THE PREDICTIVE RELATION BETWEEN DEPRESSION AND COMORBID PSYCHOPATHOLOGY IN ADOLESCENTS AT VARIED RISK FOR DEPRESSION

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CHAPTER I

INTRODUCTION

Depression in youth rarely occurs in "pure" forms (Angold, Costello, & Erkanli, 1999; Biederman, Faraone, Mick, & Lelon, 1995; Sorensen, Nissen, Mors, & Thomsen, 2005). Comorbidity is the rule rather than the exception. The presence of major depressive disorder (MDD) or dysthymia in children and adolescents is estimated to increase the likelihood of another disorder at least twenty-fold (Angold & Costello, 1993). Comorbidity affects risk for recurrent depression, duration of depressive episodes, suicide attempts and behaviors, utilization of mental health services, and functional impairment (Birmaher et al., 1996; Hammen & Compas, 1994, Ezpeleta, Domenech, & Angold, 2006). Diagnoses frequently found to be comorbid with major depression in both clinical and nonclinical samples of youth include anxiety disorders, conduct disorders, and substance abuse and dependence (Wagner, 2003).

Depression and anxiety are the most commonly co-occurring conditions (Angold & Costello, 2001). Epidemiological studies have reported estimates of the comorbidity of MDD with anxiety ranging from 16% to 50% (Angold et al., 1999; Seligman & Ollendick, 1998). In clinical samples, the rate of comorbid anxiety disorders in depressed youth has been found to be as high as 70% (Birmaher et al., 1996). A meta-analysis of studies of comorbidity in children revealed that the median odds ratio between anxiety and depression was 8.2, between conduct disorder and depression was 6.6, and between

substance use disorders and depression was about 3.3 (Armstrong & Costello, 2002; Angold et al., 1999).

Studies of offspring of parents diagnosed with depressive disorders indicate that this high risk sample not only has increased rates of depression (about three-fold higher), but also of anxiety (about three-fold higher), conduct (over one-fold higher), and substance use disorders (about two-fold higher) compared to offspring of nondepressed parents (Beardslee et al., 1996; Weissman et al., 1997; 2000). Thus, offspring of depressed parents are a particularly appropriate population in which to study comorbidity because of the high rates found among them (Avenevoli & Merikangas, 2006).

The temporal course of co-occurring disorders has been identified as a critical aspect of comorbidity in need of further study (Angold & Costello, 1993). That is, to what extent does one disorder increase the risk of others? Research in this area has yielded mixed results. In a longitudinal study of a community sample, Costello and colleagues (2003) examined the likelihood of a disorder predicting a different disorder and found that, controlling for other comorbidities, anxiety to depression, depression to anxiety, ADHD to oppositional defiant disorder, and anxiety to substance use disorders were significant. In a longitudinal follow-up of a referred sample, Kovacs et al. (1989) reported that two thirds of children with comorbid depression and anxiety disorders experienced the anxiety disorder prior to the depression. Similarly, the Oregon Adolescent Depression Project (Rohde, Lewinsohn, & Seeley, 1991) showed that anxiety, disruptive disorders, and substance use disorders all preceded depression. Additionally, Weissman et al. (1992) found that among offspring of depressed parents, 28.6% of those

with an initial diagnosis of conduct disorder developed depression over the next two years.

The literature on the developmental sequence of depression and conduct disorders is somewhat contradictory. Some have found that conduct and anxiety disorders precede MDD (Kovacs et al., 1984, 1989), whereas others (e.g., Geller et al., 1985) have found that anxiety and conduct disorder occur following MDD. Few studies, however, have examined in the same individuals the prospective relation between prior psychopathology and subsequent depression as well as the reverse (i.e., prior depression predicting subsequent psychopathology). The purpose of the present prospective study was to investigate the temporal relations of depression with anxiety, disruptive disorders, and substance use disorders through adolescence. Given the episodic nature of depressive disorders, examining these diagnoses longitudinally with the same individuals decreased our chances of inadvertently missing disorders when they occurred.

