a genetically informed sample that could parse out the independent contribution of genetic and environmental influences would move us further towards an understanding of where to intervene. If the effect is found to have a substantial environmental component, specific parenting behaviors may be investigated

as contributing factors. As previously stated, there is mounting evidence of shared genetic etiological factors across externalizing disorders, as well as shared specific environmental risk factors, and shared neural substrates, biomarkers, and cognitive and emotional processing abnormalities in externalizing disorders (Krueger and South, 2009). These etiological variables should be studied in a familial aggregation context, to evaluate if they contribute to the aggregation of disorders in families, and not just to the comorbidity of disorders within individuals.

It is notable that most effects in this study (and in other metastructure modeling studies) were in the small to medium range, according to Cohen's (1988) characterization of effect sizes. Genetic studies (Young et al. 2000; Krueger et al. 2002; Kendler et al. 2003) find the genetic effect on the general latent externalizing propensity in these studies (the heritability), in the range of 80% (albeit a portion of this high heritability may be traced to the factor being latent and therefore free of stochastic measurement error). Most studies have found variance explained by parent diagnoses to be much smaller. If so much variance in externalizing is explained by genetic and heritable factors, it is interesting that in this study and other studies, variance explained by parent disorder is quite low, although significant. Future studies should investigate other variables that contribute unique variance to offspring psychopathology, controlling for parent disorders, and using a multivariate metastructure approach, to preserve clinical utility of findings.

Finally, understanding how and why disorders differentiate from these latent factors is potentially informative. Most environmental risk factors appear to confer general risk, and so are not likely to be the source of diagnostic differentiation. Several

authors have found that environmental effects that enhance risk, like maltreatment and family violence, family disruption, poor parental monitoring, or low social class of rearing, tend to be non-specific, impacting risk for disorders in a general way, as opposed to impacting specific syndromes in a highly specific manner (Moffitt, Caspi, Rutter and Silva, 2001; Zucker, 2006). Within syndromal groups, exposure to unique environmental experiences may explain why one disorder vs another develops in vulnerable individuals (Kendler et al., 2003). Understanding why these disorders differentiate as they do may yield insight into etiological variables that can lead to early intervention.

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Appendix A: Table Legends and Tables

Table Legends

Table 1. Legend: *Note.* Total Ns are provided for each sample. Prevalence rates are provided in percentages, followed by Ns in parentheses, for males and females separately, and then for the complete samples. Disorders are measured differently across samples, so that not every sample provides prevalence rates for every diagnosis. Data are missing for some diagnoses, so prevalence rates and Ns do not necessarily correspond to total Ns. Disorder prevalence rates are provided for maternal, paternal, and offspring dichotomous diagnoses. GAD= Generalized anxiety disorder.

Table 2. Legend: *Note.* Prevalence rates are provided for participants with symptom counts falling in each of the four quartiles (0-24.9%, 25-49.9%, 50-74.9%, 75-100%), for male and female offspring separately, and then for the total sample. Prevalence rates are provided for offspring, paternal, and maternal diagnoses. Some disorders have no cases in the upper quartiles, including maternal conduct disorder and maternal antisocial behavior in male and female offspring and adult antisocial behavior in male offspring. Dx=Disorder; Bx= Behavior; GAD=Generalized anxiety disorder; Dep, Depend= dependence.

Table 3. Legend: *Note.* RMSEA= Root Mean Square Error of Approximation; CFI= Comparative Fit Index; TLI= Tucker-Lewis Index. Free parameters are the number of freely estimated parameters, after all model parameters are estimated. Model fit is adequate in both models, separately in males and females.

Table 4. Legend: *Note.* Models in this table replicate diagnoses used in NESARC (sample 1). These models do not extend or add additional diagnoses to those used in the NESARC model. RMSEA= Root Mean Square Error of Approximation; CFI= Comparative Fit Index; TLI= Tucker-Lewis Index. Free parameters are the number of freely estimated parameters, after all model parameters are estimated. Model fit is adequate in both models, separately in males and females.

Table 5. Legend: *Note.* In addition to models included in the NESARC replication, this extended model loaded parent conduct disorder, alcohol abuse, drug abuse, and nicotine dependence on parent externalizing, and loaded conduct disorder, alcohol abuse and drug abuse on offspring externalizing. Model fit was significantly worse in the extended model, as compared to the replication model which included fewer diagnoses loaded on the externalizing factor in parents and offspring. RMSEA= Root Mean Square Error of Approximation; CFI= Comparative Fit Index; TLI= Tucker-Lewis Index. Free parameters are the number of freely estimated parameters, after all model parameters are estimated. Model fit is adequate in both models, separately in males and females.

Table 6. Legend: *Note.* Models in this table replicate diagnoses used in NESARC (sample 1), but use symptom count instead of dichotomous diagnostic variables. These models do

not extend or add additional diagnoses to those used in the NESARC model. RMSEA= Root Mean Square Error of Approximation; CFI= Comparative Fit Index; TLI= Tucker-Lewis Index. Free parameters are the number of freely estimated parameters, after all model parameters are estimated. Model fit is adequate in both models, separately in males and females. Model fit in the models using symptom count diagnoses is poorer than in models using dichotomous diagnostic variables.

Table 7. Legend: *Note.* In addition to models included in the NESARC replication, this extended model loaded parent conduct disorder, alcohol abuse, drug abuse, and nicotine dependence on parent externalizing, and loaded conduct disorder, alcohol abuse and drug abuse on offspring externalizing. Model fit is adequate in both models, separately in males and females. However, model fit was significantly worse in the extended model, as compared to the replication model which included fewer diagnoses loaded on the externalizing factor in parents and offspring. RMSEA= Root Mean Square Error of Approximation; CFI= Comparative Fit Index; TLI= Tucker-Lewis Index. Free parameters are the number of freely estimated parameters, after all model parameters are estimated.

Table 8. Legend: *Note.* Table compares a model where manifest variable loadings on latent factors, and thresholds, are constrained across offspring gender (Constrained model) to a model where loadings and thresholds are allowed to vary across offspring gender, and only structural constrains were imposed (Less Constrained Model; only number of factors and which observed variables loaded on which latent factors was constrained). DIFFTEST value, degrees of freedom, and significance is also included in the table. The less constrained model is selected as the preferred model and bolded, because a significant DIFFTEST indicates the model fit suffers significantly from the addition of threshold and loading constraints. Male and female offspring are treated as separate groups for subsequent analyses. Model fit is not significantly different according to fit statistics.

Table 9. Legend: *Note.* Table compares a model where manifest variable loadings on latent factors, and thresholds, are constrained across offspring gender (Constrained model) to a model where loadings and thresholds are allowed to vary across offspring gender, and only structural constrains were imposed (Less Constrained Model; only number of factors and which observed variables loaded on which latent factors was constrained). DIFFTEST value, degrees of freedom, and significance is also included in the table. The less constrained model is selected as the preferred model and bolded, because a significant DIFFTEST indicates the model fit suffers significantly from the addition of threshold and loading constraints. Male and female offspring are treated as separate groups for subsequent analyses. Model fit is not significantly different according to fit statistics.

Table 10. Legend: *Note.* Table compares a model where manifest variable loadings on latent factors, and thresholds, are constrained across offspring gender (Constrained model) to a model where loadings and thresholds are allowed to vary across offspring gender, and only structural constrains were imposed (Less Constrained Model; only number of factors and which observed variables loaded on which latent factors was constrained). DIFFTEST value, degrees of freedom, and significance is also included in the table. The less constrained model is selected as the preferred model and bolded, because a significant DIFFTEST indicates the model fit suffers significantly from the addition of threshold and loading constraints. Male and female offspring are treated as separate groups for subsequent analyses. Model fit is not significantly different according to fit statistics.

Table 11. Legend: *Note.* Table presents results from DIFFTESTS where regressions of offspring latent factors onto parent latent factors were either constrained across gender or free to vary. Regressions under 'main effects' constrain regressions across both offspring and parent gender. Regressions under 'interactions' constrain across either parent or offspring gender. The column labeled 'outcome' describes if constraints could be applied, according to DIFFTEST. Models could not be constrained if DIFFTEST was significant. The final model is bolded, and was selected because it was the most constrained model that survived DIFFTEST testing without decrement to model fit.

Table 12. Legend: *Note.* Table presents standardized regression coefficients, standard errors in parentheses, and *p*-values for regressions of offspring latent externalizing, fear, and distress factors on maternal and paternal latent externalizing factors. In the unconstrained model, the regression coefficients are free to vary across both parent and offspring gender, yielding four regression coefficients for each regression of offspring latent factor on parent externalizing. In the constrained regressions, coefficients were constrained according to results of previous analyses shown in table 11. If main effect regression coefficients could be constrained across gender in table 11, a single regression coefficient is reported for male and female offspring, for maternal and paternal externalizing. If regressions could be partially constrained across gender in interactions in table 11, regression coefficients are presented for the regressions that could be constrained. For offspring externalizing and fear regressed onto parent externalizing, regressions were constrained across parent and offspring gender, and this was the preferred model according to DIFFTEST. For offspring distress regressed onto parent externalizing, the regression could be constrained across male and female offspring for paternal externalizing, and across female offspring for paternal externalizing. Regressions differ between male and female offspring regressed onto paternal externalizing because of measurement variance. Female offspring distress regressed onto maternal externalizing could not be constrained across parent or offspring gender, so is presented separately. *p<.05

Table 13. Legend: *Note.* Table presents results from DIFFTESTS where regressions of offspring latent factors onto parent latent factors were either constrained across gender or free to vary. Regressions under 'main effects' constrain regressions across both offspring and parent gender. Regressions under 'interactions' constrain across either parent or offspring gender. The column labeled 'outcome' describes if constraints could be applied, according to DIFFTEST. Models could not be constrained if DIFFTEST was significant. The final model is bolded, and was selected because it was the most constrained model that survived DIFFTEST testing without decrement to model fit, and because regression coefficients were most similar in the unconstrained model. Regressions were constrained across all main effect regressions that were allowed by DIFFTEST, and then additionally constrained across interactions as showed in the bolded model. CFI= Comparative Fit Index; TLI= Tucker-Lewis Index; RMSEA= Root Mean Square Error of Approximation; Free Param= Free parameters; DF= Degrees of Freedom.

Table 14. Legend: *Note.* Table presents standardized regression coefficients, standard errors in parentheses, and *p*-values for regressions of offspring latent externalizing, fear, and distress factors on maternal and paternal latent externalizing factors. In the unconstrained model, the regression coefficients are free to vary across both parent and offspring gender, yielding four regression coefficients for each regression of offspring latent factor on parent externalizing. In the constrained regressions, coefficients were constrained according to results of previous analyses shown in table 16. If main effect regression coefficients could be constrained across gender in table 16, a single regression coefficient is reported for male and female offspring, across maternal and paternal externalizing. If regressions could be partially constrained across gender in interactions in table 16, regression coefficients are presented for the regressions that could be constrained. For offspring externalizing and fear regressed onto parent externalizing, regressions were constrained across parent and offspring gender, and this was the preferred model according to DIFFTEST. For offspring distress regressed onto parent externalizing, the regression could be constrained across male and female offspring for paternal externalizing, and separately across male and female offspring for paternal externalizing. *p<.05

Table 15. Legend: *Note.* Table presents results from DIFFTESTS where regressions of offspring latent factors onto parent latent factors were either constrained across gender or free to vary. Regressions under 'main effects' constrain regressions across both offspring and parent gender. Regressions under 'interactions' constrain across either parent or offspring gender. The column labeled 'outcome' describes if constraints could be applied, according to DIFFTEST. Models could not be constrained if DIFFTEST was significant. The final model is bolded, and was selected because it was the most constrained model that survived DIFFTEST testing without decrement to model fit, and because regression coefficients were most similar in the unconstrained model. Regressions in the final model were constrained across all main effect regressions that were allowed by DIFFTEST, and then additionally constrained across interactions as showed in the bolded model. CFI=

Comparative Fit Index; TLI= Tucker-Lewis Index; RMSEA= Root Mean Square Error of Approximation; Free Param= Free parameters; DF= Degrees of Freedom.

Table 16. Legend: *Note.* Table presents standardized regression coefficients, standard errors in parentheses, and *p*-values for regressions of offspring latent externalizing, fear, and distress factors on maternal and paternal latent externalizing factors. In the unconstrained model, the regression coefficients are free to vary across both parent and offspring gender, yielding four regression coefficients for each regression of offspring latent factor on parent externalizing. In the constrained regressions, coefficients were constrained according to results of previous analyses shown in table 21. If main effect regression coefficients could be constrained across gender in table 21, a single regression coefficient is reported for male and female offspring, across maternal and paternal externalizing. If regressions could be partially constrained across gender in interactions in table 21, regression coefficients are presented for the regressions that could be constrained. *p<.05

Table 17. Legend: *Note.* Table presents results from DIFFTESTS for pairs of regressions that investigate the presence of stronger associations between same-sex parents and offspring for externalizing. These regressions are reported for the regression of offspring externalizing on parent externalizing. The first two regressions presented in each regression cluster are the coefficients when the regressions are free to vary across gender. The third coefficients in the third model in each cluster (labeled constrained) presents the coefficients for males/females when the regressions are constrained. Values sometimes differ slightly due to measurement variance. Where DIFFTEST is significant, regression coefficients are significantly different across regression pairs and cannot be constrained. When DIFFTEST is non-significant, as it is in all regressions presented in this table, the regressions are constrainable, indicating no significant increase in association between parent and same-sex offspring. S.E. = Standard Error. DF= Degrees of freedom.

Table 18. Legend: *Note.* Table presents results from DIFFTESTS for pairs of regressions that investigate the presence of stronger associations between same-sex parents and offspring for fear. These regressions are reported for the regression of offspring fear on parent externalizing. The first two regressions presented in each regression cluster are the coefficients when the regressions are free to vary across gender. The third coefficients in the third model in each cluster (labeled constrained) presents the coefficients for males/females when the regressions are constrained. Values sometimes differ slightly due to measurement variance. Where DIFFTEST is significant, regression coefficients are significantly different across regression pairs and cannot be constrained. When DIFFTEST is non-significant, as it is in all regressions presented in this table, the regressions are constrainable, indicating no significant increase in association between parent and same-sex offspring. S.E. = Standard Error. DF= Degrees of freedom.

Table 19. Legend: *Note.* Table presents results from DIFFTESTS for pairs of regressions that investigate the presence of stronger associations between same-sex parents and offspring for distress. These regressions are reported for the regression of offspring distress on parent externalizing. The first two regressions presented in each regression cluster are the coefficients when the regressions are free to vary across gender. The third coefficients in the third model in each cluster (labeled constrained) presents the coefficients for males/females when the regressions are constrained. Values sometimes differ slightly due to measurement variance. Where DIFFTEST is significant (bolded), regression coefficients are significantly different across regression pairs and cannot be constrained. When DIFFTEST is non-significant, the regressions are constrainable, indicating no significant increase in association between parent and same-sex offspring. S.E. = Standard Error. DF= Degrees of freedom.

Table 20. Legend: *Note.* Table presents results from DIFFTESTS for pairs of regressions that investigate the presence of stronger associations between same-sex parents and offspring for externalizing. These regressions are reported for the regression of offspring externalizing on parent externalizing. The first two regressions presented in each regression cluster are the coefficients when the regressions are free to vary across gender. The third coefficients in the third model in each cluster (labeled constrained) presents the coefficients for males/females when the regressions are constrained. Values sometimes differ slightly due to measurement variance. Where DIFFTEST is significant (bolded), regression coefficients are significantly different across regression pairs and cannot be constrained. When DIFFTEST is non-significant, the regressions are constrainable, indicating no significant increase in association between parent and same-sex offspring. S.E. = Standard Error. DF= Degrees of freedom.

Table 21. Legend: *Note.* Table presents results from DIFFTESTS for pairs of regressions that investigate the presence of stronger associations between same-sex parents and offspring for fear. These regressions are reported for the regression of offspring fear on parent externalizing. The first two regressions presented in each regression cluster are the coefficients when the regressions are free to vary across gender. The third coefficients in the third model in each cluster (labeled constrained) presents the coefficients for males/females when the regressions are constrained. Values sometimes differ slightly due to measurement variance. Where DIFFTEST is significant, regression coefficients are significantly different across regression pairs and cannot be constrained. When DIFFTEST is non-significant, the regressions are constrainable, indicating no significant increase in association between parent and same-sex offspring. S.E. = Standard Error. DF= Degrees of freedom.

Table 22. Legend: *Note.* Table presents results from DIFFTESTS for pairs of regressions that investigate the presence of stronger associations between same-sex parents and offspring for distress. These regressions are reported for the regression of offspring

distress on parent externalizing. The first two regressions presented in each regression cluster are the coefficients when the regressions are free to vary across gender. The third coefficients in the third model in each cluster (labeled constrained) presents the coefficients for males/females when the regressions are constrained. Values sometimes differ slightly due to measurement variance. Where DIFFTEST is significant (bolded), regression coefficients are significantly different across regression pairs and cannot be constrained. When DIFFTEST is non-significant, the regressions are constrainable, indicating no significant increase in association between parent and same-sex offspring. S.E. = Standard Error. DF= Degrees of freedom.

