



Published in final edited form as:

Psychol Bull. 2014 May ; 140(3): 816–845. doi:10.1037/a0034733.

Comorbidity of Anxiety and Depression in Children and Adolescents: 20 Years After

Colleen M. Cummings, Nicole E. Caporino, and Philip C. Kendall

Temple University

Abstract

Brady and Kendall (1992) concluded that although anxiety and depression in youth are meaningfully linked, there are important distinctions, and additional research was needed. Since then, studies of anxiety-depression comorbidity in youth have increased exponentially. Following a discussion of comorbidity, we review existing conceptual models and propose a multiple pathways model to anxiety-depression comorbidity. Pathway 1 describes youth with a diathesis for anxiety, with subsequent comorbid depression resulting from anxiety-related impairment. Pathway 2 refers to youth with a shared diathesis for anxiety and depression, who may experience both disorders simultaneously. Pathway 3 describes youth with a diathesis for depression, with subsequent comorbid anxiety resulting from depression-related impairment. Additionally, shared and stratified risk factors contribute to the development of the comorbid disorder, either by interacting with disorder-related impairment or by predicting the simultaneous development of the disorders. Our review addresses descriptive and developmental factors, gender differences, suicidality, assessments, and treatment-outcome research as they relate to comorbid anxiety and depression, and to our proposed pathways. Research since 1992 indicates that comorbidity varies depending on the specific anxiety disorder, with Pathway 1 describing youth with either social phobia or separation anxiety disorder and subsequent depression, Pathway 2 applying to youth with co-primary generalized anxiety disorder and depression, and Pathway 3 including depressed youth with subsequent social phobia. The need to test the proposed multiple pathways model and to examine (a) developmental change and (b) specific anxiety disorders is highlighted.

Keywords

comorbidity; anxiety; depression; children; adolescents; youth

Anxiety and depression are common in youth (Chavira, Stein, Bailey, & Stein, 2004; Costello, Mustillo, Erkanli, Keeler, & Angold, 2003), and each is associated with substantial functional impairment (e.g., Kendall et al., 2010) and future mental health problems (e.g., substance use, bipolar disorders; Lopez, Turner, & Saavedra, 2005; Weissman et al., 1999). Anxiety and depression often co-occur (i.e., Axelson & Birmaher, 2001; Essau, 2008) and their comorbidity is common in children and adolescents (Garber & Weersing, 2010).

Among youth with depression¹, anxiety disorders are the most common comorbid mental health disorders, with comorbidity estimates ranging from 15% to 75% (Angold, Costello, & Erkanli, 1999; Avenevoli, Stolar, Dierker, & Merikangas, 2001; Yorbik, Birmaher, Axelson, Williamson, & Ryan, 2004). In youth with anxiety disorders, rates of comorbid depressive disorders are generally lower, ranging from 10% to 15% (Angold et al., 1999; Axelson & Birmaher, 2001; Costello et al., 2003). Garber and Weersing (2010) suggested several explanations for this imbalance. First, anxiety-disordered youth may present with subsyndromal depressive symptoms (Van Voorhees, Melkonian, Marko, Humensky, & Fogel, 2010) that are not captured by diagnostic interviews. Second, and important to this review, studies have combined anxiety disorders that are heterogeneous (e.g., panic disorder; social phobia), which obfuscates the relationship between specific anxiety disorders and depression. Third, anxiety has an earlier age of onset (e.g., Fichter, Quadflieg, Fischer, & Kohlboeck, 2010) and is overall more prevalent in childhood than depression, whereas depression is more prevalent in adolescence (Cohen, Cohen, & Brooke, 1993; Woodward & Fergusson, 2001); thus, the degree of comorbidity may vary based on age. Fourth, many studies have not differentiated between concurrent comorbidity (both disorders occurring at the same time) and sequential comorbidity (one disorder preceding or predicting the other).

Brady and Kendall (1992), in this journal, reviewed the research on the comorbidity of anxiety and depression in youth and concluded that although anxiety and depression are meaningfully linked, there are important distinctions, and additional research was needed to further understand these differences. Since that review, the number of studies on the topic has increased exponentially. For Brady and Kendall, a PsycINFO search of the phrases, “depression,” “anxiety,” and “comorbidity” among children and adolescents yielded 37 journal articles published between 1972 and 1992. The same search yielded over 650 journal articles published between 1992 and 2012. Given the information now available, and the fact that the field continues to struggle to understand the distinctive and overlapping features of these disorders (Belzer & Schneier, 2004), we updated the 1992 review. We examined the full literature, but cite illustrative studies. We considered all studies that advanced knowledge on the relationship between depression and specific anxiety disorders (i.e., generalized anxiety disorder, GAD; separation anxiety disorder, SAD; social phobia, SoP) in children and adolescents, particularly those regarding theoretical models.