The present study explored the predictive relations of depression with anxiety, externalizing, and substance use disorders in a sample of offspring of mothers who had a history of mood disorders (high risk) and youth whose mothers were life-time free of psychiatric disorders (low risk). In addition, given that the rates of depression increase in girls during adolescence (Hankin et al., 1998; Lewinsohn et al., 1993; Reinherz et al., 1993), we explored whether the relations between depression and comorbid psychopathology varied as a function of gender. Few studies have examined this issue, although evidence exists that the developmental trajectories of comorbid disorders differ for initially depressed male and female adolescents (Kovacs, Obrosky, and Sherrill, 2003). In contrast, Sorensen and colleagues (2005) found no gender differences in

disorders comorbid with depression at the symptom level. Research that clarifies the complex temporal picture of comorbidity in males and females could inform intervention efforts, particularly whom to target for which disorders. For example, if substance abuse tends to occur before depressive symptoms in females, then interventions aimed at preventing and treating substance abuse could reduce the subsequent occurrence of depressive disorders, particularly in females.

Finally, studies have highlighted the importance of investigating subsyndromal levels of symptoms, that is, symptoms that do not meet all the criteria for a threshold diagnosis (Georgiades, Lewinsohn, Monroe, & Seeley, 2006; Lewinsohn et al., 2004). Adolescents with subthreshold depression are at elevated risk of developing MDD, substance use, and anxiety disorders (Gotlib et al., 1995; Lewinsohn et al., 2000; Pickles et al., 2001; Pine et al., 1999), and subthreshold depressive disorders are associated with impaired psychosocial functioning (Rapaport & Judd, 1998). Therefore, we examined the relations between depression and other psychopathology both including and excluding subthreshold levels of the disorders.

CHAPTER II

METHOD

Participants

Participants were 240 adolescents and their mothers. Children were first assessed in 6th grade (mean age = 11.86, *SD* = .57). The sample of adolescents was 54.2% female, 82% Caucasian, 14.7% African-American, and 3.3% other (Hispanic, Asian, Native American). The sample was predominantly working class (e.g., clerical) to middle-class (e.g., sales) with a mean socioeconomic status of 41.84 (SD = 13.25) (Hollingshead, 1975).

Procedure

Parents of 5th grade children from public schools were invited to participate in a study about parents and children. A brief health history questionnaire comprised of 24 medical conditions (e.g., heart disease, depression) and 34 medications (e.g., Prozac, Elavil) and a letter describing the project was sent to over 3500 families. Of the 1495 parents who responded, telephone screening interviews were conducted with the 587 who had endorsed either a history of depression, use of antidepressants, or no history of psychopathology. The remaining families were excluded because the mother either did not indicate depression or indicated other kinds of psychiatric problems without depression, or had a serious medical illness (e.g., cancer, multiple sclerosis). Based on these screening calls, 349 mothers were identified who reported either a history of depressive symptoms (n=247) or no history of psychiatric problems (n=102). They then were interviewed in

person with the Structured Clinical Interview for *DSM* diagnoses (SCID; Spitzer, Williams, Gibbon, & First, 1990) to confirm the diagnosis of a depressive disorder. Based on these SCID interviews, 109 families then were excluded because they did not indicate sufficient symptoms to meet criteria for a depressive disorder (38%), had other psychiatric disorders that did not also include a depressive disorder (19%), they or the target child had a serious medical condition (14%), they were no longer interested (21%), the target child was in the wrong grade (6%), or the family had moved out of the area (2%). The final sample of 240 families consisted of 185 mothers who had histories of mood disorders (e.g., Major Depressive Disorder, Dysthymia) and 55 mothers who were lifetime free of psychiatric disorders.