Table 23. Legend: *Note.* Table presents results from DIFFTESTS for pairs of regressions that investigate the presence of stronger associations between same-sex parents and offspring for distress. These regressions are reported for the regression of offspring distress on parent externalizing. The first two regressions presented in each regression cluster are the coefficients when the regressions are free to vary across gender. The third coefficients in the third model in each cluster (labeled constrained) presents the coefficients for males/females when the regressions are constrained. Values sometimes differ slightly due to measurement variance. Where DIFFTEST is significant (bolded), regression coefficients are significantly different across regression pairs and cannot be constrained. When DIFFTEST is non-significant, the regressions are constrainable, indicating no significant increase in association between parent and same-sex offspring. S.E. = Standard Error. DF= Degrees of freedom.

Table 24. Legend: *Note.* Table presents results from DIFFTESTS for pairs of regressions that investigate the presence of stronger associations between same-sex parents and offspring for fear. These regressions are reported for the regression of offspring fear on parent externalizing. The first two regressions presented in each regression cluster are the coefficients when the regressions are free to vary across gender. The third coefficients in the third model in each cluster (labeled constrained) presents the coefficients for males/females when the regressions are constrained. Values sometimes differ slightly due to measurement variance. Where DIFFTEST is significant, regression coefficients are significantly different across regression pairs and cannot be constrained. When DIFFTEST is non-significant, as with all regressions in this model, the regressions are constrainable, indicating no significant increase in association between parent and same-sex offspring. S.E. = Standard Error. DF= Degrees of freedom.

Table 25. Legend: *Note.* Table presents results from DIFFTESTS for pairs of regressions that investigate the presence of stronger associations between same-sex parents and offspring for externalizing. These regressions are reported for the regression of offspring externalizing on parent externalizing. The first two regressions presented in each regression cluster are the coefficients when the regressions are free to vary across gender. The third coefficients in the third model in each cluster (labeled constrained) presents the coefficients for males/females when the regressions are constrained. Values sometimes

differ slightly due to measurement variance. Where DIFFTEST is significant (bolded), regression coefficients are significantly different across regression pairs and cannot be constrained. When DIFFTEST is non-significant, the regressions are constrainable, indicating no significant increase in association between parent and same-sex offspring. S.E. = Standard Error. DF= Degrees of freedom.

Table 26. Legend: *Note.* Table presents results from correlations of residual variance of offspring diagnoses on residuals of the same parent diagnoses. Because multiple tests were run for these analyses, required p-value was corrected using a Bonferroni correction (.05/12=.004). Significant correlations are bolded. Off. = Offspring; In offspring, ASPD= Antisocial Personality Disorder; Alcohol= Alcohol dependence; Drug= Drug dependence; In parents, ASPD= Antisocial traits; Alcohol= Alcohol use disorder traits; Drug= Drug use disorder traits; CFI= Comparative Fit Index; TLI= Tucker-Lewis Index; RMSEA= Root Mean Square Error of Approximation; Free Param.= Free parameters; S.E. = Standard Error.

Table 27. Legend: *Note.* Table presents results from correlations of residual variance of offspring diagnoses on residuals of parent antisocial traits. Because multiple models were run for each diagnosis, a conservative p-value corrected for multiple tests was used to determine significance, where p<.001 was considered significant. Significant correlations are bolded. Off. = Offspring; In offspring, Alcohol= Alcohol dependence; Drug= Drug dependence; Nicotine= Nicotine dependence; Panic= Panic disorder; Social Ph= Social phobia; Specific Ph. =Specific phobia; MDD= Major Depressive Disorder; GAD= Generalized Anxiety Disorder; In parents, ASPD= Antisocial traits; CFI= Comparative Fit Index; TLI= Tucker-Lewis Index; RMSEA= Root Mean Square Error of Approximation; Free Param.= Free parameters; S.E. = Standard Error.

Table 28. Legend: *Note.* Table presents results from correlations of residual variance of offspring diagnoses on residuals of parent antisocial traits. Because multiple models were run for each diagnosis, a conservative p-value corrected for multiple tests was used to determine significance, where p<.001 was considered significant. Significant correlations are bolded. Off. = Offspring; In offspring, Alcohol= Alcohol dependence; ASPD= Antisocial Personality Disorder; Nicotine= Nicotine dependence; Panic= Panic disorder; Social Ph= Social phobia; Specific Ph. =Specific phobia; MDD= Major Depressive Disorder; GAD= Generalized Anxiety Disorder; In parents, Drug= Drug use disorder traits; CFI= Comparative Fit Index; TLI= Tucker-Lewis Index; RMSEA= Root Mean Square Error of Approximation; Free Param.= Free parameters; S.E. = Standard Error.

Table 29. Legend: *Note.* Table presents results from correlations of residual variance of offspring diagnoses on residuals of parent antisocial traits. Because multiple models were run for each diagnosis, a conservative p-value corrected for multiple tests was used to determine significance, where p<.001 was considered significant. Significant correlations are bolded. Off. = Offspring; In offspring, Drug= Drug dependence; ASPD= Antisocial

Personality Disorder; Nicotine= Nicotine dependence; Panic= Panic disorder; Social Ph= Social phobia; Specific Ph. =Specific phobia; MDD= Major Depressive Disorder; GAD= Generalized Anxiety Disorder; In parents, Alcohol= Alcohol use disorder traits; CFI= Comparative Fit Index; TLI= Tucker-Lewis Index; RMSEA= Root Mean Square Error of Approximation; Free Param.= Free parameters; S.E. = Standard Error.

Table 30. Legend: *Note.* Table presents results from correlations of residual variance of offspring diagnoses on residuals of the same parent diagnoses. Because multiple tests were run for these analyses, required p-value was corrected using a Bonferroni correction (.05/12=.004). Significant correlations are bolded. Off. = Offspring; In offspring, ASPD= Adult Antisocial Behavior; Alcohol= Alcohol dependence; Drug= Drug dependence; In parents, ASPD= Adult Antisocial Behavior; Alcohol= Alcohol dependence; Drug= Drug dependence; CFI= Comparative Fit Index; TLI= Tucker-Lewis Index; RMSEA= Root Mean Square Error of Approximation; Free Param.= Free parameters; S.E. = Standard Error.

Table 31. Legend: *Note.* Table presents results from correlations of residual variance of offspring diagnoses on residuals of the same parent diagnoses. Because multiple tests were run for these analyses, required p-value was corrected using a Bonferroni correction (.05/12=.004). Significant correlations are bolded. Off. = Offspring; In offspring, ASPD= Adult Antisocial Behavior symptoms; Alcohol= Alcohol dependence symptoms; Drug= Drug dependence symptoms; In parents, ASPD= Adult Antisocial Behavior symptoms; Alcohol= Alcohol dependence symptoms; Drug= Drug dependence symptoms; CFI= Comparative Fit Index; TLI= Tucker-Lewis Index; RMSEA= Root Mean Square Error of Approximation; Free Param.= Free parameters; S.E. = Standard Error.

Table 32. Legend: *Note.* Table presents results from correlations of residual variance of offspring diagnoses on residuals of parent antisocial traits. Because multiple models were run for each diagnosis, a conservative p-value corrected for multiple tests was used to determine significance, where p<.001 was considered significant. Significant correlations are bolded. Off. = Offspring; In offspring, Alcohol= Alcohol dependence; Drug= Drug dependence; Nicotine= Nicotine dependence; Panic= Panic disorder; Social Ph= Social phobia; Specific Ph. =Specific phobia; MDD= Major Depressive Disorder; GAD= Generalized Anxiety Disorder; In parents, ASPD= Adult Antisocial Behavior; CFI= Comparative Fit Index; TLI= Tucker-Lewis Index; RMSEA= Root Mean Square Error of Approximation; Free Param.= Free parameters; S.E. = Standard Error.

Table 33. Legend: *Note.* Table presents results from correlations of residual variance of offspring diagnoses on residuals of parent antisocial traits. Because multiple models were run for each diagnosis, a conservative p-value corrected for multiple tests was used to determine significance, where p<.001 was considered significant. Significant correlations are bolded. Off. = Offspring; In offspring, Alcohol= Alcohol dependence; ASPD= Adult Antisocial Behavior; Nicotine= Nicotine dependence; Panic= Panic disorder; Social Ph=

Social phobia; Specific Ph. =Specific phobia; MDD= Major Depressive Disorder; GAD= Generalized Anxiety Disorder; In parents, Drug= Drug dependence; CFI= Comparative Fit Index; TLI= Tucker-Lewis Index; RMSEA= Root Mean Square Error of Approximation; Free Param.= Free parameters; S.E. = Standard Error.

Table 34. Legend: *Note.* Table presents results from correlations of residual variance of offspring diagnoses on residuals of parent antisocial traits. Because multiple models were run for each diagnosis, a conservative p-value corrected for multiple tests was used to determine significance, where p<.001 was considered significant. Significant correlations are bolded. Off. = Offspring; In offspring, Drug= Drug dependence; ASPD= Adult Antisocial Behavior; Nicotine= Nicotine dependence; Panic= Panic disorder; Social Ph= Social phobia; Specific Ph. =Specific phobia; MDD= Major Depressive Disorder; GAD= Generalized Anxiety Disorder; In parents, Alcohol= Alcohol dependence; CFI= Comparative Fit Index; TLI= Tucker-Lewis Index; RMSEA= Root Mean Square Error of Approximation; Free Param.= Free parameters; S.E. = Standard Error.

Table 35. Legend: *Note.* Table presents results from correlations of residual variance of offspring diagnoses on residuals of parent antisocial traits. Because multiple models were run for each diagnosis, a conservative p-value corrected for multiple tests was used to determine significance, where p<.001 was considered significant. Significant correlations are bolded. Off. = Offspring; In offspring, Alcohol= Alcohol dependence symptoms; Drug= Drug dependence symptoms; Nicotine= Nicotine dependence symptoms; Panic= Panic disorder symptoms; Social Ph= Social phobia symptoms; Specific Ph. =Specific phobia symptoms; MDD= Major Depressive Disorder symptoms; GAD= Generalized Anxiety Disorder symptoms; In parents, ASPD= Adult Antisocial Behavior symptoms; CFI= Comparative Fit Index; TLI= Tucker-Lewis Index; RMSEA= Root Mean Square Error of Approximation; Free Param.= Free parameters; S.E. = Standard Error.

Table 36. Legend: *Note.* Table presents results from correlations of residual variance of offspring diagnoses on residuals of parent antisocial traits. Because multiple models were run for each diagnosis, a conservative p-value corrected for multiple tests was used to determine significance, where p<.001 was considered significant. Significant correlations are bolded. Off. = Offspring; In offspring, Alcohol= Alcohol dependence symptoms; ASPD= Adult Antisocial Behavior symptoms; Nicotine= Nicotine dependence symptoms; Panic= Panic disorder symptoms; Social Ph= Social phobia symptoms; Specific Ph. =Specific phobia symptoms; MDD= Major Depressive Disorder symptoms; GAD= Generalized Anxiety Disorder symptoms; In parents, Drug= Drug dependence symptoms; CFI= Comparative Fit Index; TLI= Tucker-Lewis Index; RMSEA= Root Mean Square Error of Approximation; Free Param.= Free parameters; S.E. = Standard Error.

Table 37. Legend: *Note.* Table presents results from correlations of residual variance of offspring diagnoses on residuals of parent antisocial traits. Because multiple models were

run for each diagnosis, a conservative p-value corrected for multiple tests was used to determine significance, where p<.001 was considered significant. Significant correlations are bolded. Off. = Offspring; In offspring, Drug= Drug dependence symptoms; ASPD= Adult Antisocial Behavior symptoms; Nicotine= Nicotine dependence symptoms; Panic= Panic disorder symptoms; Social Ph= Social phobia symptoms; Specific Ph. =Specific phobia symptoms; MDD= Major Depressive Disorder symptoms; GAD= Generalized Anxiety Disorder symptoms; In parents, Alcohol= Alcohol dependence symptoms; CFI= Comparative Fit Index; TLI= Tucker-Lewis Index; RMSEA= Root Mean Square Error of Approximation; Free Param.= Free parameters; S.E. = Standard Error.

Table 1. Prevalence Rates of Disorders in NESARC and Twin Sample using Dichotomous Diagnostic Variables

	NESARC Males	NESARC Females	NESARC Total	Twin Sample Males	Twin Sample Females	Twin Sample Total
Total Number	16048	20814	36862	2368	2631	4999
			Maternal Disorders/Traits			
Maternal Antisocial Traits	2.0 (299)	2.8 (556)	2.4 (841)	1.3 (28)	1.4 (32)	1.3(60)
Maternal Drug Depend. Traits	1.4 (217)	1.7 (350)	1.6 (561)	-	-	-
Maternal Alcohol Depend. Traits	4.7 (749)	5.8 (1186)	5.3 (1917)	-	-	-
Maternal Drug Abuse	-	-	-	5.4 (119)	6.4 (149)	5.9 (268)
Maternal Drug Dependence	-	-	-	3.4 (74)	2.3 (54)	2.8 (128)
Maternal Alcohol Abuse	-	-	-	5.7 (125)	6.5 (152)	6.1 (277)
Maternal Alcohol Dependence	-	-	-	4.1 (90)	4.4 (104)	4.3 (194)
Maternal Nicotine Dependence	-	-	-	17.2 (376)	17.9 (419)	17.3 (795)
Maternal Conduct Disorder	-	-	-	2.2 (47)	2.7 (63)	2.4 (110)
			Paternal Disorders/Traits			
Paternal Antisocial Traits	6.8 (1014)	7.8 (1525)	7.3 (2522)	7.9 (173)	10.6 (249)	9.3 (422)
Paternal Drug Depend. Traits	1.9 (297)	2.5 (496)	2.2 (783)	-	-	-
Paternal Alcohol Depend. Traits	17.7 (2766)	20.7 (4206)	19.2 (6921)	-	-	-
Paternal Drug Abuse	-	-	-	13.6 (298)	19.7 (458)	16.7 (756)
Paternal Drug Dependence	-	-	-	4.3 (95)	8.0 (187)	6.2 (282)
Paternal Alcohol Abuse	-	-	-	29.0 (638)	34.4 (804)	30.8 (1442)
Paternal Alcohol Dependence	-	-	-	17.9 (394)	20.1 (470)	19.0 (864)
Paternal Nicotine Dependence	-	-	-	29.9 (657)	30.7 (718)	30.3 (1375)
Paternal Conduct Disorder	-	-	-	12.6 (274)	15.7 (364)	14.1 (638)
			Offspring Disorders/Traits			
Alcohol Abuse	-	-	-	45.9 (1087)	24.6 (646)	34.7 (1733)
Alcohol Dependence	16.3 (2618)	7.1 (1479)	11.5 (4257)	19.3 (456)	8.6 (227)	13.7 (683)

Antisocial PD	5.0 (798)	1.6 (340)	3.2 (1196)	-	-	-
Adult Antisocial Behavior	-	-	-	26.8 (510)	11.2 (255)	18.3 (765)
Conduct Disorder	-	-	-	20.1 (475)	5.7 (149)	12.5 (624)
Drug Dependence	2.7 (426)	1.6 (341)	2.1 (785)	16.8 (397)	8.7 (229)	13.7 (696)
Drug Abuse	-	-	-	29.1 (689)	15.8 (416)	22.1 (1105)
Nicotine Dependence	20.1 (3221)	15.1 (3140)	17.5 (6447)	30.2 (714)	20.8 (547)	25.2 (1261)
Panic Disorder	3.7 (590)	7.1 (1472)	5.4 (2002)	1.8 (40)	4.4 (112)	3.2 (152)
Social Phobia	4.3 (686)	5.8 (1206)	5.1 (1867)	5.7 (129)	7.7 (197)	6.7 (326)
Specific Phobia	6.2 (997)	12.3 (2566)	9.4 (3457)	2.4 (53)	4.3 (108)	3.4 (161)
Major Depressive Disorder	13.1 (2106)	22.8 (4741)	18.1 (6680)	20.7 (491)	31.3 (822)	26.3 (1313)
Dysthmia	3.5 (563)	6.1 (1260)	4.8 (1779)	-	-	-
GAD	3.2 (510)	5.8 (1209)	4.5 (1674)	0.9 (20)	2.0 (52)	1.5 (72)

Table 2: Prevalence Rates of Disorders using Symptom Count Variables in Twin Sample