We focused on GAD, SAD, and SoP because they are commonly occurring anxiety disorders in youth (Beesdo, Knappe, & Pine, 2009; Benjamin et al., 2011; Essau, Conradt, & Petermann, 1999) and their comorbidity with depression has been extensively studied. Other childhood anxiety disorders, such as panic disorder and specific phobia, differ from GAD, SAD, and SoP. We refer interested readers to studies of comorbidity among individuals with specific phobia and panic disorder (e.g., Burnstein et al., Choy, Feyer, & Goodwin, 2007; Roy-Byrne et al., 2000).

Although several theoretical models describe the co-occurrence of anxiety and depression in adults (e.g., Alloy, 1991; Alloy, Kelly, Mineka & Clements, 1990; Barlow, 1991; Barlow,

¹Throughout the paper, the term depression is used to refer to symptoms and diagnoses of persistent depressive disorder (previously dysthymic disorder) and major depressive disorder.

Chorpita, & Turovksy, 1996; Mineka, Watson, & Clark, 1998; Watson, 2005; Clark & Watson, 2006; Chorpita, Albano, & Barlow, 1998), there is a need for models that address their development in youth. The identification of developmental pathways, precursors, and protective factors has implications for prevention of further comorbidity and related impairment and complications to treatment (Silk, Davis, McMakin, Dahl, & Forbes, 2012). We hold a developmental psychopathology perspective (Cummings, Davies, & Campbell, 2000), considering principles of equifinality (different pathways or risk factors may lead to the same outcome) and multifinality (the same risk factor may lead to different outcomes) in examining the interactive processes that may lead to the emergence of psychopathology (Cicchetti & Toth, 2009). These principles apply to mood and anxiety disorders in youth, as they are commonly comorbid and may share similar risk and protective factors (Epkins & Heckler, 2011).

The advances since 1992 in our understanding of the comorbidity of anxiety and depression in youth are described and detailed in sections on theoretical models, descriptive and developmental variables, gender differences, suicidality, assessment, and treatment response, with a summary (see Table 1) provided to highlight both key findings and an agenda for future research. We review the literature relative to our proposed multiple pathways model. Pathway 1 describes youth with a diathesis for anxiety, with subsequent comorbid depression resulting from anxiety-related impairment. Pathway 2 refers to youth with a shared diathesis for anxiety and depression who experience both disorders simultaneously. Pathway 3 describes youth with a diathesis for depression, with subsequent comorbid anxiety resulting from depression-related impairment. Additionally, we suggest shared and stratified (i.e., unshared) risk factors (Klein & Riso, 1993) that play a role, either through interacting with disorder-related impairment or predicting the simultaneous development of the disorders. As evident following the review, these pathways are differentially applicable to specific disorders.

Comorbidity

Comorbidity typically refers to the presence of two or more distinct, co-occurring disorders in one person simultaneously (Klein & Riso, 1993). Brady and Kendall (1992) noted that the comorbidity of anxiety and depression may have been a result of the diagnostic system at that time, the Diagnostic and Statistical Manual of Mental Disorders (DSM), Third Edition, Revised (DSM-III; American Psychiatric Association, 1987). Comorbidity within the DSM-IV-Text Revision (American Psychiatric Association, 2000) continues, with some suggesting that comorbidity is “largely the product of a nosological system that classifies mental disorders categorically, presupposing discrete diagnostic entities or disease states” (Belzer & Scheier, 2004, p. 297). Indeed, comorbidity may be nothing more than an artifact of an imperfect diagnostic system. Although its merits are debatable, the literature considers the comorbidity of depression and anxiety within the context of the diagnostic system. The majority of studies since Brady and Kendall’s (1992) review used DSM-IV criteria. Although there were few changes to criteria for anxiety and depressive disorders in DSM-5 (American Psychiatric Association, 2013), changes in the required duration of symptoms (e.g., “fear, anxiety, or avoidance is persistent, *typically* lasting for 6 months or more”) might slightly elevate comorbidity rates.