Youth were first assessed when they were in sixth grade (Time 1), and then annually through 12th grade. Interviewers were unaware of the mothers' psychiatric history. At the baseline interview, mothers and youth were interviewed separately about the teen's history of psychiatric disorders, and at each follow-up evaluation, mothers and youth were interviewed separately about the adolescent's psychopathology since the last assessment.

Measures

Youth Psychopathology. To assess children's current and lifetime history of psychopathology, mothers and youth were interviewed with the Schedule for Affective Disorders and Schizophrenia for School-aged Children – Present and Lifetime Version (K-SADS-PL; Kaufman et al., 1997) at the first evaluation. Interviews were conducted annually through the end of their senior year of high school using the Longitudinal Interval

Follow-up Evaluation for children (K-LIFE; Keller and Nielsen, 1988), which parallels the K-SADS and assesses disorders since the previous interview. All interviews were audio taped. A second rater who was unaware of the ratings of the primary interviewer reviewed a random 25% of the interview audiotapes. Inter-rater reliability for all diagnoses yielded kappas $\geq$ .78.

Based on the K-SADS-PL, disorders were rated on a 3-point scale (1 = no diagnosis; 2 = subthreshold diagnosis; 3 = threshold diagnosis). To receive a subthreshold diagnosis, at least half of the criterion symptoms plus impairment had to be present. For each disorder, we examined both threshold diagnoses (threshold only) and combined sub- and threshold diagnoses (inclusive). Unless otherwise noted by the modifier "threshold," we refer here to the more inclusive categories (combined sub- and threshold) denoted by "depression," "anxiety," "externalizing disorders," and "substance use disorders."

Threshold depression included diagnoses of major depressive disorder (MDD) or dysthymia. Subthreshold depression included Depression not otherwise specified (D-NOS) and Adjustment Disorders with Depressed Mood (ADDM). Thus, here *Depression* (sub- and threshold) included MDD, dysthymia, D-NOS, and ADDM. Threshold anxiety included diagnoses of separation anxiety, overanxious, generalized anxiety, panic, phobias (social, simple), obsessive-compulsive disorder, or post-traumatic stress disorder. *Anxiety* was defined here as threshold and subthreshold anxiety disorders. *Externalizing* disorders were defined here as threshold and subthreshold oppositional defiant disorder (ODD) or conduct disorder (CD). Finally, due to the overall low frequency of threshold *substance use disorders*, we combined the subthreshold and threshold substance use into

one inclusive category, which consisted of sub- and threshold alcohol abuse and dependence and sub- and threshold drug abuse and dependence. In order to assess the temporal sequence of disorders, analyses included the *first* lifetime occurrence of the diagnosis (either sub- or threshold). Thus, the focus of this study was on sequential rather than concurrent comorbidity.

CHAPTER III

RESULTS

Data Analyses

A series of logistic regression models was fit to examine if prior anxiety (sub- and threshold), predicted subsequent depression (sub- and threshold), controlling for gender and risk. Parallel logistic regression models were fit to examine if prior depression predicted subsequent anxiety. Similar analyses were conducted to examine the predictive relation between externalizing disorders and depression, and between substance use disorders and depression (see Table 1). Finally, in each logistic regression analysis we added the interaction between gender and prior psychopathology (i.e., depression, anxiety, externalizing, or substance use) to test for gender differences in the temporal relations between these other disorders and depression. See Table 2 for results of the analyses of the main effects of risk and sex.

Odds of Psychopathology as a Function of Risk. High-risk youth had more than 13 times the fitted odds of ever having a depressive disorder compared to low-risk children, controlling for prior anxiety and gender (mean OR = 13.48, $p < .05$), controlling for prior externalizing disorders and gender (mean OR=13.46, $p < .05$), and controlling for prior substance use disorders and gender (mean OR = 14.11, $p < .05$). In addition, compared to low-risk youth, controlling for prior depression and gender, high-risk youth had more than 5 times the fitted odds of ever having an anxiety disorder