	Male Offspring				Female Offspring			
	0-24.9%	25-49.5%	50-74.9%	75-100%	0-24.9%	25-49.5%	50-74.9%	75-100%
Conduct Disorder	82.9 (1964)	13.1 (310)	3.3 (79)	0.6 (15)	96.2 (2531)	3.4 (89)	0.4 (10)	<0.0 (1)
Adult Antisocial Beh.	37 (705)	10.2 (194)	2.9 (56)	0 (0)	77.4 (1756)	18.1 (412)	4.1 (92)	0.4 (10)
Drug Abuse	70.5 (1670)	10.2 (241)	10.6 (252)	8.7 (205)	84.1 (2212)	8.3 (217)	4.7 (123)	3.0 (78)
Drug Dependence	78.2 (1851)	9.8 (231)	6.9 (163)	5.2 (123)	88.2 (2320)	5.7 (149)	3.5 (92)	2.6 (69)
Alcohol Abuse	54.1 (1280)	19.8 (469)	14.7 (349)	11.4 (270)	75.4 (1982)	15.1 (398)	5.9 (154)	3.7 (96)
Alcohol Dependence	67.6 (1601)	22.6 (534)	7.4 (175)	2.4 (58)	85.0 (2235)	11.1 (293)	2.6 (69)	1.3 (33)
Nicotine Dependence	62.7 (1485)	17.1 (406)	17.9 (424)	2.2 (53)	73.7 (1938)	13.8 (364)	11.2 (294)	1.3 (34)
Major Depressive Dx	69.2 (1639)	9.3 (220)	11.1 (263)	10.4 (246)	57 (1498)	11.1 (292)	13 (342)	18.9 (498)
GAD	97.6 (2202)	0.4 (9)	1.1 (24)	0.9 (21)	95.2 (2450)	0.9 (22)	1.8 (46)	2.2 (56)
Social Phobia	83.7 (1890)	2.4 (54)	3.4 (77)	10.5 (236)	85.1 (2190)	1.3 (33)	2.3 (60)	11.3 (291)
Specific Phobia	94.3 (2094)	0.7 (15)	1.3 (29)	3.7 (82)	93.5 (2359)	0.2 (6)	0.8 (20)	5.4 (137)
Panic Disorder	94.5 (2099)	3.1 (68)	2.1 (47)	0.3 (6)	89.1 (2245)	5.6 (140)	4.6 (116)	0.8 (20)
Paternal Conduct Dx	88.2 (1935)	11 (241)	0.7 (15)	0.1 (2)	85 (1990)	12.5 (293)	2.2 (51)	0.3 (6)
Paternal Antisocial Bx	68.6 (1508)	26.8 (589)	4.3 (94)	0.3 (6)	67.4 (1582)	26.1 (612)	5.9 (138)	0.6 (14)
Paternal Drug Abuse	77 (1685)	4 (88)	11.7 (255)	7.3 (159)	71.4 (1663)	4.6 (108)	13.5 (314)	10.5 (245)
Paternal Drug Depend	91 (1990)	5.2 (114)	2.2 (48)	1.6 (35)	86.4 (2012)	6.4 (148)	5.1 (119)	2.2 (51)
Paternal Alcohol Abuse	55 (1209)	5.3 (116)	21.3 (467)	18.4 (405)	53.2 (1245)	5.3 (124)	21.6 (505)	19.9 (466)
Paternal Alcohol Dep.	69.8 (1533)	17.3 (380)	7.7 (169)	5.1 (113)	67.8 (1584)	16.8 (393)	9.7 (226)	5.8 (135)
Paternal Nicotine Dep.	57.2 (1256)	25 (550)	17.2 (378)	0.6 (13)	59.4 (1389)	22.5 (527)	16.6 (387)	1.5 (35)
Maternal Conduct Dx	97.9 (2144)	2.1 (46)	-	-	97.4 (2281)	2.6 (60)	-	-
Maternal Antisocial Bx	91.1 (1996)	7.9 (174)	0.9 (20)	-	90.5 (2118)	8.1 (189)	1.5 (34)	-

Maternal Drug Abuse	88.8 (1945)	2.1 (46)	5.8 (128)	3.2 (71)	86.6 (2028)	1.9 (44)	7.8 (182)	3.7 (87)
Maternal Drug Depend	94.7 (2074)	2.2 (48)	2.3 (51)	0.8 (17)	94.1 (2203)	3 (70)	1.3 (31)	1.6 (37)
Maternal Alcohol Abuse	86.7 (1899)	2.6 (57)	8.6 (189)	2.1 (45)	86.5 (2025)	2 (47)	8.5 (198)	3 (71)
Maternal Alcohol Dep.	91.2 (1997)	5.7 (125)	2.3 (51)	0.8 (17)	90.6 (2121)	5.7 (134)	2.3 (53)	1.4 (33)
Maternal Nicotine Dep.	72.5 (1586)	16.2 (354)	10.1 (220)	1.3 (28)	71.1 (1665)	15.4 (360)	12 (282)	1.5 (34)

Table 2: Continued Prevalence Rates of Disorders using Symptom Count Variables in Twin Sample

	Prevalence Rate (n)			
	0-24.9%	25-49.5%	50-74.9%	75-100%
Conduct Disorder	89.9 (4495)	8 (399)	1.8 (89)	0.3 (16)
Adult Antisocial Beh.	26.8 (1117)	6.9 (286)	1.6 (66)	0 (0)
Drug Abuse	77.7 (3882)	9.2 (458)	7.5 (375)	5.7 (283)
Drug Dependence	83.5 (4171)	7.6 (380)	5.1 (255)	3.8 (192)
Alcohol Abuse	65.3 (3262)	17.3 (867)	10.1 (503)	7.3 (366)
Alcohol Dependence	76.8 (3836)	16.5 (827)	4.9 (244)	1.8 (91)
Nicotine Dependence	68.5 (3423)	15.4 (770)	14.4 (718)	1.7 (87)
Major Depressive Dx	62.8 (3137)	10.2 (512)	12.1 (605)	14.9 (744)
GAD	96.3 (4652)	0.6 (31)	1.4 (70)	1.6 (77)
Social Phobia	84.5 (4080)	1.8 (87)	2.8 (137)	10.9 (527)
Specific Phobia	93.9 (4453)	0.4 (21)	1 (49)	4.6 (219)
Panic Disorder	91.6 (4344)	4.4 (208)	3.4 (163)	0.5 (26)
Paternal Conduct Dx	86.6 (3925)	11.8 (534)	1.5 (66)	0.2 (8)
Paternal Antisocial Bx	68.0 (3090)	26.4 (1201)	5.1 (232)	0.4 (20)
Paternal Drug Abuse	74.1 (3348)	4.3 (196)	12.6 (569)	8.9 (404)
Paternal Drug Depend	88.6 (4002)	5.8 (262)	3.7 (167)	1.9 (86)
Paternal Alcohol Abuse	54.1 (2454)	5.3 (240)	21.4 (972)	19.2 (871)
Paternal Alcohol Dep.	68.8 (3117)	17.1 (773)	8.7 (395)	5.5 (248)
Paternal Nicotine Dep.	58.3 (2645)	23.7 (1077)	16.9 (765)	1.1 (48)
Maternal Conduct Dx	97.7 (4425)	2.3 (106)	-	-
Maternal Antisocial Bx	90.8 (4114)	8 (363)	1.2 (54)	-
Maternal Drug Abuse	87.7 (3973)	2 (90)	6.8 (310)	3.5 (158)
Maternal Drug Depend	94.4 (4277)	2.6 (118)	1.8 (82)	1.2 (54)

Maternal Alcohol Abuse	86.6 (3924)	2.3 (104)	8.5 (387)	2.6 (116)
Maternal Alcohol Dep.	90.9 (4118)	5.7 (259)	2.3 (104)	1.1 (50)
Maternal Nicotine Dep.	71.8 (3251)	15.8 (714)	11.1 (502)	1.4 (62)

Table 3: Model Fit in Male and Female Offspring Separately in NESARC

Model	RMSEA	CFI	TLI	Free Parameters
Base Model in Male Offspring	0.015	0.977	0.970	42
Base Model in Female Offspring	0.015	0.980	0.975	42

Table 4: Model Fit Statistics in Twin and Sibling Sample using Dichotomous Diagnostic Variables, Replicating Diagnoses used in NESARC Sample.

Model:	RMSEA	CFI	TLI	Free Parameters
Base Model in Male Offspring	.010	.990	.988	44
Base Model in Female Offspring	.016	.978	.973	44

Table 5: Model Fit Statistics for the Extended Model in Twin and Sibling Sample using Dichotomous Diagnostic Variables

Model:	RMSEA	CFI	TLI	Free Parameters
Base Model in Male Offspring	.025	.967	.963	62
Base Model in Female Offspring	.022	.965	.961	62

Table 6: Model Fit Statistics in Twin and Sibling Sample using Symptom Count Variables, Replicating Diagnoses used in NESARC.

Model	RMSEA	CFI	TLI	Free Parameters
Base Model in Male Offspring	0.024	0.973	0.965	69
Base Model in Female Offspring	0.017	.987	.983	69

Table 7: Model Fit Statistics for the Extended Model in Twin and Sibling Sample using Symptom Count Diagnostic Variables

Model	RMSEA	CFI	TLI	Free Parameters
Base Model in Male Offspring	.034	.956	.951	111
Base Model in Female Offspring	.030	.960	.955	111

Table 8: Testing Invariance across Gender in NESARC by Comparing Less to More Constrained Models				
Model:	RMSEA	CFI	TLI	Free Parameters
Less Constrained Model	**0.015**	**0.979**	**0.973**	**84**
Constrained Model	0.014	0.979	0.974	78
	DIFFTEST Value	df	*p*-value	
DIFFTEST	30.721	6	<0.0001	

Table 9: Testing Invariance across Gender by Comparing Less to More Constrained Models in Twin and Sibling Sample using Dichotomous Diagnostic Variables

Model:	RMSEA	CFI	TLI	Free Parameters
Less Constrained Model	**.009**	**.994**	**.992**	**80**
Constrained Model	.023	.955	.946	64
	value	df	P-value	
DIFFTEST	187.809	16	<.0001	

Table 10: Testing Invariance across Gender by Comparing Less to More Constrained Models in Twin and Sibling Sample using Symptom Count Variables

Model:	RMSEA	CFI	TLI	Free Parameters
Less Constrained Model	**0.022**	**0.977**	**0.972**	**124**
Constrained Model	0.033	0.936	0.934	94
	value	df	P-value	
DIFFTEST	344.064	30	<0.0001	

Table 11: Associations between Parent and Offspring Latent Liability Compared Across Gender in NESARC

Main effects	CFI	TLI	RMSEA	Free Parameters	DIFFTEST	DF	*p*-value	Outcome
Externalizing constrained across parent and offspring gender	0.979	0.974	0.014	81	5.125	3	0.1629	Constrain
Fear constrained across parent and offspring gender	0.98	0.974	0.014	81	2.883	3	0.4100	Constrain
Fear and Externalizing constrained across parent and offspring gender	0.98	0.975	0.014	78	7.735	6	0.2582	Constrain
Distress constrained across parent and offspring gender	0.979	0.974	0.014	81	8.919	3	0.0304	Do not constrain
Interactions								
Distress constrained across mothers and fathers in female offspring	0.98	0.975	0.014	77	5.302	1	0.0213	Do not constrain
Distress constrained across male offspring	0.98	0.976	0.014	77	0.666	1	0.4144	Constrain
Distress constrained across fathers in male and female offspring	0.98	0.976	0.014	77	2.769	1	0.0961	Constrain
Distress constrained across moms in male vs female offspring	0.98	0.976	0.014	77	4.454	1	0.0348	Do not constrain
Final model: Distress constrained across mothers and fathers in male offspring and fathers in female offspring	**0.98**	**0.976**	**0.014**	**76**	**3.345**	**2**	**0.1878**	**Constrain**

Table 12: Comparing Regressions of Offspring Latent Factors on Parent Latent Externalizing in NESARC

		Paternal regressions: Regression Coefficient (St. error)				Maternal regressions: Regression Coefficient (St. error)			
		Male offspring	*p*-value	Female offspring	*p*- value	Male offspring	*p*- value	Female offspring	*p*- value
Offspring Ext. on Parent Ext.	Unconstrained	.469* (.099)	<.001	.372* (.079)	<.001	.161 (.105)	0.126	.313* (.083)	<.001
	Constrained	**.331 (.008), *p* <.001**							
Offspring Fear on Parent Ext.	Unconstrained	.266* (.135)	0.048	.358* (.104)	<0.001	.170 (.143)	0.235	.121 (.111)	0.276
	Constrained	**.233 (.000), *p* <.001**							
Offspring Distress on Parent Ext.	Unconstrained	.327* (.110)	0.003	.122 (.077)	0.155	.116 (.120)	0.336	.394* (.081)	<.001
	Constrained	**.222*(.012)**	**<.001**	**0.214* (.015)**	**<.001**	**.222*(.012)**	**<.001**	**.301* (.025)**	**<.001**

Table 13: Associations between Parent and Offspring Latent Liability Compared across Gender in Twin and Sibling Study using Dichotomous Diagnostic Variables

Main effects	CFI	TLI	RMSEA	Free Param.	DIFFTEST	DF	p-value	Outcome
Externalizing constrained across parent and offspring gender	0.993	0.991	0.009	77	4.429	3	0.2187	Constrain
Fear constrained across parent and offspring gender	0.993	0.991	0.009	77	6.100	3	0.1068	Constrain
Fear and Externalizing constrained across parent and offspring gender	0.993	0.991	0.009	74	9.798	6	0.1334	Constrain
Distress constrained across parent and offspring gender	0.992	0.990	0.010	77	9.418	3	0.0242	Do not constrain
Interactions								
Maternal and Paternal distress constrained across female offspring	0.992	0.990	0.010	73	2.905	1	0.0883	Constrain
Maternal and Paternal distress constrained across male offspring	0.993	0.991	0.009	73	1.147	1	0.2842	Constrain
Distress constrained across fathers in male and female offspring	0.993	0.991	0.009	73	2.769	1	0.2781	Constrain
Distress constrained across moms in male vs female offspring	0.993	0.991	0.009	73	0.064	1	0.8000	Constrain
Distress constrained across mothers and fathers in female offspring and fathers in male offspring	0.993	0.991	0.009	72	3.021	2	0.2208	Constrain
Distress constrained across mother and fathers in female offspring and mothers in male offspring	0.992	0.990	0.010	72	6.695	2	0.0352	Do Not Constrain

Distress constrained across mothers and fathers in male offspring and mothers in female offspring	0.993	0.991	0.009	72	1.332	2	0.5138	Constrain
Distress constrained across mothers and fathers in male offspring and fathers in female offspring	0.992	0.989	0.010	72	8.427	2	0.0148	Do Not Constrain
Distress constrained across mothers and fathers in male offspring, separately constrained in mothers and fathers in female offspring	**0.992**	**0.990**	**0.010**	**72**	**4.327**	**2**	**0.1149**	**Constrain**
Distress constrained across male and female offspring for mothers and male and female offspring for fathers.	0.992	0.990	0.010	72	5.294	2	0.0709	Constrain

Table 14: Comparing Regressions of Offspring Latent Factors on Parent Latent Externalizing in Twin and Sibling Study using Dichotomous Diagnostic Variables

		Paternal regressions: Regression Coefficient (St. error)				Maternal regressions: Regression Coefficient (St. error)			
		Male offspring	*p*-value	Female offspring	*p*-value	Male offspring	*p*-value	Female offspring	*p*-value
Offspring Ext. on Parent Externalizing	unconstrained	.305* (.078)	<.001	.043 (.110)	0.692	.020 (.092)	0.825	.312* (.125)	0.013
	constrained	**0.170* (.021), p<.001**							
Offspring Fear on Parent Externalizing	unconstrained	.110 (.127)	0.385	-.326 (.174)	0.062	.023 (.153)	0.883	.492* (.204)	0.016
	constrained	**0.055 (.033), p=.099**							
Offspring Distress on Parent Externalizing	unconstrained	.101 (.122)	0.408	-.136 (.123)	0.269	.291* (.126)	0.021	.300* (.147)	0.041
	constrained	**-0.045 (.081), p=.580**				**0.289* (.093), p=.002**			

Table 15: Associations between Parent and Offspring Latent Liability Compared across Gender in Twin and Sibling Study using Symptom Count Variables

Main effects	CFI	TLI	RMSEA	Free Param.	DIFFTEST	DF	*p*-value	Outcome
Externalizing constrained across parent and offspring gender	0.979	0.975	0.020	121	3.342	3	0.3418	Constrain
Fear constrained across parent and offspring gender	0.976	0.971	0.022	121	9.506	3	0.0233	Do not constrain
Distress constrained across parent and offspring gender	0.977	0.973	0.021	121	4.919	3	0.1778	Constrain
Externalizing and Distress constrained across parent and offspring gender	0.979	0.975	0.020	118	7.611	6	0.2680	Constrain
Interactions								
Maternal and Paternal fear constrained across female offspring	0.979	0.976	0.020	117	1.185	1	0.2764	Constrain
Maternal and Paternal fear constrained across male offspring	0.979	0.976	0.020	117	0.160	1	0.6895	Constrain
Fear constrained across fathers in male and female offspring	0.979	0.976	0.020	117	0.222	1	0.6377	Constrain
Fear constrained across moms in male vs female offspring	0.979	0.976	0.020	117	0.997	1	0.3181	Constrain
Fear constrained across mothers and fathers in female offspring and fathers in male offspring	0.979	0.976	0.020	116	3.149	2	0.2072	Constrain
Fear constrained across mother and fathers in female offspring and mothers in male offspring	0.979	0.976	0.020	116	1.338	2	0.5122	Constrain