Since Brady and Kendall (1992), concepts of comorbidity have developed, with distinctions made between epidemiologic and clinical comorbidity (Kraemer, 1995). Epidemiologic comorbidity refers to the non-independence of, or association between, two disorders in a population, and is relevant to efforts to define the boundaries of each disorder and identify their etiologies. Clinical comorbidity refers to the presence of two disorders in one person and is relevant to discussions of prognosis, course, and treatment response. Clinical comorbidity can occur without epidemiologic comorbidity and vice versa. Although studies have examined epidemiologic comorbidity by assessing lifetime prevalence using mixed-age samples (versus the simultaneous presence of more than one disorder), this approach has been criticized for inflating estimates of the association between disorders (Kraemer, Wilson, & Hayward, 2006). For this review, we highlight clinical comorbidity. However, we also report studies that describe the broader relationship between depression and anxiety (i.e., anxiety leading to subsequent depression and vice versa). In the multiple pathways model, comorbidity refers to the simultaneous presence of depression and anxiety, although onset of one disorder may precede the other.

Individuals who are generally comorbid (i.e., those with more than one concurrent diagnosis) have been found more likely than single-diagnosis individuals to use mental health services and to report more suicide attempts, periods of disability, greater life dissatisfaction, less job satisfaction, and less social stability (Newman, Moffitt, Caspi, & Silva, 1998). Comorbid individuals have more physical health problems and are less likely to attend college (Newman et al., 1998). Among adolescents, general comorbidity has been associated with greater overall impairment (Karlsson et al., 2006), academic difficulties, and suicide attempts (Lewinsohn, Rohde, & Seeley, 1995). Comorbidity (in general) may influence the clinical presentation of anxiety-disordered youth more than that of other disorders; Lewinsohn and colleagues (1995) found that comorbidity had the greatest effect on mental health treatment utilization, suicide attempts, academic problems, and conflict with parents for anxiety-disordered youth, as compared to youth with other disorders.

Brady and Kendall (1992) found rates of overlap of anxiety and depression ranging from 16% to 62%, a large range that was attributed to the samples studied (Anderson, Williams, McGee, & Silva, 1987; Bernstein & Garfinkel, 1986; Carey, Finch, & Imm, 1989; Costello et al., 1988; Kovacs, Gatsonis, Paulaukas, & Richards, 1989; Strauss, Last, Hersen, & Kazdin, 1988). The studies reviewed (i.e., Carey et al., 1989; Mitchell, McCauley, Burke, & Moss, 1988; Strauss et al., 1988) reported greater levels of impairment among comorbidly depressed-anxious youth versus single diagnosis youth. However, methodological limitations and the paucity of studies limited the conclusions drawn in 1992.

Research has since confirmed that comorbid anxiety and depression are associated with greater impairment and symptom severity related to the primary diagnosis, and even more so when anxiety is the primary concern (e.g., O'Neil, Podell, Benjamin, & Kendall, 2010; Strauss et al., 1988; Masi, Favilla, Mucci, Millepiedi, 2000; Franco, Saavedra, & Silverman, 2007; Fichter et al., 2010). O'Neil and colleagues (2010) found that among youth with a principal anxiety diagnosis, comorbid depression was associated with lower global functioning, poorer family functioning, more severe social anxiety, and greater severity of

specific depressive symptoms (i.e., negative mood, ineffectiveness, and anhedonia, but not interpersonal problems or negative self-esteem).

Research on the impact of comorbid anxiety disorders on depression is mixed (Guberman & Manassis, 2011; Rohde, Clarke, Lewinsohn, Seeley, & Kaufman, 2001) and suggests that comorbid anxiety may not be associated with worsened functioning among depressed youth. For example, Guberman and Manassis (2011) found that anxious youth with comorbid depression evidenced greater anxiety severity than youth with anxiety alone, but depressed youth with comorbid anxiety did not evidence greater depression severity or family dysfunction than youth with depression alone. This finding is consistent with the notion that severely anxious youth are more prone to comorbid depression than non-anxiety-disordered youth, but not necessarily more severe depression. However, severely depressed youth appear to consistently demonstrate severe anxiety. A latent class analysis indicated that the vast majority of adolescents with high levels of depression also had high levels of anxiety, but that the reverse was not true: adolescents with high levels of anxiety had either high or low levels of depression (Ferdinand, De Nijs, van Lier, & Verhulst, 2005). These results are in line with previous conclusions (Brady & Kendall, 1992) that depressed youth tend to report high levels of both depression and anxiety, whereas anxious youth tend to report high levels of anxiety but relatively low levels of depression.