Table 1. The odds ratio of one disorder given the prior presence of the other disorder for sub- and threshold depression, anxiety, externalizing disorders, and substance use disorders, controlling for risk and sex

	Prior Psychopathology Predicts: / Outcomes	Odds Ratio	95% CI
Anxiety to Depression	Prior Threshold Anxiety Predicts:		
	Threshold Depression	1.12	.45-2.78
	Sub- and Threshold Depression	1.91	.74-4.95
	Prior Sub- and Threshold Anxiety Predicts:		
	Threshold Depression	1.30	.71-2.40
	Sub- and Threshold Depression	1.41	.76-2.60
Depression to Anxiety	Prior Threshold Depression Predicts:		
	Threshold Anxiety	.59	.24-1.47
	Sub- and Threshold Anxiety	.50~	.23-1.08
	Prior Sub- and Threshold Depression Predicts:		
	Threshold Anxiety	.47	.20-1.10
	Sub- and Threshold Anxiety	.63	.33-1.20
Externalizing to Depression	Prior Threshold Externalizing Predicts:		
	Threshold Depression	.96	.38-2.45
	Sub- and Threshold Depression	.88	.34-2.27
	Prior Sub- and Threshold Externalizing Predicts		
	Threshold Depression	1.99*	1.02-3.89
	Sub- and Threshold Depression	1.33	.66-2.66
Depression to Externalizing	Prior Threshold Depression Predicts:		
	Threshold Externalizing	1.00	.45-2.23
	Sub- and Threshold Externalizing	.90	.43-1.89
	Prior Sub- and Threshold Depression Predicts:		
	Threshold Externalizing	.80	.37-1.69
	Sub- and Threshold Externalizing	.88	.47-1.65
Substance Use to Depression	Prior Substance Use Disorder Predicts:		
	Threshold Depression	1.05	.45-2.45
	Sub- and Threshold Depression	.98	.41-2.38
Depression to Substance Use	Prior Threshold Depression Predicts:		
	Substance Use Disorder	1.81~	.90-3.64
	Prior Sub- and Threshold Depression Predicts:		
	Substance Use Disorder	1.46	.75-2.84

~ $p < .10$; *$p < .05$

Table 2. Odds ratios of the main effects of risk and sex, controlling for prior sub- and threshold depression, anxiety, externalizing, and substance use disorders (and controlling for risk in main effect of sex, controlling for sex in the main effect of risk)

Psychopathology	Risk		Sex	
Controlling for Prior Threshold Anxiety	**OR**	**95% CI**	**OR**	**95% CI**
Threshold Depression	15.06***	3.54-63.95	1.45	.80-2.64
Sub- and Threshold Depression	12.32***	4.26-35.67	1.53	.87-2.70
Controlling for Prior Sub- and Threshold Anxiety				
Threshold Depression	14.56***	3.42-61.93	1.43	.79-2.60
Sub- and Threshold Depression	12.68***	4.38-36.66	1.56	.89-2.75
Controlling for Prior Threshold Depression				
Threshold Anxiety	5.81*	1.33-25.71	2.49*	1.09-5.68
Sub- and Threshold Anxiety	4.15***	1.94-8.91	2.08**	1.20-3.62
Controlling for Prior Sub- and Threshold Depression				
Threshold Anxiety	6.43*	1.46-28.46	2.57*	1.12-5.89
Sub- and Threshold Anxiety	4.19***	1.93-9.06	2.12**	1.22-3.69
Controlling for Prior Threshold Externalizing				
Threshold Depression	15.28***	3.59-65.06	1.45	.79-2.68
Sub- and Threshold Depression	13.26***	4.57-38.44	1.57	.89-2.78
Controlling for Prior Sub- and Threshold Externalizing				
Threshold Depression	12.89***	3.01-55.11	1.69~	.91-3.16
Sub- and Threshold Depression	12.45***	4.29-36.19	1.66~	.93-2.94
Controlling for Prior Threshold Depression				
Threshold Externalizing	--[a]	---	.44*	.21-.91
Sub- and Threshold Externalizing	11.80***	3.50-39.74	.55*	.31-.99
Controlling for Prior Sub- and Threshold Depression				
Threshold Externalizing	--[a]	---	.45*	.22-.95
Sub- and Threshold Externalizing	12.01***	3.54-40.70	.55*	.31-.99
Controlling for Prior Substance Use Disorder				
Threshold Depression	15.13***	3.56-64.28	1.47	.81-2.66
Sub- and Threshold Depression	13.09***	4.53-37.87	1.59	.91-2.79
Controlling for Prior Threshold Depression				
Substance Use Disorder	5.25**	1.53-18.05	.53~	.28-1.02
Controlling for Prior Sub- and Threshold Depression				
Substance Use Disorder	5.39**	1.55-18.73	.53~	.28-1.02