Fear constrained across mothers and fathers in male offspring and mothers in female offspring	0.979	0.976	0.020	116	4.423	2	0.1096	Constrain
Fear constrained across mothers and fathers in male offspring and fathers in female offspring	0.980	0.976	0.020	116	0.219	2	0.8965	Constrain
Fear constrained across mothers and fathers in male offspring, separately constrained in mothers and fathers in female offspring	**0.979**	**0.976**	**0.020**	**116**	**1.262**	**2**	**0.5320**	**Constrain**
Fear constrained across male and female offspring for mothers and male and female offspring for fathers.	0.978	0.975	0.020	116	7.560	2	0.0228	Do Not Constrain

Table 16: Comparing Regressions of Offspring Latent Factors on Parent Latent Externalizing in Twin and Sibling Study using Symptom Count Variables

		Paternal regressions: Regression Coefficient (St. error)				Maternal regressions: Regression Coefficient (St. error)			
		Male offspring	*p*-value	Female offspring	*p*-value	Male offspring	*p*-value	Female offspring	*p*-value
Offspring Ext. on Parent Externalizing	unconstrained	.270* (.067)	<.001	.067 (.073)	.353	.063 (.080)	.431	.261 (.085)	.066
	constrained	**.167* (.017), p<.001**							
Offspring Fear on Parent Externalizing	unconstrained	-.079 (.111)	.478	-.016 (.095)	.864	.018 (.127)	.888	.200(.109)	.066
	constrained	**-.035 (.036)**	**.341**	**.086* (.028)**	**.002**	**-.035* (.036)**	**.341**	**.086*(.028)**	**.002**
Offspring Distress on Parent Externalizing	unconstrained	.039 (.090)	.667	-.064 (.079)	.424	.213* (.097)	.028	.274*(.093)	.003
	constrained	**.104* (.020), p<.001**							

Table 17: Associations between Parent Externalizing and Externalizing in Same- and Opposite- Sex Offspring in NESARC

Interaction: Externalizing	Loading	S.E.	P-value	DIFFTEST	
Male offspring with Fathers	0.469	0.099	<.001	Value	0.456
Female offspring with Fathers	0.372	0.079	<.001	df	1
Constrained	0.434/.414	0.063/0.060	<.001	P-value	0.4997
Male offspring with Fathers	0.469	0.099	<.001	Value	2.615
Male offspring with Mothers	0.161	0.105	0.126	df	1
Constrained	0.318	0.013	<.001	P-value	0.1059
Female offspring with Mothers	0.313	0.083	<.001	Value	1.489
Male offspring with Mothers	0.161	0.105	0.126	df	1
Constrained	0.250/240	0.066/0.063	<.001	P-value	0.2224
Female offspring with Mothers	0.313	0.083	<.001	Value	0.173
Female offspring with Fathers	0.372	0.104	<.001	df	1
Constrained	0.343	0.011	<.001	P-value	0.6773
Female offspring with Mothers	0.313	0.083	<.001	Value	1.351
Male offspring with Fathers	0.469	0.099	<.001	df	1
Constrained	0.385/0.366	0.068/0.062	<.001	P-value	0.2451

Table 18: Associations between Parent Externalizing and Fear in Same and Opposite-Sex Offspring in NESARC

Interaction: Fear	Loading	S.E.	P-value	DIFFTEST	
Male offspring with Fathers	0.266	0.135	0.048	Value	0.232
Female offspring with Fathers	0.358	0.104	0.001	df	1
Constrained	0.331/0.324	0.084/0.083	<.001	P-value	0.6299
Male offspring with Fathers	0.266	0.135	0.048	Value	0.173
Male offspring with Mothers	0.170	0.143	0.235	df	1
Constrained	0.219	0.016	<.001	P-value	0.6776
Female offspring with Mothers	0.121	0.111	0.276	Value	0.027
Male offspring with Mothers	0.170	0.143	0.235	df	1
Constrained	0.136/0.133	0.089/0.088	0.129	P-value	0.8699
Female offspring with Mothers	0.121	0.111	0.276	Value	1.089
Female offspring with Fathers	0.358	0.104	0.001	df	1
Constrained	0.224	0.012	<.001	P-value	0.2968
Female offspring with Mothers	0.121	0.111	0.276	Value	0.687
Male offspring with Fathers	0.266	0.135	0.048	df	1
Constrained	0.178/0.174	0.089/0.086	0.042	P-value	0.4073

Table 19: Associations between Parent Externalizing and Distress in Same- and Opposite-Sex Offspring in NESARC

Interaction: Distress	Loading	S.E.	P-value	DIFFTEST	
Male offspring with Fathers	0.327	0.110	0.003	Value	2.466
Female offspring with Fathers	0.122	0.077	0.115	df	1
Constrained	0.1870.180	0.062/0.059	0.002	P-value	0.1163
Male offspring with Fathers	0.327	0.110	0.003	Value	0.924
Male offspring with Mothers	0.116	0.120	0.336	df	1
Constrained	0.224	0.013	<.001	P-value	0.3366
Female offspring with Mothers	**0.394**	**0.081**	**<.001**	**Value**	**4.238**
Male offspring with Mothers	**0.116**	**0.120**	**0.336**	**df**	**1**
Constrained	0.327/0.318	0.066/0.064	<.001	**P-value**	**0.0395**
Female offspring with Mothers	0.394	0.081	<.001	Value	3.824
Female offspring with Fathers	0.122	0.077	0.115	df	1
Constrained	0.255	0.099	<.001	P-value	0.0505
Female offspring with Mothers	0.394	0.081	<.001	Value	0.309
Male offspring with Fathers	0.327	0.110	0.003	df	1
Constrained	0.380/0.366	0.067/0.063	<.001	P-value	0.5783

Table 20: Associations between Parent Externalizing and Externalizing in Same- and Opposite- Sex Offspring in Twin and Sibling Study using Dichotomous Diagnostic Variables

Interaction: Externalizing	Loading	S.E.	P-value	DIFFTEST	
Male offspring with Fathers	**0.305**	**.078**	**<.001**	**Value**	**4.035**
Female offspring with Fathers	**0.043**	**.110**	**.692**	**df**	**1**
Constrained	0.209/0.207	0.060/0.060	<.001	**P-value**	**.0446**
Male offspring with Fathers	0.305	.078	<.001	Value	3.326
Male offspring with Mothers	0.020	.092	.825	df	1
Constrained	0.176	.030	<.001	P-value	.0682
Female offspring with Mothers	0.312	.125	.013	Value	3.719
Male offspring with Mothers	0.020	.092	.825	df	1
Constrained	0.124/0.126	0.069/0.070	.071	P-value	.0638
Female offspring with Mothers	0.312	.125	.013	Value	1.516
Female offspring with Fathers	0.043	.110	.692	df	1
Constrained	.165	.028	<.001	P-value	.2182
Female offspring with Mothers	0.312	.125	.013	Value	0.005
Male offspring with Fathers	0.305	.078	<.001	df	1
Constrained	0.307/0.305	0.066/0.066	<.001	P-value	.9464

Table 21: Associations between Parent Externalizing and Fear in Same- and Opposite- Sex Offspring in Twin and Sibling Study using Dichotomous Diagnostic Variables

Interaction: Fear	Loading	S.E.	P-value	DIFFTEST	
Male offspring with Fathers	**0.110**	**.127**	**.385**	**Value**	**4.644**
Female offspring with Fathers	**-0.326**	**.174**	**.062**	**df**	**1**
Constrained	-0.094/-0.094	0.100/0.100	0.348	**P-value**	**0.0312**
Male offspring with Fathers	0.110	.127	.385	Value	0.113
Male offspring with Mothers	0.023	.153	.883	df	1
Constrained	0.071	0.054	0.186	P-value	0.7371
Female offspring with Mothers	0.492	.204	.016	Value	3.670
Male offspring with Mothers	0.023	.153	.883	df	1
Constrained	0.237/0.238	0.120/0.121	0.048	P-value	0.0554
Female offspring with Mothers	**0.492**	**.204**	**.016**	**Value**	**7.013**
Female offspring with Fathers	**-0.326**	**.174**	**.062**	**df**	**1**
Constrained	0.043	0.042	0.312	**P-value**	**0.0081**
Female offspring with Mothers	0.492	.204	.016	Value	2.887
Male offspring with Fathers	0.110	.127	.385	df	1
Constrained	0.252/0.252	0.107/0/108	0.019	P-value	0.0893

Table 22: Associations between Parent Externalizing and Distress in Same- and Opposite- Sex Offspring in Twin and Sibling Study using Dichotomous Diagnostic Variables

Interaction: Distress	Loading	S.E.	P-value	DIFFTEST	
Male offspring with Fathers	0.101	.122	.408	Value	1.744
Female offspring with Fathers	-0.136	.123	.269	df	1
Constrained	-0.040/-0.043	0.085/0.091	.636	P-value	0.1867
Male offspring with Fathers	0.101	.122	.408	Value	0.804
Male offspring with Mothers	0.291	.126	.021	df	1
Constrained	0.190	0.054	<.001	P-value	0.3699
Female offspring with Mothers	0.492	.204	.016	Value	.001
Male offspring with Mothers	0.291	.126	.021	df	1
Constrained	0.290/0.301	0.094/0.099	.002	P-value	0.9700
Female offspring with Mothers	0.492	.204	.016	Value	3.024
Female offspring with Fathers	-0.136	.123	.269	df	1
Constrained	0.060	.033	.064	P-value	0.0820
Female offspring with Mothers	0.492	.204	.016	Value	1.031
Male offspring with Fathers	0.101	.122	.408	df	1
Constrained	0.187/0.197	0.089/0.094	.036	P-value	0.3100

Table 23: Associations between Parent Externalizing and Distress in Same- and Opposite- Sex Offspring in Twin and Sibling Study using Symptom Count Variables

Interaction: Distress	Loading	S.E.	P-value	DIFFTEST	
Male offspring with Fathers	0.039	.090	.667	Value	.679
Female offspring with Fathers	-0.064	.079	.424	df	1
Constrained	-0.015/-0.015	0.060/0.060	.797	P-value	.4098
Male offspring with Fathers	0.039	.090	.667	Value	1.050
Male offspring with Mothers	0.213	.097	.028	df	1
Constrained	0.120	.031	<.001	P-value	.3054
Female offspring with Mothers	0.274	.093	.003	Value	.176
Male offspring with Mothers	0.213	.097	.028	df	1
Constrained	0.243/0.245	0.067/0.068	<.001	P-value	.6750
Female offspring with Mothers	**0.274**	**.093**	**.003**	**Value**	**4.731**
Female offspring with Fathers	**-0.064**	**.079**	**.424**	**df**	**1**
Constrained	0.093	.026	<.001	**P-value**	**.0296**
Female offspring with Mothers	0.274	.093	.003	Value	3.411
Male offspring with Fathers	0.039	.090	.667	df	1
Constrained	0.144/0.145	0.063/0.063	.022	P-value	.0648

Table 24: Associations between Parent Externalizing and Fear in Same- and Opposite- Sex Offspring in Twin and Sibling Study using Symptom Count Variables

Interaction: Fear	Loading	S.E.	P-value	DIFFTEST	
Male offspring with Fathers	-0.079	.111	.478	Value	.171
Female offspring with Fathers	-0.016	.095	.864	df	1
Constrained	-0.046/-0.045	0.074/0.072	0.533	P-value	0.6792
Male offspring with Fathers	-0.079	.111	.478	Value	0.170
Male offspring with Mothers	0.018	.127	.888	df	1
Constrained	-0.035	.037	0.344	P-value	0.6804
Female offspring with Mothers	0.200	.109	.066	Value	1.159
Male offspring with Mothers	0.018	.127	.888	df	1
Constrained	0.124/0.123	0.083/0.083	0.138	P-value	0.2816
Female offspring with Mothers	0.200	.109	.066	Value	1.264
Female offspring with Fathers	-0.016	.095	.864	df	1
Constrained	0.085	.028	0.002	P-value	0.2609
Female offspring with Mothers	0.200	.109	.066	Value	3.306
Male offspring with Fathers	-0.079	.111	.478	df	1
Constrained	0.060/0.059	0.077/0/077	0.440	P-value	0.0690

Table 25: Associations between Parent Externalizing and Externalizing in Same- and Opposite- Sex Offspring in Twin and Sibling Study using Symptom Count Variables

Interaction: Externalizing	Loading	S.E.	P-value	DIFFTEST	
Male offspring with Fathers	**0.270**	**.067**	**<.001**	**Value**	**4.158**
Female offspring with Fathers	**0.067**	**.073**	**.353**	**df**	**1**
Constrained	0.181/0.180	0.050/0.050	<.001	**P-value**	**0.0414**
Male offspring with Fathers	0.270	.067	<.001	Value	2.075
Male offspring with Mothers	0.063	.080	.431	df	1
Constrained	0.176	.025	<.001	P-value	0.1498
Female offspring with Mothers	0.261	.085	.002	Value	2.721
Male offspring with Mothers	0.063	.080	.431	df	1
Constrained	0.156/0.158	0.058/0.059	.007	P-value	0.0991
Female offspring with Mothers	0.261	.085	.002	Value	1.713
Female offspring with Fathers	0.067	.073	.353	df	1
Constrained	.159	.025	<.001	P-value	0.1906
Female offspring with Mothers	0.261	.085	.002	Value	0.004
Male offspring with Fathers	0.270	.067	<.001	df	1
Constrained	0.267/0.266	0.053/0.052	<.001	P-value	0.9523

Table 26: Specific Liability Conferred from Parent Diagnoses to Same Offspring Diagnoses in NESARC

		Model fit						
Model:	Correlated with:	RMSEA	CFI	TLI	Correlation	SE	*p*-value	Free Param.
Male off. ASPD	**Maternal ASPD**	**0.014**	**0.981**	**0.976**	**0.416***	**0.097**	**<.001**	**78**
Female off. ASPD					**0.304***	**0.045**	**<.001**	**78**
Male off. Alcohol	Maternal Alcohol	0.014	0.98	0.975	0.026	0.048	0.583	78
Female off. Alcohol					0.063	0.049	0.199	78
Male off. Drug	Maternal Drug	0.014	0.98	0.975	-0.128	0.17	0.452	78
Female off. Drug					0.141	0.117	0.228	78
Male off. ASPD	**Paternal ASPD**	**0.013**	**0.983**	**0.979**	**0.401***	**0.075**	**<.001**	**78**
Female off. ASPD					**0.434***	**0.117**	**<.001**	**78**
Male off. Alcohol	Paternal Alcohol	0.014	0.98	0.975	0.101	0.041	0.013	78
Female off. Alcohol					0.048	0.038	0.204	78
Male off. Drug	Paternal Drug	0.014	0.98	0.975	0.036	0.127	0.779	78
Female off. Drug					0.034	0.044	0.438	78

Table 27: Residual Correlations between Parent Antisocial Traits and Offspring Diagnoses in NESARC

Model:	Correlated with:	RMSEA	CFI	TLI	Correlation	SE	*p*-value	Free param
Male off. Alcohol	Maternal ASPD	0.014	0.98	0.976	-0.316	0.107	0.003	78
Female off. Alcohol					-0.147	0.085	0.085	78
Male off. Alcohol	Paternal ASPD	0.014	0.98	0.976	-0.099	0.076	0.190	78
Female off. Alcohol					-0.322	0.093	0.001	78
Male off. Drug	Maternal ASPD	0.014	0.98	0.975	-0.057	0.122	0.638	78
Female off. Drug					-0.198	0.139	0.156	78
Male off. Drug	Paternal ASPD	0.014	0.98	0.975	-0.024	0.147	0.869	78
Female off. Drug					-0.282	0.126	0.026	78
Male off. Nicotine	Maternal ASPD	0.014	0.98	0.976	-0.196	0.092	0.033	78
Female off. Nicotine					-0.219	0.073	0.003	78
Male off. Nicotine	**Paternal ASPD**	**0.014**	**0.98**	**0.976**	**-0.254**	**0.071**	**<.001**	**78**
Female off. Nicotine					-0.054	0.074	0.461	78
Male off. Panic	Maternal ASPD	0.014	0.98	0.975	0.115	0.134	0.392	78
Female off. Panic					0.154	0.088	0.080	78
Male off. Panic	Paternal ASPD	0.014	0.98	0.975	-0.018	0.091	0.840	78
Female off. Panic					0.029	0.082	0.727	78
Male off. Social Ph.	Maternal ASPD	0.014	0.98	0.976	0.041	0.114	0.719	78
Female off. Social Ph					0.170	0.086	0.048	78
Male off. Social Ph.	Paternal ASPD	0.014	0.98	0.975	0.169	0.083	0.043	78
Female off. Social Ph					0.277	0.081	0.001	78