Existing Theoretical Models

Several models have been proposed to explain the frequent co-occurrence of depression and anxiety. Seligman and Ollendick (1998) offered four explanations: (1) comorbidity between anxiety and depression in youth is due to overlap in definitions; (2) anxiety and depression represent two indicators of a single construct; (3) comorbidity is due to overlap in risk factors; (4) anxiety causes or puts youth at risk for depression. Similarly, Klein and Riso (1993) offered explanations for comorbidity, including comorbidity by chance, population stratification (i.e., separate risk factors associated with each disorder tend to co-occur in subsets of the population), one disorder serving as a risk factor for the other, and overlapping risk factors between the two disorders.

At the same time, the etiology of anxiety and depression may not be best captured by a single model (Issler, Sant'Anna, Kapczinski, & Lafer, 2004), and it is likely that more than one of Seligman and Ollendick's (1998) or Klein and Riso's (1993) explanations apply to the complex relationship between depression and the various anxiety disorders. The multiple pathways model builds on these explanations by applying them to comorbid depression and *specific* anxiety disorders in youth.

There is some evidence for distinct factors of depression and anxiety that are stable across time and gender (Boylan, Miller, Vaillancourt, & Szatmari, 2011) but the co-occurrence of disorders may be explained by a shared factor, negative affectivity (NA; Watson, Clark, & Carey, 1988; Murphy, Marelich, & Hoffman, 2000), particularly for depression and GAD (Troster, Whitton, Brown, & Pincus, 2012). NA may involve "transdiagnostic factors," including neuroticism (Griffith et al., 2010), rumination (Hankin, 2008b; McLaughlin & Nolen-Hoeksema, 2011), and intolerance of uncertainty (Mahoney & McEvoy, 2012).

Models that strive to explain comorbidities and have been tested include the Tripartite Model (Clark & Watson, 1991) and behavioral inhibition/activation (Gray, 1987, 1991). Newer models, including the Quadripartite Model (Watson, 2009), have not yet been empirically tested.

The Tripartite Model

The Tripartite Model (Clark & Watson, 1991) states that anxiety and depression share a general NA factor, whereas physiological hyperarousal (PH) is specific to anxiety and low positive affect (PA) is specific to depression. The shared NA factor links sadness/depression and anxiety/fearfulness, thus accounting for comorbidity between anxiety and depression. Brady and Kendall (1992) noted only a few studies supporting its application in adults (Watson et al., 1988) and youth (Finch, Lipovksy, & Casat, 1989). Since then, numerous studies have further examined the Tripartite Model in youth. Several studies have demonstrated support for the Tripartite Model in youth (Cannon & Weems, 2006; Cole, Truglio, & Peeke, 1997; Joiner, Catanzaro, & Laurent, 1996; Tully, Zajac, & Venning, 2009). Olino, Klein, Lewinsohn, Rohde, and Seeley (2008), for example, compared one- and three-factor models in adolescents followed up to 30 years of age. The one-factor model was an “internalizing” factor, whereas the three-factor model included depressive, anxious, and common factors. The three-factor model fit best, supporting the idea that depression and anxiety can be explained by a combination of shared and unique factors. Lonigan, Phillips, and Hooe’s (2003) longitudinal study of youth in grades 4 through 11 found that NA and PA were stable over time, related to each other, and provided a good fit to children’s self-reported affect. Studying outpatient adolescents, Steer, Clar, Kumar and Beck (2007) provided support for NA with their finding that a second-order factor (representing general symptom distress) best explained the common variance between anxiety and depression measures.

Other studies have suggested the Tripartite Model to be an imperfect fit to anxiety and depression. For instance, PH and PA may not be specific to anxiety and/or depression. An examination of parent- and child-reported anxiety and automatic arousal measures found PH in both anxiety and depression (Greaves-Lord et al., 2007). De Bolle, Decuyper, De Clercq, and De Fruyt (2010) found that PH and PA did not account for the unique aspects of anxiety and depression, and that PH (rather than NA) was the shared factor. In a study of perceived arousal and hypothalamic-pituitary-adrenal (HPA)-axis functioning (an indicant of PH), perceived arousal was related to both depression and anxiety. Additionally, reactive HPA-axis functioning (high PH) was reduced in depressed youth (Dieleman, van der Ende, Verhulst, & Huizink, 2010). These findings suggest that PH is not unique to anxiety.