~ $p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$

[a] = not able to calculate; OR = Odds Ratio

(mean OR = 5.26, $p < .05$), or a substance use disorder (mean OR = 5.32, $p < .05$), and more than 11 times the fitted odds of ever having an externalizing disorder (mean OR = 11.90, $p < .05$).

Odds of Psychopathology as a Function of Sex. Girls were twice as likely as boys to have been diagnosed with an anxiety disorder, controlling for prior depression and risk (mean OR = 2.33, $p < .05$), and about one and a half times as likely as boys to have been diagnosed with a depressive disorder, controlling for prior anxiety and risk, although this was not significant (mean OR = 1.53, $p < .24$). In addition, boys were almost twice as likely as girls to have been diagnosed with an externalizing disorder, controlling for prior depression and risk (mean OR=1.82, $p < .05$). No main effect gender differences were found for substance use disorders.

Relation between Depression and Anxiety. Gender moderated the relation between anxiety and depression. For girls, the rates of depression were high regardless of prior anxiety, whereas for boys, those with prior anxiety were more than three times as likely to have subsequent depression compared to boys with no prior anxiety, controlling for risk (OR = 3.33, $p < .05$). That is, among youth *with* a prior history of anxiety, the fitted odds that males would have subsequent depression were 1.72 times the fitted odds for females. The proportional improvement in fit when the gender by anxiety interaction was added to the model with the main effects of these predictors and risk was a 2% reduction in the X^2 statistic (X^2 difference = 5.19, df difference = 1, $p < .05$).

Relation between Depression and Externalizing Disorders. Overall, prior externalizing disorders significantly predicted subsequent threshold depressive disorders (OR = 1.99, $p < .05$), controlling for gender and risk. The addition of the gender by prior depressive disorder interaction resulted in a significant improvement in the main effect model that included these predictors and risk, and yielded a 2% reduction in the X^2 statistic (X^2 difference = 4.60, df difference = 1, $p < .05$). For boys, the rates of externalizing disorders were elevated regardless of prior depression, whereas for girls, those with prior threshold depressive disorders (i.e., MDD or dysthymia) were about one and half times as likely to have a subsequent externalizing disorder compared to girls with no prior threshold depression, controlling for risk (OR = 1.64, $p < .05$). That is, among youth with a prior history of threshold depressive disorder, the fitted odds that girls would have a subsequent externalizing disorder were 2.25 times the fitted odds for boys. Additionally, girls with prior threshold depression were over twice as likely to have a subsequent diagnosis of a threshold externalizing disorder compared to girls with no prior threshold depression, controlling for risk (OR = 2.33, $p < .05$).

Relation between Depression and Substance Use Disorders. The gender by prior substance use disorder interaction significantly incremented the main effect model that included risk, gender, and prior substance use as predictors. Girls with prior substance use disorders were over 3 times more likely to have a subsequent diagnosis of MDD or dysthymia, controlling for risk (OR = 3.36, $p < .05$). That is, among youth with a prior history of substance use disorders, the fitted odds that girls would have a subsequent threshold depressive disorder were 13.24 times the fitted odds for boys. The proportional

improvement in fit when the gender by substance abuse interaction was included was a 3% reduction in the X^2 statistic (X^2 difference = 57.16, df difference = 1, $p < .05$).