Male off. Specific Ph.	Maternal ASPD	0.014	0.98	0.975	0.073	0.103	0.482	78
Female off. Specific Ph					0.027	0.064	0.678	78
Male off. Specific Ph.	Paternal ASPD	0.014	0.98	0.976	0.145	0.074	0.050	78
Female off. Specific Ph					0.163	0.069	0.018	78
Male off. MDD	Maternal ASPD	0.014	0.98	0.975	-0.017	0.154	0.911	78
Female off. MDD					0.223	0.101	0.028	78
Male off. MDD	Paternal ASPD	0.014	0.98	0.975	0.131	0.103	0.203	78
Female off. MDD					0.287	0.096	0.003	78
Male off. Dysthymia	**Maternal ASPD**	**0.014**	**0.98**	**0.976**	-0.081	0.167	0.628	78
Female off. Dysthymia					**0.331**	**0.093**	**<.001**	**78**
Male off. Dysthymia	Paternal ASPD	0.014	0.98	0.975	-0.085	0.130	0.516	78
Female off. Dysthymia					0.143	0.098	0.146	78
Male off. GAD	Maternal ASPD	0.014	0.98	0.975	-0.082	0.131	0.534	78
Female off. GAD					0.190	0.090	0.035	78
Male off. GAD	Paternal ASPD	0.014	0.98	0.975	-0.073	0.107	0.497	78
Female off. GAD					0.017	0.095	0.856	78

Table 28: Residual Correlations between Parent Drug Use Disorder Traits and Offspring Diagnoses in NESARC

Model:	Correlated with:	RMSEA	CFI	TLI	Correlation	SE	*p*-value	Free Param.
Male off. Alcohol	Maternal Drug	0.014	0.98	0.976	-0.351	0.106	0.001	78
Female off. Alcohol					-0.114	0.079	0.148	78
Male off. Alcohol	Paternal Drug	0.014	0.98	0.976	-0.268	0.088	0.002	78
Female off. Alcohol					-0.122	0.072	0.090	78
Male off. ASPD	Maternal Drug	0.014	0.98	0.976	0.308	0.101	0.002	78
Female off. ASPD					0.160	0.095	0.094	78
Male off. ASPD	**Paternal Drug**	**0.014**	**0.98**	**0.976**	**0.339**	**0.095**	**<.001**	**78**
Female off. ASPD					0.275	0.093	0.003	78
Male off. Nicotine	Maternal Drug	0.014	0.98	0.976	-0.075	0.099	0.448	78
Female off. Nicotine					-0.218	0.075	0.004	78
Male off. Nicotine	Paternal Drug	0.014	0.98	0.976	-0.200	0.071	0.005	78
Female off. Nicotine					-0.072	0.053	0.174	78
Male off. Panic	Maternal Drug	0.014	0.98	0.975	-0.102	0.154	0.507	78
Female off. Panic					-0.065	0.092	0.478	78
Male off. Panic	Paternal Drug	0.013	0.983	0.979	-0.115	0.138	0.403	78
Female off. Panic					-0.004	0.085	0.959	78
Male off. Social Ph.	Maternal Drug	0.014	0.98	0.975	-0.143	0.151	0.343	78
Female off. Social Ph					-0.159	0.095	0.093	78
Male off. Social Ph.	Paternal Drug	0.014	0.98	0.975	-0.120	0.116	0.302	78
Female off. Social Ph					-0.161	0.079	0.041	78

Male off. Specific Ph.	Maternal Drug	0.014	0.98	0.975	-0.039	0.107	0.715	78
Female off. Specific Ph					-0.069	0.067	0.308	78
Male off. Specific Ph.	Paternal Drug	0.014	0.98	0.975	0.112	0.091	0.219	78
Female off. Specific Ph					-0.022	0.061	0.716	78
Male off. MDD	Maternal Drug	0.014	0.98	0.975	-0.172	0.169	0.307	78
Female off. MDD					0.101	0.106	0.342	78
Male off. MDD	Paternal Drug	0.014	0.98	0.975	-0.029	0.139	0.837	78
Female off. MDD					0.058	0.100	0.560	78
Male off. Dysthymia	Maternal Drug	0.014	0.98	0.975	-0.223	0.206	0.278	78
Female off. Dysthymia					0.042	0.101	0.678	78
Male off. Dysthymia	Paternal Drug	0.014	0.98	0.975	-0.167	0.141	0.235	78
Female off. Dysthymia					-0.168	0.097	0.081	78
Male off. GAD	Maternal Drug	0.014	0.98	0.975	-0.176	0.167	0.294	78
Female off. GAD					-0.085	0.093	0.364	78
Male off. GAD	**Paternal Drug**	**0.014**	**0.98**	**0.976**	-0.151	0.145	0.300	78
Female off. GAD					**-0.405**	**0.096**	**<.001**	**78**

Table 29: Residual Correlations between Parent Alcohol Use Disorder Traits and Offspring Diagnoses in NESARC

	Correlated with:	RMSEA	CFI	TLI	Correlation	SE	*p*-value	Free Param.
Male off. ASPD	Maternal Alcohol	0.014	0.98	0.975	0.093	0.059	0.112	78
Female off. ASPD					0.100	0.076	0.191	78
Male off. ASPD	Paternal Alcohol	0.014	0.98	0.975	0.073	0.048	0.129	78
Female off. ASPD					0.023	0.066	0.726	78
Male off. Drug	Maternal Alcohol	0.014	0.98	0.975	-0.163	0.105	0.120	78
Female off. Drug					-0.006	0.099	0.951	78
Male off. Drug	Paternal Alcohol	0.014	0.98	0.975	-0.014	0.076	0.859	78
Female off. Drug					-0.069	0.078	0.380	78
Male off. Nicotine	Maternal Alcohol	0.014	0.98	0.976	-0.153	0.048	0.001	78
Female off. Nicotine					-0.044	0.043	0.301	78
Male off. Nicotine	Paternal Alcohol	0.014	0.98	0.975	0.031	0.036	0.388	78
Female off. Nicotine					0.049	0.028	0.080	78
Male off. Panic	Maternal Alcohol	0.014	0.98	0.975	0.025	0.087	0.776	78
Female off. Panic					-0.135	0.053	0.011	78
Male off. Panic	Paternal Alcohol	0.014	0.98	0.975	-0.011	0.058	0.058	78
Female off. Panic					-0.028	0.040	0.475	78
Male off. Social Ph.	Maternal Alcohol	0.014	0.98	0.975	-0.136	0.075	0.070	78
Female off. Social Ph					-0.024	0.059	0.683	78
Male off. Social Ph.	Paternal Alcohol	0.014	0.98	0.975	-0.109	0.056	0.052	78
Female off. Social Ph					0.004	0.042	0.927	78

Male off. Specific Ph.	Maternal Alcohol	0.014	0.98	0.975	-0.108	0.061	0.074	78
Female off. Specific Ph					-0.028	0.046	0.550	78
Male off. Specific Ph.	Paternal Alcohol	0.014	0.98	0.975	-0.074	0.043	0.089	78
Female off. Specific Ph					0.022	0.032	0.502	78
Male off. MDD	Maternal Alcohol	0.014	0.98	0.975	-0.131	0.089	0.142	78
Female off. MDD					-0.014	0.069	0.839	78
Male off. MDD	Paternal Alcohol	0.014	0.98	0.975	-0.089	0.062	0.153	78
Female off. MDD					-0.031	0.046	0.507	78
Male off. Dysthymia	Maternal Alcohol	0.014	0.98	0.975	-0.064	0.105	0.544	78
Female off. Dysthymia					0.097	0.061	0.115	78
Male off. Dysthymia	Paternal Alcohol	0.014	0.98	0.975	-0.084	0.075	0.257	78
Female off. Dysthymia					-0.077	0.050	0.122	78
Male off. GAD	Maternal Alcohol	0.014	0.98	0.975	-0.077	0.082	0.351	78
Female off. GAD					-0.032	0.057	0.571	78
Male off. GAD	Paternal Alcohol	0.014	0.98	0.975	-0.058	0.065	0.376	78
Female off. GAD					-0.081	0.047	0.086	78

Table 30: Specific Liability Conferred from Parent Diagnoses to Same Offspring Diagnoses in Twin Study using Dichotomous Diagnostic Variable

		Model fit						
Model:	Correlated with:	RMSEA	CFI	TLI	Correlation	SE	*p*-value	Free param
Male off. ASPD	Maternal ASPD	0.010	0.992	0.990	-0.125	0.157	0.426	74
Female off. ASPD					0.421	0.300	0.160	74
Male off. Alcohol	Maternal Alcohol	0.010	0.992	0.990	-0.057	0.157	0.719	74
Female off. Alcohol					0.028	0.219	0.899	74
Male off. Drug	Maternal Drug	0.010	0.992	0.990	-0.120	0.233	0.607	74
Female off. Drug					-0.147	0.300	0.624	74
Male off. ASPD	Paternal ASPD	0.009	0.993	0.991	0.290	0.124	0.019	74
Female off. ASPD					-0.423	0.186	0.023	74
Male off. Alcohol	Paternal Alcohol	0.009	0.993	0.991	0.147	0.085	0.083	74
Female off. Alcohol					0.243	0.124	0.050	74
Male off. Drug	Paternal Drug	0.010	0.992	0.990	0.257	0.176	0.145	74
Female off. Drug					-0.104	0.278	0.710	74

Table 31: Specific Liability Conferred from Parent Diagnoses to Same Offspring Diagnoses in Twin Study using Symptom Count Variable

		Model fit			Correlation	SE	*p*-value	Free Param.
Model:	Correlated with:	RMSEA	CFI	TLI				
Male off. ASPD	Maternal ASPD	0.026	0.962	0.960	-0.057	0.144	0.691	103
Female off. ASPD					0.133	0.132	0.314	103
Male off. Alcohol	Maternal Alc	0.026	0.962	0.960	-0.019	0.097	0.848	103
Female off. Alcohol					-0.144	0.106	0.172	103
Male off. Drug	Maternal Drug	0.026	0.962	0.959	0.030	0.195	0.877	103
Female off. Drug					0.177	0.170	0.298	103
Male off. ASPD	**Paternal ASPD**	**0.026**	**0.964**	**0.961**	**0.347**	**0.094**	**<.001**	**103**
Female off. ASPD					-0.053	0.098	0.587	103
Male off. Alcohol	Paternal Alc	0.026	0.962	0.960	0.073	0.067	0.274	103
Female off. Alcohol					0.058	0.081	0.469	103
Male off. Drug	Paternal Drug	0.026	0.962	0.960	0.251	0.187	0.180	103
Female off. Drug					-0.007	0.157	0.964	103

Table 32: Residual Correlations Between Parent Adult Antisocial Behavior and Offspring Diagnoses in Twin Study using Dichotomous Diagnostic Variables

Model:	Correlated with:	RMSEA	CFI	TLI	Correlation	SE	*p*-value	Free param
Male off. Alcohol	Maternal ASPD	0.010	0.992	0.990	-0.030	0.268	0.911	74
Female off. Alcohol					0.138	0.207	0.503	74
Male off. Alcohol	Paternal ASPD	0.010	0.992	0.990	-0.050	0.134	0.711	74
Female off. Alcohol					0.016	0.145	0.914	74
Male off. Drug	Maternal ASPD	0.009	0.994	0.992	-0.671	0.271	0.013	74
Female off. Drug					0.744	0.265	0.005	74
Male off. Drug	Paternal ASPD	0.010	0.992	0.990	0.008	0.154	0.961	74
Female off. Drug					-0.074	0.171	0.667	74
Male off. Nicotine	Maternal ASPD	0.010	0.993	0.991	-0.132	0.202	0.516	74
Female off. Nicotine					0.493	0.208	0.017	74
Male off. Nicotine	Paternal ASPD	0.010	0.992	0.990	0.088	0.142	0.537	74
Female off. Nicotine					-0.070	0.128	0.583	74
Male off. Panic	Maternal ASPD	0.010	0.992	0.990	-0.026	1.234	0.983	74
Female off. Panic					0.113	0.261	0.666	74
Male off. Panic	Paternal ASPD	0.010	0.992	0.990	0.247	0.374	0.509	74
Female off. Panic					-0.197	0.162	0.225	74
Male off. Social Ph.	Maternal ASPD	0.010	0.992	0.990	0.082	0.238	0.730	74
Female off. Social Ph					0.084	0.208	0.687	74
Male off. Social Ph.	Paternal ASPD	0.010	0.992	0.990	-0.208	0.191	0.278	74
Female off. Social Ph					-0.048	0.122	0.691	74
Male off. Specific Ph.	Maternal ASPD	0.010	0.992	0.990	0.082	0.332	0.800	74

Female off. Specific Ph.					0.249	0.184	0.175	74
Male off. Specific Ph.	Paternal ASPD	0.010	0.992	0.990	-0.370	0.251	0.141	74
Female off. Specific Ph					-0.178	0.127	0.163	74
Male off. MDD	Maternal ASPD	0.010	0.992	0.990	0.074	0.232	0.752	74
Female off. MDD					-0.226	0.230	0.325	74
Male off. MDD	Paternal ASPD	0.010	0.992	0.990	0.197	0.152	0.195	74
Female off. MDD					-0.089	0.107	0.405	74
Male off. GAD	Maternal ASPD	0.010	0.992	0.990	0.033	0.756	0.965	74
Female off. GAD					-0.148	0.962	0.877	74
Male off. GAD	Paternal ASPD	0.010	0.992	0.990	-0.240	0.354	0.499	74
Female off. GAD					-0.205	0.244	0.401	74

Table 33: Residual Correlations between Parent Drug Dependence and Offspring Diagnoses in Twin Study using Dichotomous Diagnostic Variables

Model:	Correlated with:	RMSEA	CFI	TLI	Correlation	SE	*p*-value	Free Param
Male off. Alcohol	Maternal Drug	0.010	0.992	0.990	-0.425	0.264	0.107	74
Female off. Alcohol					-0.006	0.240	0.979	74
Male off. Alcohol	Paternal Drug	0.010	0.992	0.990	0.073	0.151	0.631	74
Female off. Alcohol					-0.219	0.257	0.393	74
Male off. ASPD	Maternal Drug	0.010	0.992	0.990	0.013	0.208	0.951	74
Female off. ASPD					0.138	0.313	0.659	74
Male off. ASPD	Paternal Drug	0.010	0.993	0.991	0.178	0.142	0.211	74
Female off. ASPD					-0.596	0.318	0.061	74
Male off. Nicotine	Maternal Drug	0.010	0.992	0.990	-0.120	0.208	0.564	74
Female off. Nicotine					-0.204	0.215	0.343	74
Male off. Nicotine	Paternal Drug	0.010	0.992	0.990	-0.245	0.192	0.203	74
Female off. Nicotine					-0.210	0.234	0.369	74
Male off. Panic	Maternal Drug	0.010	0.992	0.990	-0.136	0.493	0.782	74
Female off. Panic					0.414	0.214	0.053	74
Male off. Panic	Paternal Drug	0.010	0.992	0.990	0.014	0.376	0.970	74
Female off. Panic					-0.009	0.240	0.969	74

Male off. Social Ph.	Maternal Drug	0.010	0.992	0.990	0.177	0.226	0.434	74
Female off. Social Ph					0.259	0.188	0.168	74
Male off. Social Ph.	Paternal Drug	0.010	0.993	0.991	0.160	0.168	0.340	74
Female off. Social Ph					-0.417	0.204	0.041	74
Male off. Specific Ph.	Maternal Drug	0.010	0.992	0.990	-0.229	0.369	0.534	74
Female off. Specific Ph.					0.011	0.223	0.960	74
Male off. Specific Ph.	Paternal Drug	0.010	0.992	0.990	0.080	0.235	0.733	74
Female off. Specific Ph					0.184	0.183	0.317	74
Male off. MDD	Maternal Drug	0.010	0.992	0.990	0.260	0.185	0.160	74
Female off. MDD					0.075	0.148	0.610	74
Male off. MDD	Paternal Drug	0.010	0.992	0.990	0.126	0.147	0.394	74
Female off. MDD					-0.206	0.175	0.239	74
Male off. GAD	Maternal Drug	0.010	0.992	0.990	0.010	0.422	0.981	74
Female off. GAD					0.021	0.250	0.933	74
Male off. GAD	Paternal Drug	0.010	0.992	0.990	0.481	0.269	0.074	74
Female off. GAD					0.002	0.324	0.995	74

Table 34: Residual Correlations between Parent Alcohol Dependence and Offspring Diagnoses in Twin Study using Dichotomous Diagnostic Variables