Still other studies have offered partial support for the Tripartite Model: PA, NA, and PH are not independent of each other. In a study that sampled elementary and high school boys and girls (Jacques & Mash, 2004), NA correlated positively with both depression and anxiety (consistent with the model). Contrary to the model, PA was negatively correlated with both depression and anxiety, and PH was positively correlated with both depression and anxiety. The Tripartite Model best fit data from high school girls. Using an elementary school sample, Lee and Rebok (2002) found that PA and NA scales were negatively correlated,

cross-sectionally and longitudinally. In a study that sampled African-American, urban youth in grades six through nine, the model was said to be supported but the dimensions were highly correlated (Lambert, McCreary, Joiner, Schmidt, & Ialongo, 2004; Gaylord-Harden, Elmore, Campbell, & Wethington, 2011).

Consistent with Jacques and Mash's (2004) findings that the Tripartite Model fit best for older girls, Ollendick, Seligman, Goza, Byrd, and Singh (2003) found that the two-factor model fit data from boys and younger (fourth grade) children. Anxiety and depression may be best differentiated among older girls. Nevertheless, findings examining whether the Tripartite Model applies across age groups are mixed. Cole and colleagues (1997) factor analyzed anxiety and depression measures administered to sixth graders and found both shared and unique factors, consistent with the model. However, constructs of anxiety and depression were indistinguishable in a third grade sample. Contrary to Cole and colleagues' findings and the notion that depression and anxiety may differentiate with increasing age, Turner and Barrett (2003) found that a Tripartite Model provided a good fit to data across third, sixth, and ninth grade age groups.

One of our main concerns, that anxiety disorders are diverse (not one anxiety disorder), merits consideration in terms of the Tripartite Model and whether it applies to the various anxiety disorders (Anderson & Hope, 2008). In a sample of 1,578 school children, NA was positively related to anxiety and depression, and PA was negatively correlated with depression (as expected). However, PH was positively related to panic only (Chorpita, 2002). In relation to social anxiety, Anderson, Veed, Inderbitzen-Nolan and Hansen (2010) found that low PA, high NA, and high PH characterized adolescents diagnosed with SoP, whereas adolescents with elevated symptoms of social anxiety (but not meeting diagnostic criteria) evidenced only high PH and high NA.

Thus, evaluations of the Tripartite Model have had varying results, possibly due to methodological and sampling differences. Nonetheless, a few conclusions can be drawn. First, anxiety and depression are difficult to discriminate in community samples with available measures but are more easily differentiated as symptomatology reaches diagnosable levels. Second, the model may not apply across developmental levels. Third, the model does not fully account for heterogeneity among anxiety disorders, with suggestions that PH only applies to panic. Research and a modified model (Chorpita, Plummer, & Moffitt, 2000; Laurent, Catanzaro, & Joiner, 2004) are needed to understand the relationship between anxiety and depression in youth. It is essential that such work recognize the heterogeneity among the anxiety disorders and call researchers to determine the unique components of each anxiety disorder.

Within the adult literature, concerns about the Tripartite Model are that PH does not capture the heterogeneity among the anxiety disorders (e.g., PH is found in panic, but not other disorders; Brown, Chorpita, & Barlow, 1998); and that the anxiety disorders show varying levels of overlap with depression. Alternative models, for adult disorders (i.e., Barlow, 1991; Barlow, Chorpita, & Turovsky, 1996; Mineka, Watson, & Clark, 1998; Watson, 2005; Clark & Watson, 2006; Chorpita, Albano, & Barlow, 1998), offer three factors that include (a) anxious apprehension, (b) fear, and (c) depression; with anxious apprehension (general

distress or NA factor) a nonspecific component of both anxiety and depression, fear (autonomic arousal and panic) a specific feature of anxiety, and depression (anhedonia, low PA) a specific feature of depression. Mineka et al.'s (1998) model accounts for heterogeneity among the anxiety disorders by specifying that PH is a feature of panic only. Each anxiety disorder is proposed to have a unique component, though not yet identified, and the amount of variance attributed to general distress differs across specific anxiety disorders. Watson (2005) distinguished between fear and distress in his disorder-based model for DSM. Distress disorders (i.e., GAD, PTSD, MDD, & DD) contain a large amount of the NA component and the model implies that GAD and PTSD are more related to depression than they are to fear disorders (i.e., panic disorder, agoraphobia, SoP, and specific phobia). Watson's symptom-level Quadripartite Model (Watson, 2009) includes (a) high distress symptoms with limited specificity to depression versus anxiety (e.g., dysphoric mood in MDD), (b) high distress symptoms with greater specificity (e.g., suicidality in MDD), (c) low distress symptoms with greater specificity (e.g., psychomotor retardation in MDD), (d) low distress symptoms with limited specificity (e.g., insomnia in MDD).