CHAPTER IV

DISCUSSION

The present study examined the predictive relations of depression with anxiety, externalizing, and substance use disorders in a sample of youth who varied with regard to their risk of mood disorders. In addition, given that the rates of depression increase in girls during adolescence (Hankin et al., 1998), we explored whether the relation between depression and comorbid psychopathology varied as a function of gender. Finally, several studies have highlighted the importance of investigating subthreshold levels of symptoms because of their link with subsequent psychopathology and impairment (Gotlib, Lewinsohn, & Seeley, 1995; Lewinsohn et al., 2004). Therefore, the temporal relations between depression and other disorders were examined both including and excluding subthreshold levels of the disorders.

As would be expected based on previous literature (e.g., Beardslee, Versage, & Gladstone, 1998; Weissman et al., 1992), offspring of mothers with a history of mood disorders (high risk) were more likely to have had depressive, anxiety, externalizing, and substance use disorders, controlling for prior psychopathology and gender, compared to offspring of mothers who were lifetime-free of psychiatric diagnoses (low risk). This finding held true with regard to both threshold and subthreshold disorders. In terms of the main effect of gender, girls were twice as likely as boys to have been diagnosed with an anxiety disorder, controlling for prior depression and risk, and about one and a half times as likely as boys to have been diagnosed with a depressive disorder, controlling for prior

anxiety and risk. This finding is a consistent with studies that have found that females have higher rates of anxiety and depressive disorders than males (Blazer et al., 1991; Breslau et al., 2000; Eaton et al., 1997; Weissman et al., 1984). In addition, boys were almost twice as likely as girls to have been diagnosed with an externalizing disorder, controlling for prior depression and risk, which is consistent with other studies that have found that boys have higher rates of externalizing behaviors than girls (e.g., Kovacs, 2003; Offord, Boyle, & Racine, 1989).

Regarding main effect relations of depression and other disorders, we found that prior externalizing predicted subsequent depressive disorders (i.e., MDD and Dysthymic Disorder). Although the developmental sequence of conduct disorders and depression remains unclear, these findings are consistent with the results of Ezpeleta et al. (2006) who showed that for 70% of those children with comorbid disorders, conduct disorder preceded depression, and with the suggestion by Zoccolillo (1992) that conduct disorder leads to mood disorders.

In the present student, several interesting findings emerged with regard to gender as a moderator. First, the relation between anxiety and depression differed for males and females. Consistent with the literature (Blazer et al., 1991), girls in our sample experienced higher rates of anxiety than boys. Moreover, whereas for girls the rates of depression were high regardless of prior anxiety, for boys, those with prior anxiety were more than three times as likely to have subsequent depression compared to boys with no prior anxiety, controlling for risk. Perhaps for boys, the experience of anxiety is more debilitating in a culture socialized to be "tough," which then increases their risk of developing depression over time. For anxious boys, social support and acceptance may be

less forthcoming, thereby leading to feelings of rejection and distress. Others (e.g., Frost et al., 1999) similarly have shown that anxiety predicts depressive symptoms in males, and also have suggested that males might be more vulnerable to depression after an anxiety disorder than females (Breslau et al., 2000). The precise mechanisms through which anxiety temporally predicts depression for boys remain to be identified.