Model:	Correlated with:	RMSEA	CFI	TLI	Correlation	SE	*p*-value	Free param
Male off. ASPD	Maternal Alcohol	0.010	0.992	0.990	0.038	0.142	0.789	74
Female off. ASPD					-0.016	0.282	0.954	74
Male off. ASPD	Paternal Alcohol	0.010	0.992	0.990	0.142	0.100	0.156	74
Female off. ASPD					-0.052	0.143	0.716	74
Male off. Drug	Maternal Alcohol	0.010	0.992	0.990	0.022	0.161	0.892	74
Female off. Drug					-0.465	0.338	0.169	74
Male off. Drug	Paternal Alcohol	0.010	0.992	0.990	-0.187	0.112	0.096	74
Female off. Drug					-0.144	0.153	0.345	74
Male off. Nicotine	Maternal Alcohol	0.010	0.992	0.990	-0.209	0.155	0.177	74
Female off. Nicotine					0.188	0.199	0.345	74
Male off. Nicotine	Paternal Alcohol	0.010	0.993	0.991	-0.031	0.092	0.735	74
Female off. Nicotine					0.244	0.103	0.017	74
Male off. Panic	Maternal Alcohol	0.010	0.992	0.990	0.119	0.356	0.738	74
Female off. Panic					0.240	0.272	0.377	74
Male off. Panic	Paternal Alcohol	0.010	0.992	0.990	-0.013	0.218	0.952	74
Female off. Panic					-0.025	0.128	0.847	74

Male off. Social Ph.	Maternal Alcohol	0.010	0.992	0.990	-0.076	0.185	0.682	74
Female off. Social Ph					-0.078	0.195	0.691	74
Male off. Social Ph.	Paternal Alcohol	0.010	0.992	0.990	0.004	0.118	0.971	74
Female off. Social Ph.					-0.137	0.096	0.155	74
Male off. Specific Ph.	Maternal Alcohol	0.010	0.992	0.990	-0.248	0.274	0.367	74
Female off. Specific Ph.					0.156	0.238	0.513	74
Male off. Specific Ph.	Paternal Alcohol	0.010	0.992	0.990	0.202	0.141	0.152	74
Female off. Specific Ph.					-0.035	0.112	0.752	74
Male off. MDD	Maternal Alcohol	0.010	0.992	0.990	-0.050	0.157	0.752	74
Female off. MDD					-0.149	0.217	0.491	74
Male off. MDD	Paternal Alcohol	0.010	0.992	0.990	0.037	0.095	0.696	74
Female off. MDD					-0.058	0.095	0.541	74
Male off. GAD	Maternal Alcohol	0.010	0.992	0.990	-0.054	0.341	0.875	74
Female off. GAD					-0.133	0.308	0.666	74
Male off. GAD	Paternal Alcohol	0.010	0.992	0.990	0.160	0.204	0.431	74
Female off. GAD					-0.002	0.160	0.990	74

Table 35: Residual Correlations between Parent Adult Antisocial Behavior and Offspring Diagnoses in Twin Study using Symptom Count Variables

Model:	Correlated with:	RMSEA	CFI	TLI	Correlation	SE	*p*-value	Free param.
Male off. Alcohol	Maternal ASPD	0.026	0.963	0.960	-0.276	0.114	0.016	103
Female off. Alcohol					-0.043	0.118	0.715	103
Male off. Alcohol	Paternal ASPD	0.026	0.963	0.960	-0.166	0.079	0.035	103
Female off. Alcohol					0.016	0.145	0.914	103
Male off. Drug	Maternal ASPD	0.026	0.963	0.960	-0.106	0.163	0.515	103
Female off. Drug					0.351	0.146	0.016	103
Male off. Drug	Paternal ASPD	0.026	0.962	0.960	0.095	0.120	0.431	103
Female off. Drug					-0.086	0.126	0.493	103
Male off. Nicotine	Maternal ASPD	0.026	0.962	0.960	-0.164	0.107	0.126	103
Female off. Nicotine					-0.028	0.109	0.796	103
Male off. Nicotine	Paternal ASPD	0.026	0.962	0.959	0.003	0.076	0.964	103
Female off. Nicotine					-0.062	0.080	0.437	103
Male off. Panic	Maternal ASPD	0.026	0.963	0.960	-0.106	0.174	0.542	103
Female off. Panic					0.179	0.121	0.139	103
Male off. Panic	Paternal ASPD	0.026	0.963	0.960	0.044	0.124	0.724	103
Female off. Panic					-0.082	0.100	0.413	103

Male off. Social Ph.	Maternal ASPD	0.026	0.963	0.960	0.091	0.091	0.319	103
Female off. Social Ph					0.188	0.092	0.040	103
Male off. Social Ph.	Paternal ASPD	0.026	0.963	0.960	-0.002	0.071	0.975	103
Female off. Social Ph					0.137	0.071	0.054	103
Male off. Specific Ph.	Maternal ASPD	0.026	0.962	0.959	-0.068	0.144	0.636	103
Female off. Specific Ph.					-0.026	0.199	0.825	103
Male off. Specific Ph.	Paternal ASPD	0.026	0.963	0.960	-0.292	0.100	.003	103
Female off. Specific Ph					-0.073	0.099	0.457	103
Male off. MDD	Maternal ASPD	0.026	0.963	0.960	0.090	0.093	0.329	103
Female off. MDD					0.191	0.129	0.140	103
Male off. MDD	Paternal ASPD	0.026	0.962	0.960	-0.017	0.078	0.832	103
Female off. MDD					-0.057	0.101	0.573	103
Male off. GAD	Maternal ASPD	0.010	0.992	0.990	-0.125	0.173	0.468	103
Female off. GAD					0.173	0.142	0.222	103
Male off. GAD	Paternal ASPD	0.010	0.992	0.990	-0.208	0.120	0.084	103
Female off. GAD					-0.155	0.125	0.214	103

Table 36: Residual Correlations between Parent Drug Dependence and Offspring Diagnoses in Twin Study using Symptom Count Variables

Model:	Correlated with:	RMSEA	CFI	TLI	correlation	SE	*p*-value	Free Param.
Male off. Alcohol	Maternal Drug	0.026	0.963	0.960	-0.419	0.144	0.004	103
Female off. Alcohol					-0.134	0.135	0.323	103
Male off. Alcohol	Paternal Drug	0.026	0.963	0.960	-0.081	0.117	0.487	103
Female off. Alcohol					-0.211	0.124	0.090	103
Male off. ASPD	Maternal Drug	0.026	0.962	0.959	0.000	0.183	0.999	103
Female off. ASPD					0.120	0.148	0.417	103
Male off. ASPD	Paternal Drug	0.026	0.963	0.960	0.350	0.159	0.028	103
Female off. ASPD					-0.119	0.135	0.377	103
Male off. Nicotine	Maternal Drug	0.026	0.962	0.959	-0.109	0.127	0.390	103
Female off. Nicotine					0.078	0.124	0.528	103
Male off. Nicotine	Paternal Drug	0.026	0.962	0.960	-0.159	0.124	0.201	103
Female off. Nicotine					-0.104	0.126	0.411	103
Male off. Panic	Maternal Drug	0.026	0.962	0.960	0.190	0.218	0.383	103
Female off. Panic					0.136	0.178	0.443	103
Male off. Panic	Paternal Drug	0.026	0.963	0.960	0.088	0.170	0.606	103
Female off. Panic					-0.192	0.141	0.172	103

Male off. Social Ph.	Maternal Drug	0.026	0.962	0.960	0.040	0.110	0.715	103
Female off. Social Ph.					0.078	0.114	0.495	103
Male off. Social Ph.	Paternal Drug	0.026	0.963	0.960	0.110	0.088	0.211	103
Female off. Social Ph.					0.078	0.098	0.425	103
Male off. Specific Ph.	Maternal Drug	0.026	0.962	0.960	0.064	0.166	0.701	103
Female off. Specific Ph.					-0.181	0.146	0.215	103
Male off. Specific Ph.	Paternal Drug	0.026	0.963	0.960	-0.275	0.142	0.052	103
Female off. Specific Ph.					-0.034	0.140	0.809	103
Male off. MDD	Maternal Drug	0.026	0.963	0.960	0.198	0.120	0.097	103
Female off. MDD					0.155	0.163	0.340	103
Male off. MDD	Paternal Drug	0.026	0.963	0.960	0.170	0.106	0.107	103
Female off. MDD					-0.304	0.137	0.026	103
Male off. GAD	Maternal Drug	0.026	0.962	0.959	0.070	0.185	0.706	103
Female off. GAD					0.092	0.189	0.625	103
Male off. GAD	Paternal Drug	0.026	0.963	0.960	0.188	0.169	0.266	103
Female off. GAD					-0.243	0.187	0.193	103

Table 37: Residual Correlations between Parent Alcohol Dependence and Offspring Diagnoses in Twin Study using Symptom Count Variables

Model:	Correlated with:	RMSEA	CFI	TLI	correlation	SE	*p*-value	Free param
Male off. ASPD	Maternal Alcohol	0.026	0.963	0.960	0.163	0.135	0.228	103
Female off. ASPD					0.089	0.116	0.444	103
Male off. ASPD	Paternal Alcohol	0.026	0.963	0.960	0.111	0.084	0.185	103
Female off. ASPD					-0.018	0.080	0.826	103
Male off. Drug	Maternal Alcohol	0.026	0.962	0.959	-0.151	0.157	0.337	103
Female off. Drug					0.056	0.150	0.706	103
Male off. Drug	Paternal Alcohol	0.026	0.963	0.960	-0.206	0.098	0.036	103
Female off. Drug					-0.009	0.111	0.938	103
Male off. Nicotine	Maternal Alcohol	0.026	0.963	0.960	0.010	0.112	0.930	103
Female off. Nicotine					0.167	0.103	0.103	103
Male off. Nicotine	Paternal Alcohol	0.026	0.963	0.960	0.044	0.067	0.519	103
Female off. Nicotine					0.183	0.070	0.009	103
Male off. Panic	Maternal Alcohol	0.026	0.963	0.960	0.274	0.167	0.101	103
Female off. Panic					-0.153	0.134	0.255	103
Male off. Panic	Paternal Alcohol	0.026	0.962	0.960	-0.039	0.102	0.703	103
Female off. Panic					-0.006	0.088	0.942	103

Male off. Social Ph.	Maternal Alcohol	0.026	0.963	0.960	-0.139	0.094	0.139	103
Female off. Social Ph					0.061	0.096	0.524	103
Male off. Social Ph.	Paternal Alcohol	0.026	0.963	0.960	0.061	0.061	0.314	103
Female off. Social Ph					-0.053	0.063	0.402	103
Male off. Specific Ph.	Maternal Alcohol	0.026	0.963	0.960	-0.178	0.131	0.175	103
Female off. Specific Ph					-0.034	0.129	0.793	103
Male off. Specific Ph.	Paternal Alcohol	0.026	0.962	0.960	0.008	0.088	0.926	103
Female off. Specific Ph					-0.116	0.091	0.205	103
Male off. MDD	Maternal Alcohol	0.026	0.962	0.960	0.063	0.099	0.525	103
Female off. MDD					-0.118	0.134	0.377	103
Male off. MDD	Paternal Alcohol	0.026	0.962	0.960	0.004	0.063	0.949	103
Female off. MDD					-0.036	0.086	0.674	103
Male off. GAD	Maternal Alcohol	0.026	0.963	0.960	0.215	0.135	0.111	103
Female off. GAD					0.128	0.141	0.363	103
Male off. GAD	Paternal Alcohol	0.026	0.963	0.960	-0.002	0.109	0.984	103
Female off. GAD					-0.162	0.100	0.104	103

Appendix B: Figure Legends and Figures

Figure Legends

Figure 1. Legend: *Note.* This figure presents the structural equation model of externalizing in parents associated with fear, distress, and externalizing in offspring. In NESARC, maternal and paternal latent externalizing are latent factors defined by the observed variables antisocial traits, drug dependence traits, and alcohol dependence traits. Offspring latent fear is defined by panic disorder, social phobia, and specific phobia. Offspring latent distress is defined by major depressive disorder (MDD), dysthymia, and generalized anxiety disorder (GAD). Offspring latent externalizing is defined by alcohol dependence, nicotine dependence, drug dependence, and antisocial personality disorder. Arrows without numbers indicate unique variances, including error. Correlations among latent factors in parents, and latent factors in offspring, and latent factor residual arrows, are not shown for simplicity of presentation. Offspring latent factors are regressed onto parent latent factors to compare strengths of associations between latent variables, and make comparisons across gender. In later analyses, residuals from observed variables, represented by arrows without numbers, are correlated in parents and offspring to test specificity versus generality of psychopathology aggregation in families. *p<.05.

Figure 2. Legend: *Note.* This figure presents the structural equation model of externalizing in parents associated with fear, distress, and externalizing in male offspring. Values presented for the observed variables are standardized factor loadings. For associations between parent and offspring latent factors, values are standardized regression coefficients. Arrows without numbers indicate unique variances, including error. Correlations among some latent factors, and latent factor residual arrows, are not shown for simplicity of presentation. All loadings of observed variables on latent variables are significant at p<.001. Regressions between latent variables are significant at p<.05 if marked with an asterisks. Mat. = maternal; Pat. = paternal; Antisoc=antisocial; Alc= alcohol; Panic = Panic Disorder; Social Ph. = Social Phobia; Specific Ph. = Specific Phobia; MDD = Major Depressive Disorder; GAD = Generalized Anxiety Disorder; Alc Dep = Alcohol Dependence; Nic Dep = Nicotine Dependence; Drug Dep = Drug Dependence; ASPD= Antisocial Personality Disorder. *p<.05.

Figure 3. Legend: *Note.* This figure presents the structural equation model of externalizing in parents associated with fear, distress, and externalizing in female offspring. Values presented for the observed variables are standardized factor loadings. For associations between parent and offspring latent factors, values are standardized regression coefficients. Arrows without numbers indicate unique variances, including error. Correlations among some latent factors, and latent factor residual arrows, are not shown for simplicity of presentation. All loadings of observed variables on latent variables are significant at p<.001. Regressions between latent variables are significant at p<.05 if marked with an asterisks. Mat. = maternal; Pat. = paternal; Antisoc=antisocial; Alc= alcohol; Panic = Panic Disorder; Social Ph. = Social Phobia; Specific Ph. = Specific Phobia; MDD = Major Depressive Disorder; GAD = Generalized Anxiety Disorder; Alc Dep = Alcohol Dependence; Nic Dep = Nicotine Dependence; Drug Dep = Drug Dependence; ASPD= Antisocial Personality Disorder. *p<.05.

Figure 4. Legend: *Note.* This figure highlights regressions of male and female offspring latent fear, distress, and externalizing factors onto maternal and paternal externalizing. Standardized regression coefficients for males and females are provided, separated by a slash. Values before

slash are for male offspring, while values after the slash are for female offspring. Values differ slightly across gender even when constrained, due to standardization. Regressions between latent variables are significant at p<.05 if marked with an asterisks. Correlations among some latent factors, and latent factor residual arrows, are not shown for simplicity of presentation. *p<.05.

Figure 5. Legend: *Note.* This figure presents the structural equation model of externalizing in parents associated with fear, distress, and externalizing in male offspring. Values presented for the observed variables are standardized factor loadings. For associations between parent and offspring latent factors, values are standardized regression coefficients. Arrows without numbers indicate unique variances, including error. Correlations among some latent factors, and latent factor residual arrows, are not shown for simplicity of presentation. All loadings of observed variables on latent variables are significant at p<.001. Regressions between latent variables are significant at p<.05 if marked with an asterisks. Mat. = maternal; Pat. = paternal; Antisoc=antisocial; Alc= alcohol; Panic = Panic Disorder; Social Ph. = Social Phobia; Specific Ph. = Specific Phobia; MDD = Major Depressive Disorder; GAD = Generalized Anxiety Disorder; Alc Dep = Alcohol Dependence; Nic Dep = Nicotine Dependence; Drug Dep = Drug Dependence; ASPD= Antisocial Personality Disorder. *p<.05.

Figure 6. Legend: *Note.* This figure presents the structural equation model of externalizing in parents associated with fear, distress, and externalizing in female offspring. Values presented for the observed variables are standardized factor loadings. For associations between parent and offspring latent factors, values are standardized regression coefficients. Arrows without numbers indicate unique variances, including error. Correlations among some latent factors, and latent factor residual arrows, are not shown for simplicity of presentation. All loadings of observed variables on latent variables are significant at p<.001. Regressions between latent variables are significant at p<.05 if marked with an asterisks. Mat. = maternal; Pat. = paternal; Antisoc=antisocial; Alc= alcohol; Panic = Panic Disorder; Social Ph. = Social Phobia; Specific Ph. = Specific Phobia; MDD = Major Depressive Disorder; GAD = Generalized Anxiety Disorder; Alc Dep = Alcohol Dependence; Nic Dep = Nicotine Dependence; Drug Dep = Drug Dependence; AAB= Adult Antisocial Behavior. *p<.05.

Figure 7. Legend: *Note.* This figure highlights regressions of male and female offspring latent fear, distress, and externalizing factors onto maternal and paternal externalizing. Standardized regression coefficients for males and females are provided, separated by a slash. Values before slash are for male offspring, while values after the slash are for female offspring. Values may differ slightly across gender even when constrained, due to standardization. Regressions between latent variables are significant at p<.05 if marked with an asterisks. Correlations among some latent factors, and latent factor residual arrows, are not shown for simplicity of presentation. *p<.05.