These newer models, from the adult literature, improve upon the Tripartite Model by integrating research findings supporting the heterogeneity among the anxiety disorders and calling for researchers to determine the unique components of the anxiety disorders. Such work should include longitudinal studies and would inform child, adolescent, and adult literatures.

The Behavioral Inhibition/Behavioral Activation Systems

Gray (1987, 1991) proposed a model of the behavioral activation system (BAS) and the behavioral inhibition system (BIS), two brain systems that regulate approach and withdrawal behavior, respectively, in response to the environment. Activity in the left prefrontal cortex is hypothesized to be related to BAS functioning, and activity in the right prefrontal cortex is hypothesized to be related to BIS functioning, with the BIS responding to conditioned aversive stimuli (Davidson, 1998). Over time, the model was revised to include the fight-flight system (FFS; Gray, 1987), which refers to unconditioned aversive stimuli eliciting fight or flight responses. Gray and McNaughton (2000) revised the BIS/BAS (see Bijttbier, Beck, Claes, & Vandereycken, 2009; Corr, 2008), postulating that the BAS is responsive to all positive stimuli. The FFS was renamed the fight/flight/freeze system (FFFS) and proposed to manage reactions to aversive stimuli (i.e., fear), with the BIS managing goal conflicts (i.e., situations involving both reward and threat; anxiety). Although the BIS is proposed to underlie all anxiety disorders, the FFFS is proposed to relate specifically to panic disorder, SoP, and specific phobia (Kimbrel, 2008; Zinbarg & Yoon, 2008). Theory proposes that the BAS and BIS function independently; however, Corr (2002) suggested that the BIS and BAS jointly influence behavior.

BIS and BAS are considered relevant for understanding behavior in response to the environment. Individuals with BIS/BAS functioning at either extreme are at risk for psychopathology (Pickering & Gray, 1999). BIS activity is said to cause feelings of anxiety that lead to withdrawal behavior, whereas BAS activity produces impulsive behavior with little attention to negative consequences. Children with high levels of behavioral inhibition

show lower thresholds for fear responding to unfamiliar stimuli (Kagan, Reznick, & Snidman, 1987). By definition, undercontrolled children have high BAS sensitivity, and inhibited children have high BIS sensitivity, although BIS applies across situations and behavioral inhibition applies to novel stimuli. In one study, Caspi, Moffit, Newman, and Silva (1996) classified children at three years of age and later assessed them via diagnostic interviews at age 21. Undercontrolled (i.e., defined as children who are irritable, impulsive, labile) and inhibited (i.e., defined as children who are socially reticent; distinct from behaviorally inhibited) children at age 3 were most at risk for psychopathology and suicide attempts 18 years later. Inhibited children were more likely than well-adjusted children to have depression but not anxiety.

Data on BIS/BAS were unavailable at the time of Brady and Kendall's (1992) review. A relationship between BIS sensitivity and anxiety symptoms has since been established (i.e., Campbell-Sills, Liverant, & Brown, 2004). Also, low BAS sensitivity has been linked to depression in clinical (i.e., Kasch, Rottenberg, Arnow, & Gotlib, 2002) and community samples (Beevers & Meyer, 2002) of adults. Among MDD adults, self-reported BAS sensitivity scores predicted depression at 6 month follow-up (McFarland, Shankman, Tenke, Bruder, & Klein, 2006). However, other studies have not found a relationship between BAS sensitivity and depression (i.e., Johnson, Turner, & Iwata, 2003; Jorm et al., 1999), and some have found a relationship between BIS sensitivity and symptoms of depression (i.e., Beevers & Meyer, 2002; Campbell-Sills et al., 2004). It can be argued that BIS sensitivity is a common factor to anxiety and depression, whereas BAS hypoactivity is specific to depression with anhedonic symptoms (Hundt, Nelson-Gray, Kimbrel, Mitchell, & Kwapil, 2007). Impaired reward sensitivity (i.e., anhedonia) is said to differentiate depression from anxiety (Pizzagalli, Jahn, & O'Shea, 2005).