Gender also moderated the relation between externalizing and depression. For boys, the rates of externalizing disorders were elevated regardless of prior depression, whereas for girls, those with prior threshold depressive disorders were about one and half times as likely to have a subsequent externalizing disorder compared to girls with no prior threshold depression, controlling for risk. Few gender differences in the comorbidity rates of externalizing and depressive symptoms have been found (e.g., Angold & Rutter, 1992; Bird et al., 1993; Meller & Borchardt, 1996), although the relation between depressive and externalizing disorders has been shown to increase for girls from childhood to early adolescence (Little, 2001). Some studies have found only limited evidence that depression precedes conduct problems in community (Capaldi, 1992; Garber et al., 1991) and high risk samples (Weissman et al., 1992), although these studies did not specifically examine gender differences. When more severe disruptive behaviors have been studied, depression has been found to precede externalizing problems (Geller et al., 1985). Kovacs and Devlin (1998) suggested that conduct disorders that follow internalizing disorders may reflect heightened affective and behavior dysregulation. Girls with high levels of irritability and anger, often expressed by depressed youth, may be particularly likely to engage in behaviors that get them into trouble as one means of expressing their frustration.

Finally, gender moderated the relation between substance use disorders and depression. Girls with prior substance use disorders were over three times more likely to have a subsequent diagnosis of MDD or dysthymia, controlling for risk. These results parallel those of several other studies that have found that comorbid substance use and depression in adolescents is particularly high among females (Clark et al., 1997; Whitmore et al., 1997). Rao, Daley, and Hammen (2000) reported that for adolescent girls, substance use disorder predicted MDD over time, but the reverse was not true. Roberts, Roberts, and Xing (2007) found that alcohol dependence conferred an increased risk for depression, particularly for females (odds of 8.0 for females and 3.7 for males). Similarly, the use of illegal substances in adolescent girls predicted an increased risk of depressive symptoms three years later (Frost et al., 1999).

Thus, the developmental trajectories of temporally comorbid anxiety, externalizing, and substance disorders with depression differed for males and females. Comorbidity may arise as a consequence of trying to cope with stress, albeit maladaptively (Hammen & Compas, 1994). These results may have important implications for early detection of vulnerable individuals who can be targeted for intervention efforts.

One limitation as well as strength of this study was that the sample consisted primarily of offspring of depressed mothers. Given the increased rates of psychopathology in children of depressed parents (Beardslee et al., 1998), this high-risk sample allowed for greater variability in the occurrence of symptoms and disorders than would be found in a community sample. Thus, this increased the likelihood of diagnosing sufficient numbers of disorders and thereby examining the complex relations among them over time. These results may not generalize to a purely community sample, however.

Second, although a major strength of this study was the detailed information regarding psychopathology from birth through 18-years-old, the developmental trajectories of these disorders continue beyond our data collection. Therefore, following these adolescents into young adulthood might have yielded even more information about the temporal relations of one disorder to another.

Given the relatively low rates of any particular anxiety disorder, it was not possible to examine the relations between depression and specific anxiety diagnoses. Lewinsohn et al. (1997) reported that simple phobia, separation anxiety, overanxious disorder, and social phobia typically preceded the onset of MDD. Larger samples are needed to have sufficient power to detect these more specific relations. Future studies of comorbidity also should explore through what mechanisms (e.g., biological, psychosocial) one disorder precedes another. For example, how does anxiety lead to depression (Flannery-Schroeder, 2006)? Do anxiety and depression share a common underlying diathesis (Grillion et al., 2005; Kendler, Gardner, & Prescott, 2002) that just takes longer for the depression to unfold, or does being anxious create circumstances that are likely to increase the onset of depression (Hammen, 2006)?

This longitudinal study elucidated the predictive relations of depression with other commonly comorbid psychiatric disorders in a sample of adolescents who varied in their risk for psychopathology. The importance of examining gender differences in the developmental trajectories of these disorders was highlighted. These results have potential clinical implications with regard to whom and what might be targeted in interventions aimed at preventing depression. For example, depression prevention programs should target anxiety, particularly among high-risk boys, and substance use,

particularly among high-risk girls; interventions aimed at preventing externalizing disorders should focus on depression among high-risk girls. In addition, given such gender differences, the use of same sex groups might be advised, particularly if different comorbid disorders are the focus of the intervention.

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