Figure 8. Legend: *Note.* This figure presents the structural equation model of externalizing in parents associated with fear, distress, and externalizing in male offspring. Values presented for the observed variables are standardized factor loadings. For associations between parent and offspring latent factors, values are standardized regression coefficients. Arrows without

numbers indicate unique variances, including error. Correlations among some latent factors, and latent factor residual arrows, are not shown for simplicity of presentation. All loadings of observed variables on latent variables are significant at p<.001. Regressions between latent variables are significant at p<.05 if marked with an asterisks. Mat. = maternal; Pat. = paternal; Antisoc=antisocial; Alc= alcohol; Panic = Panic Disorder; Social Ph. = Social Phobia; Specific Ph. = Specific Phobia; MDD = Major Depressive Disorder; GAD = Generalized Anxiety Disorder; Alc Dep = Alcohol Dependence; Nic Dep = Nicotine Dependence; Drug Dep = Drug Dependence; AAB= Adult Antisocial Behavior. *p<.05.

Figure 9. Legend: *Note.* This figure presents the structural equation model of externalizing in parents associated with fear, distress, and externalizing in female offspring. Values presented for the observed variables are standardized factor loadings. For associations between parent and offspring latent factors, values are standardized regression coefficients. Arrows without numbers indicate unique variances, including error. Correlations among some latent factors, and latent factor residual arrows, are not shown for simplicity of presentation. All loadings of observed variables on latent variables are significant at p<.001. Regressions between latent variables are significant at p<.05 if marked with an asterisks. Mat. = maternal; Pat. = paternal; Antisoc=antisocial; Alc= alcohol; Panic = Panic Disorder; Social Ph. = Social Phobia; Specific Ph. = Specific Phobia; MDD = Major Depressive Disorder; GAD = Generalized Anxiety Disorder; Alc Dep = Alcohol Dependence; Nic Dep = Nicotine Dependence; Drug Dep = Drug Dependence; AAB= Adult Antisocial Behavior. *p<.05.

Figure 10. Legend: *Note.* This figure highlights regressions of male and female offspring latent fear, distress, and externalizing factors onto maternal and paternal externalizing. Standardized regression coefficients for males and females are provided, separated by a slash. Values before slash are for male offspring, while values after the slash are for female offspring. Values may differ slightly across gender even when constrained, due to standardization. Regressions between latent variables are significant at p<.05 if marked with an asterisks. Correlations among some latent factors, and latent factor residual arrows, are not shown for simplicity of presentation. *p<.05.

Figure 1. Structural Equation Model of Externalizing in Parents Associated with Fear, Distress, and Externalizing in Offspring

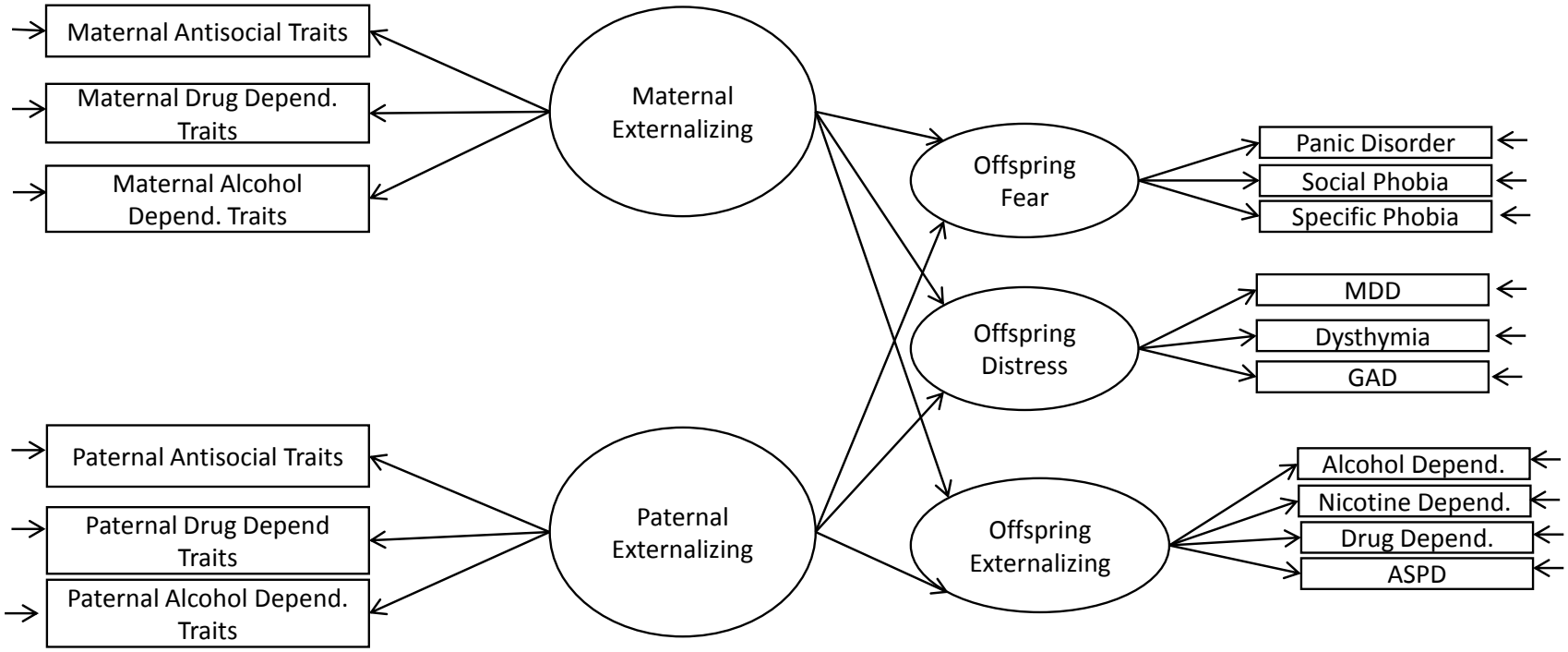

Figure 2. SEM of Externalizing in Parents Associated with Fear, Distress, and Externalizing in Male Offspring in NESARC

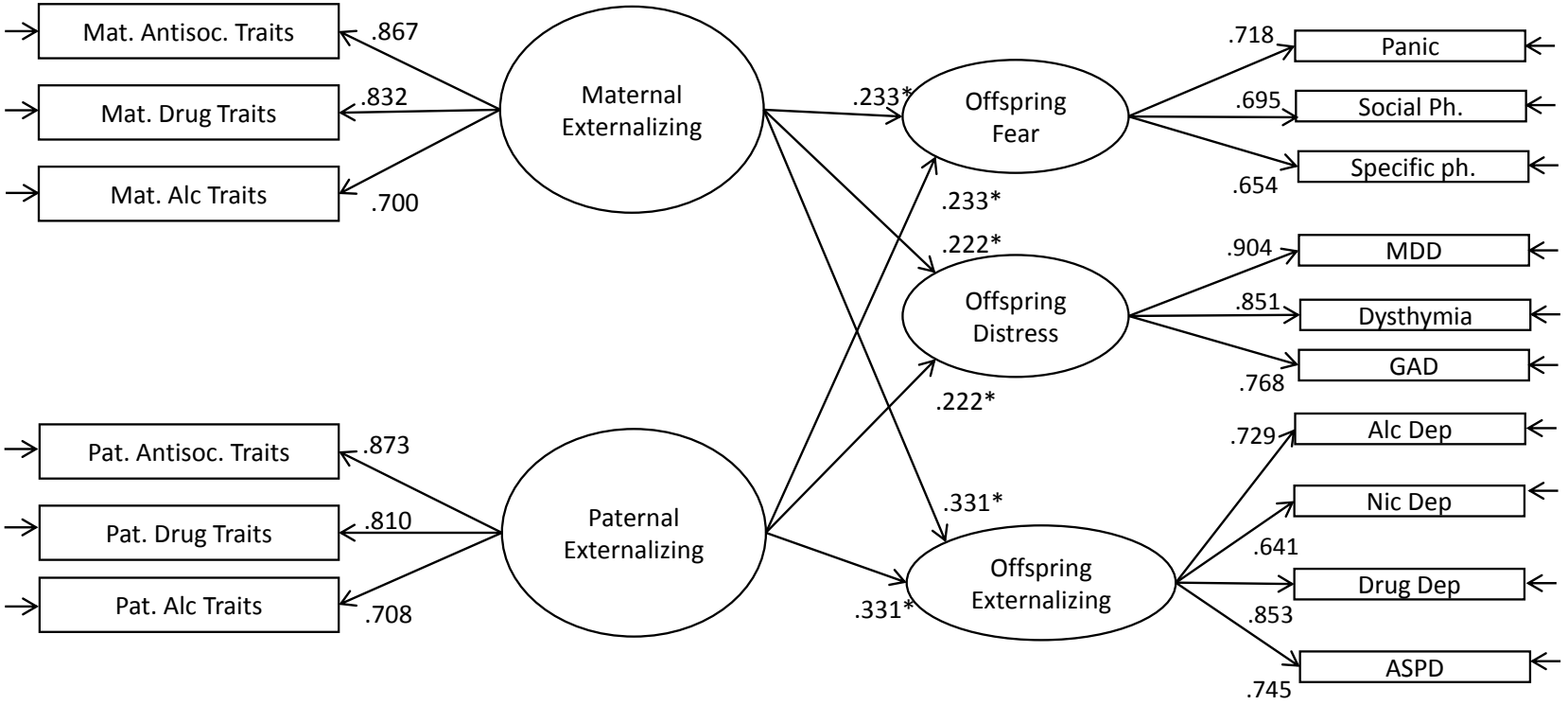

Figure 3. SEM of Externalizing in Parents Associated with Fear, Distress, and Externalizing in Female Offspring in NESARC

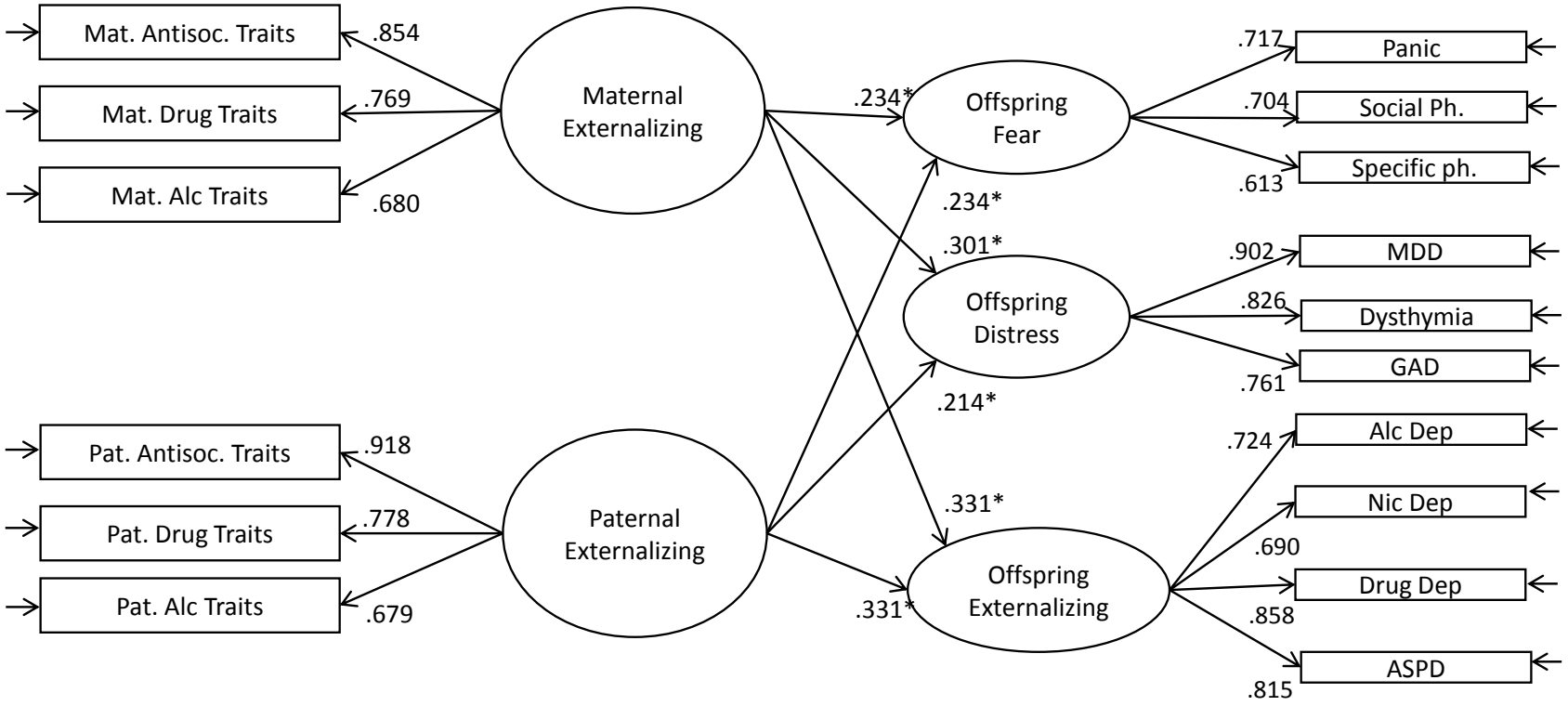

Figure 4. Offspring Latent Factors Regressed onto Parent Externalizing in Males/Females in NESARC Sample

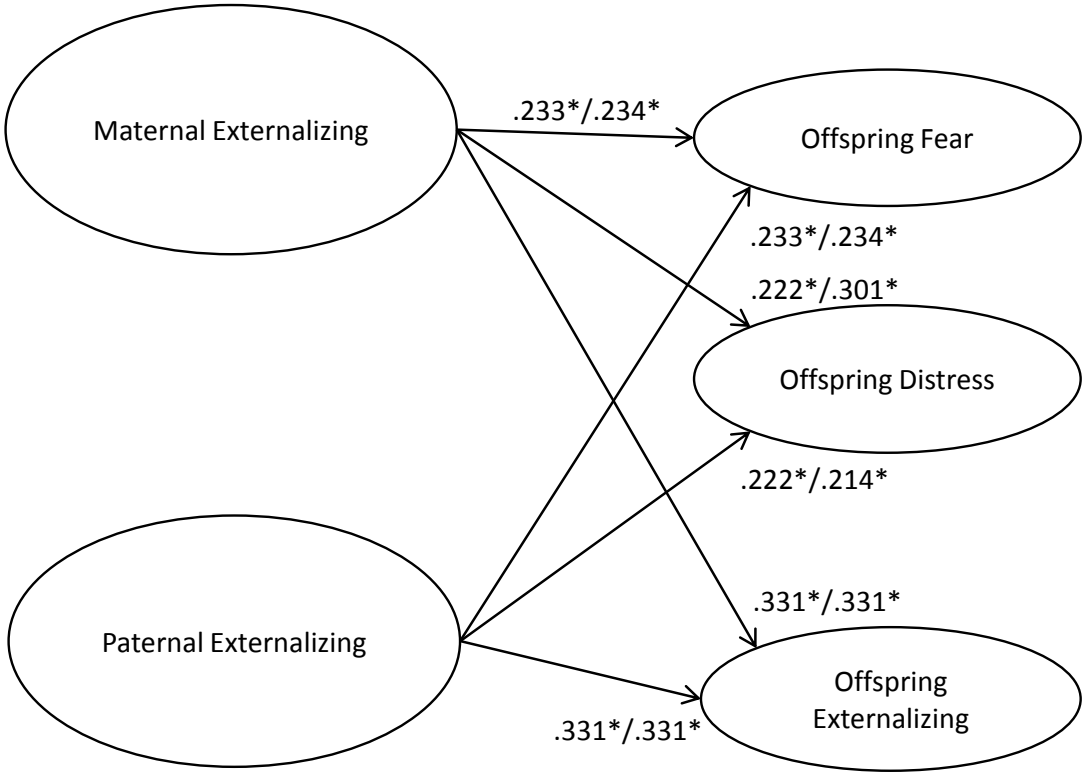

Figure 5. SEM of Externalizing in Parents Associated with Fear, Distress, and Externalizing in Male Offspring in Twin Study using Dichotomous Diagnoses