In line with findings that high BIS sensitivity is associated with both anxiety and depression (Merikangas, Swendsen, Peisig, & Chazan, 1998; Muris, Meesters, de Kanter, & Timmerman, 2005), the model may apply to their comorbidity, although little research exists on this topic in youth samples. High BIS and low BAS may be a developmental precursor to comorbid anxiety and depression, and behavioral inhibition could represent a general risk factor for both depression and anxiety (e.g., Johnson et al., 2003; Schofield, Coles, & Gibb, 2009). Little research exists on this topic, particularly in child samples. In one study, Coplan, Wilson, Frohlick, and Zelenskis (2006) found that child reports of BIS sensitivity were associated with increased depressive symptoms, greater negative affect and social anxiety, and less positive reports of subjective well-being. BAS sensitivity was negatively associated with internalizing problems but was not related to subjective well-being. Children identified as avoidant (high in BIS and low in BAS based on median splits), reported more depressive symptoms, negative affect, and social anxiety; and less PA and subjective well-being than children who were not avoidant (Coplan et al., 2006). In a study of adults with SoP, retrospective reported BIS in childhood was associated with both increased severity of adult SoP symptoms and depressive comorbidity (Rotge et al., 2011). Although direct tests of BIS/BAS to anxiety-depression comorbidity in youth are required, this line of research is promising in light of the early identification of at-risk youth. We also note that revisions to BIS/BAS theory resemble the Tripartite Model, with BIS and BAS loading on the same

factors as negative and positive affectivity, respectively (Jorm et al., 1999; Zinbarg & Yoon, 2008).

A Multiple Pathways Model

The multiple pathways model is consistent with models that emphasize the heterogeneity among the anxiety disorders (Brown et al., 1998) and with the distinction between “fear” and “distress” anxiety disorders (Watson, 2005), with distress disorders containing more overlap with depression. Additionally, we view these disorders from both categorical and dimensional perspectives, as the examination of symptoms versus diagnoses can change conclusions regarding the order of onset of anxiety and depressive disorders (e.g., Bubier & Drabick, 2009). For instance, a child may experience subsyndromal depressive symptoms, which precede and then exacerbate anxiety symptoms, contributing to a diagnosable anxiety disorder. The anxiety symptoms, in turn, exacerbate current levels of depressive symptoms, leading to a diagnosable depressive disorder. At the symptom level, depression preceded anxiety; at the level of disorder, anxiety preceded depression. Thus, dimensional approaches are necessary to capture subtle interactions between symptoms that would have otherwise been missed. Since the Brady and Kendall review (1992), promising dimensional models have been suggested for youth with externalizing disorders (Walton, Ormel, & Krueger, 2011), internalizing symptoms in general (Markon, 2010), and anxiety and depression (Lahey et al., 2008). Further, item response modeling has been used to identify the range of severity assessed by various symptom measures, allowing the selection of instruments to be tailored to specific research questions (e.g., Olino et al., 2012).

By considering the developmental processes that lead to depression, anxiety, and their comorbidity, we learn more about the specific risk and protective factors. As opposed to examining already-comorbid individuals (adults), the multiple pathways model calls attention to the interactive processes associated with depression-anxiety onset among youth. We ask, “What differentiates those individuals progressing from anxiety to depression, depression to anxiety, or experiencing the two disorders simultaneously?” And, “What differentiates anxious-only and depressed-only individuals from depressed-anxious individuals?” (Cicchetti & Toth, 2009). We maintain that anxiety and depression are separate but meaningfully related constructs. We propose that anxiety and depression differ in their “relatedness” according to three different pathways to anxiety-depression comorbidity. Consistent with previous findings, our multiple pathways model acknowledges that comorbid anxiety and depression is not a singular construct; rather, this comorbidity differs based on the type of anxiety disorder. Additionally, the multiple pathways model addresses the developmental progression of one disorder to the other. The pathways propose a diathesis to primary depression, primary anxiety, or co-primary anxiety-depression. For those with a diathesis for only anxiety or depression, comorbidity arises from both direct and indirect influences, in line with equifinality principles (Cicchetti & Toth, 2009). These influences include risk factors resulting from impairment caused by the initial disorder. Additionally, shared and unique (but stratified) risk factors contribute to depression-anxiety comorbidity (Klein & Riso, 1993). These are a combination of social/environmental (e.g., school, peer, familial-related), biological (e.g., adrenogenic exhaustion), and behavioral

(e.g., avoidance) factors. Other variables that are associated with anxiety (or depression) can also influence later depression (or anxiety).