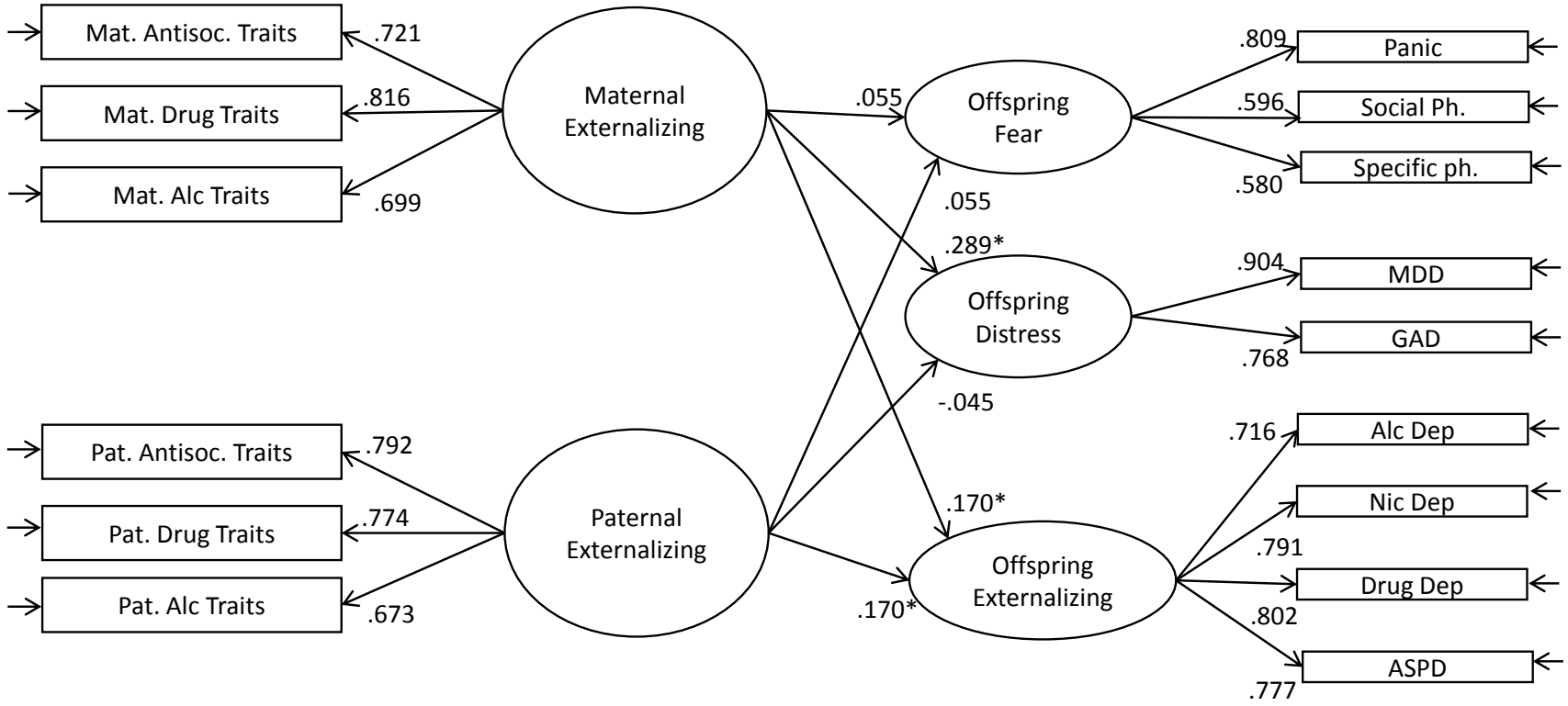

Figure 6. SEM of Externalizing in Parents Associated with Fear, Distress, and Externalizing in Female Offspring in Twin and Sibling Sample using Dichotomous Diagnoses

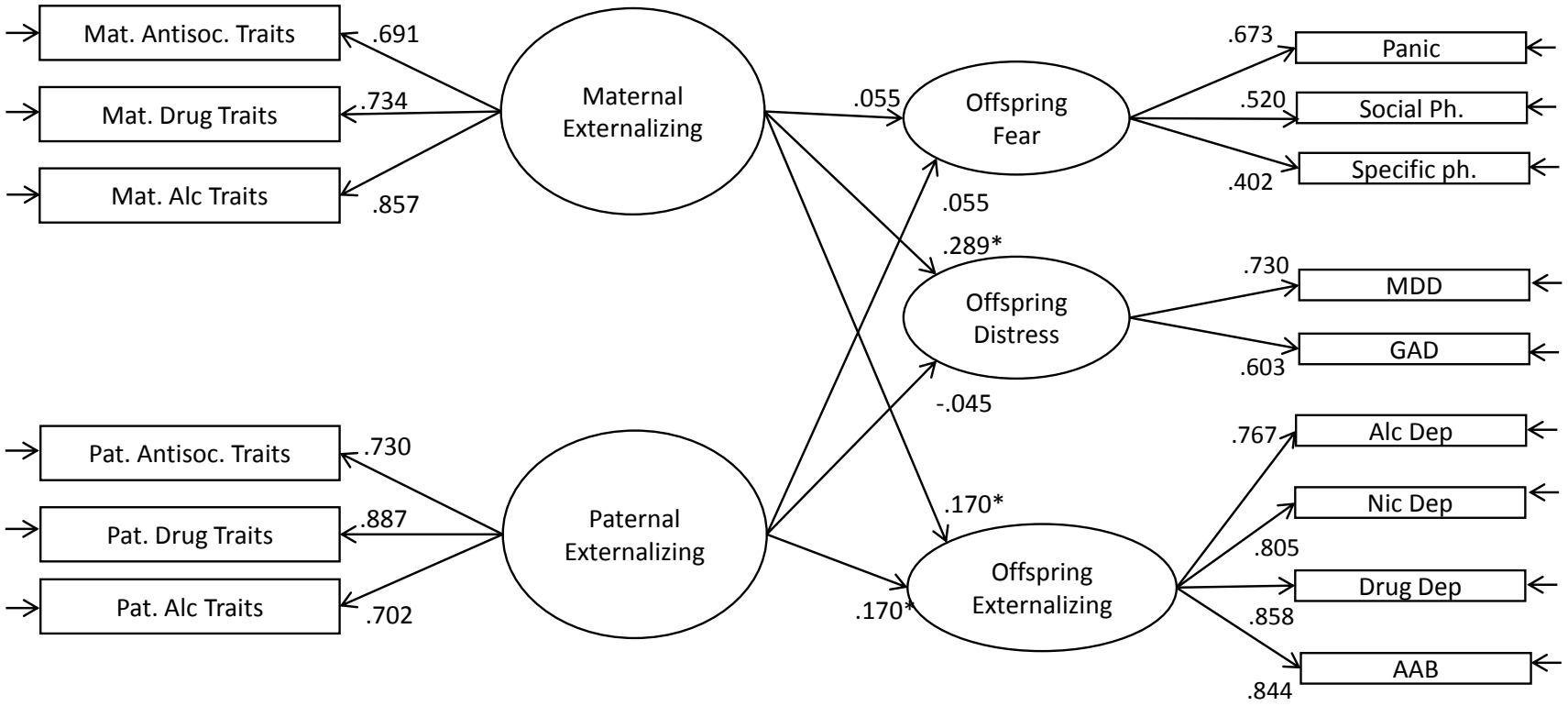

Figure 7. Offspring latent factors regressed onto Parent Externalizing in Males and Females in Twin and Sibling Sample using Dichotomous Diagnoses

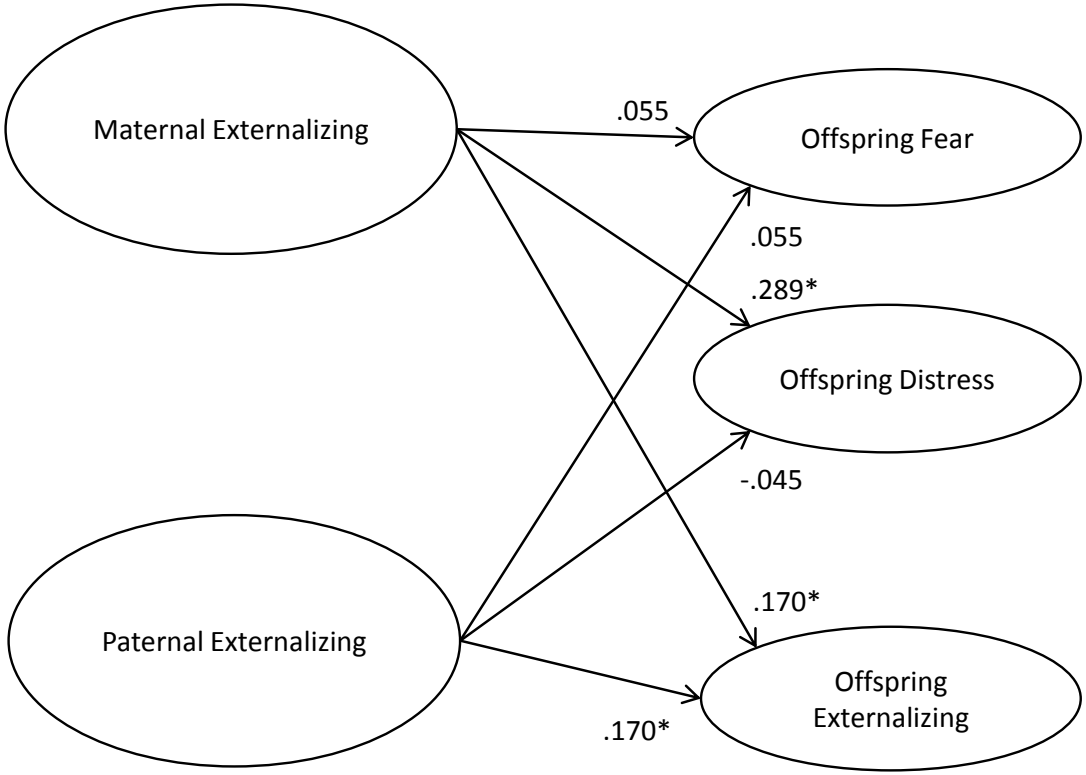

Figure 8. SEM of Externalizing in Parents Associated with Fear, Distress, and Externalizing in Male Offspring in Twin and Sibling Sample using Symptom Count Diagnostic Variables

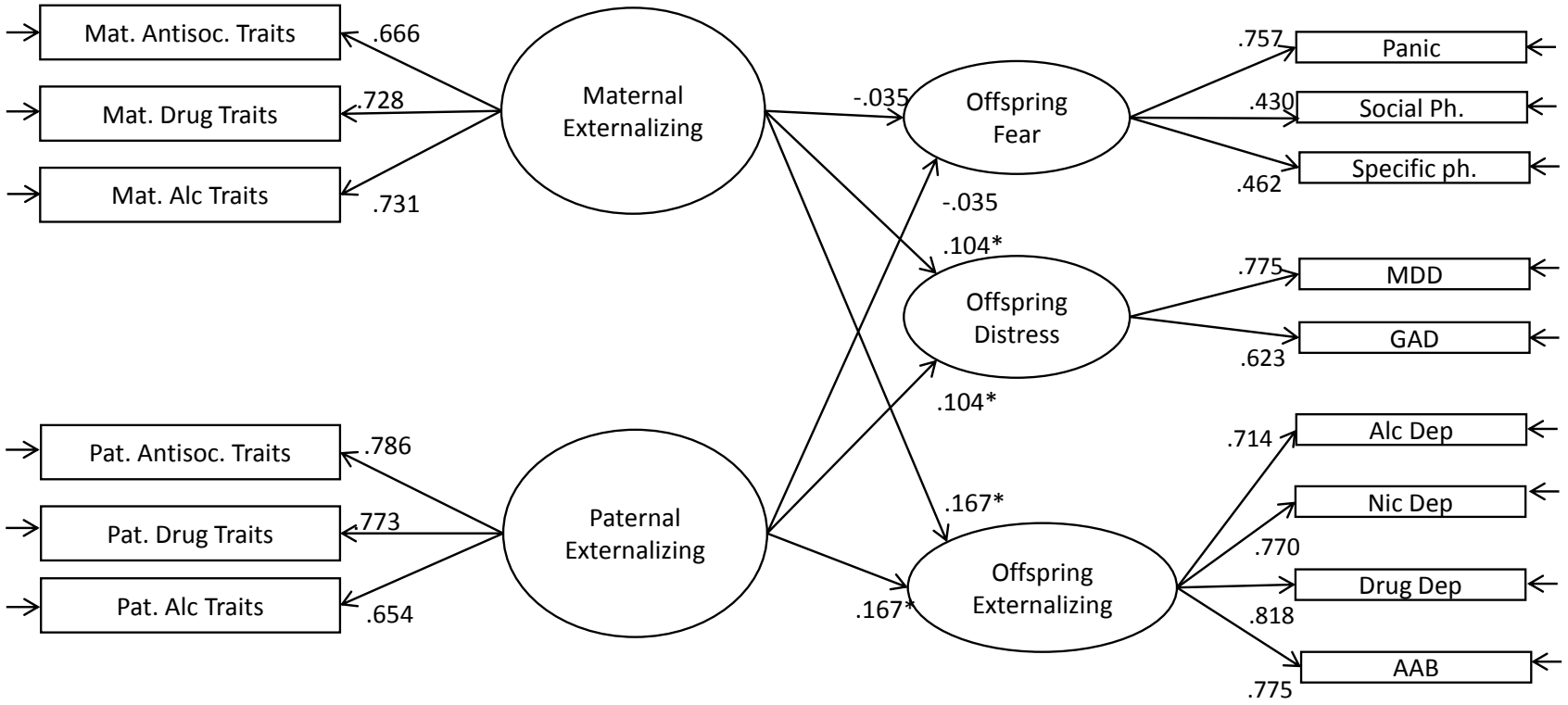

Figure 9. SEM of Externalizing in Parents Associated with Fear, Distress, and Externalizing in Female Offspring in Twin and Sibling Sample using Symptom Count Diagnostic Variables

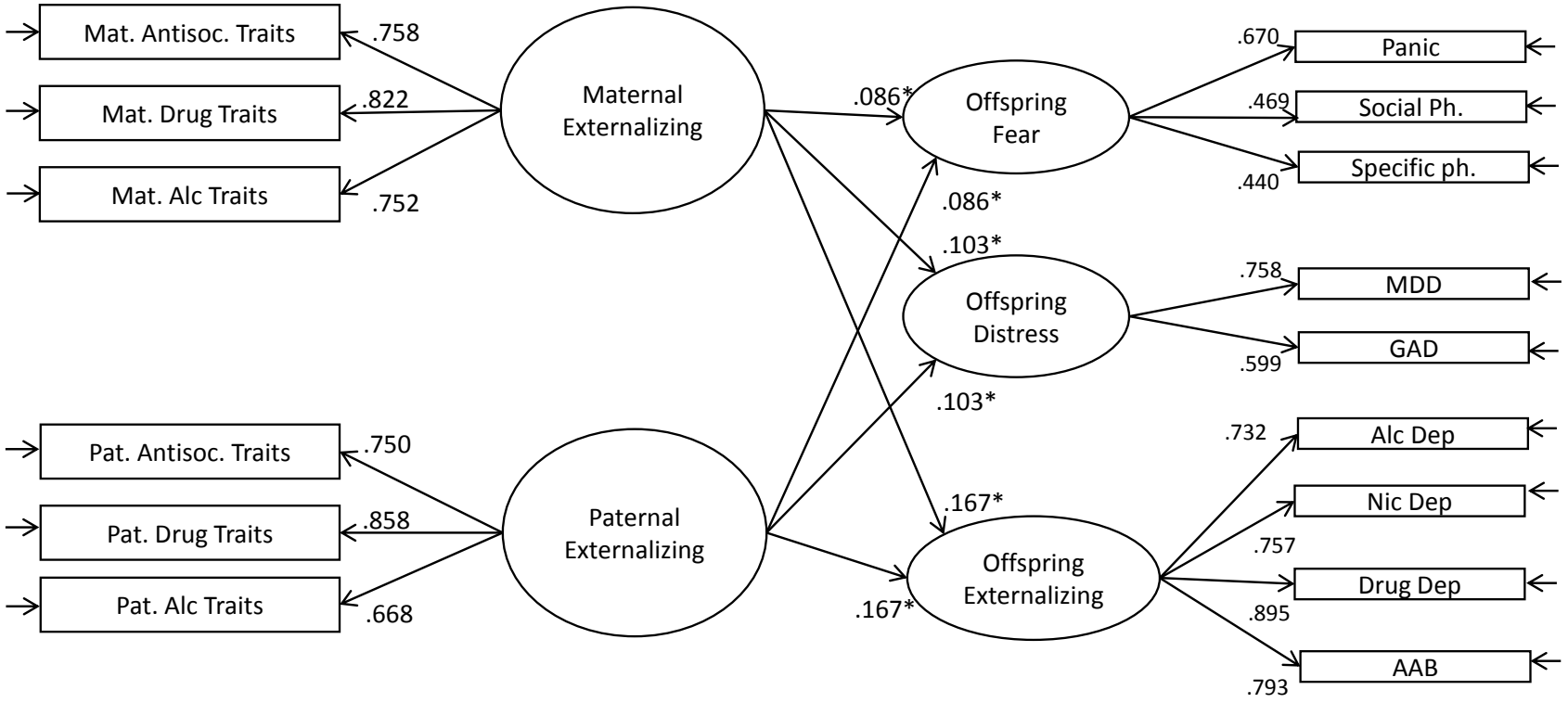

Figure 10. Offspring latent factors regressed onto Parent Externalizing in Males/Females in Twin and Sibling Sample using Symptom Count Diagnostic Variables