Pathway 1 describes youth with a general diathesis (temperamental, biological, environmental) to anxiety. When anxiety is left untreated, anxiety-related impairment becomes a risk factor for comorbid depression. This anxiety-related impairment might interact with shared risk factors for the two disorders (e.g., cognitive biases, negative affectivity), leading to the onset of depression. For instance, Silk, Davis, McMakin, Dahl, and Forbes (2012) suggest that sensitivity to social evaluative threat and alterations in reward processing are two potential vulnerabilities of anxious youth that could be associated with subsequent depression. From a diagnostic perspective, anxiety disorders that are characteristic of this pathway include SoP and SAD. Anxiety in Pathway 1 tends to be severe, rather than moderate or mild, whereas depression is mild in its presentation (relative to primary depression). For these youth, anxiety is the primary concern. Nonetheless, the presence of comorbid depression worsens the overall adjustment of these youth. Within this pathway, anxiety and depression represent separate but related conditions, with less overlap between depression (distress) and anxiety (fear-related disorders; Watson, 2005).

Pathway 2 consists of youth with the greatest shared diathesis for anxiety and depression. These individuals experience anxious and depressed feelings simultaneously in response to the same trigger. Youth experiencing comorbidity via this pathway most often show depression-GAD comorbidity. Anxiety is severe, whereas depression is moderate (relative to other forms of depression). These youth differ regarding whether anxiety or depression is identified as the principal concern (they are co-primary). Within this pathway, anxiety and depression have a high degree of overlap that is linked to worry, which is distinct from fear (e.g., Hofmann et al., 2005). This overlap may be, in part, an artifact of a diagnostic system in which anxiety and depression have shared symptoms. Given that anxiety and depression can be experienced simultaneously and their overlap is high (e.g., through the general experience of distress/anxious apprehension; Mineka, 1998; Watson, 2005), Pathway 2 includes many shared risk factors of anxiety and depression. Despite the shared diathesis, GAD and depression may not onset at the same time. As with all the pathways, it is possible that expression of depression and anxiety is influenced by age-related changes (e.g., pubertal processes; see reviews by Hyde, Mezulis, & Abramson, 2008; Reardon, Leen-Feldner, & Hayward, 2008). Additionally, reliance on categorical assessment may inflate the time interval between the onset of GAD and depression. We consider this pathway to contain the most shared risk factors.

The third pathway includes youth with a diathesis for depression, for whom depression-related impairment eventually becomes a source of anxiety. Such impairment can include poor social skills, peer victimization, or isolation resulting from depressive symptoms. Indirect influences link depression with subsequent anxiety among these youth. Although not yet extensively examined, the third pathway is the least common type of anxiety-depression comorbidity in youth. As such, we cannot rule out the extent to which comorbidity between these disorders occurs by chance (Klein & Riso, 1993), but there is some evidence of depression-related impairment linked to anxiety (e.g., Rudolph, Hammen, & Burge, 1994). Depression-anxiety comorbidity via this pathway occurs in older

adolescents (and adults) and involves SoP and GAD. As with Pathway 1, anxiety and depression are separate but related conditions, with the anxiety more in line with a “fear” presentation (Watson, 2005).

Finally, the comorbidity of anxiety and depression may be explained, in part, by shared genes. In the context of the multiple pathways model, this shared diathesis is part of Pathway 2, which involves greater degrees of overlap between anxiety and depression. Brady and Kendall (1992) reviewed family history and twin studies and concluded, cautiously, that familial genetic patterns *distinguished* depression and anxiety. Since then, some genetic studies that have capitalized on technological advances point to *shared genetics* in anxiety and depression, which may explain their frequent comorbidity (see Axelson & Birmaher, 2001; Frani, Middeldorp, Dolan, Ligthart, & Bossmas, 2010; Middeldorp, Cath, Van Dyck, & Boomsma, 2005; Williamson, Forbes, Dahl, & Ryan, 2005), although the findings from two studies suggest independent transmission of depressive and anxiety disorders (i.e., Avenevoli et al., 2001; Klein, Lewinsohn, Rohde, Seeley, & Shankman, 2003). Discrepant findings regarding the genetic transmission of anxiety/depressive disorders may be due to sampling or methodological differences (e.g., specific anxiety disorders included, early- versus later-onset MDD, diagnosed cases versus population-based samples). Below, the multiple pathways model is applied to the research findings regarding anxiety-depression comorbidity.²

Descriptive and Developmental Variables

Longitudinal Research

Research findings suggested to Brady and Kendall (1992) that a temporal relationship existed between anxiety and depression, with anxiety generally preceding depression, but only one longitudinal study had been published at that time (Kovacs, Gatsonis, Paulauskas, & Richards, 1989). An important advance in the last 20 years is the progress from cross-sectional and retrospective designs to prospective, longitudinal studies that sample community, high-risk, and diagnosed individuals, which have informed the multiple pathways model. Although there is some evidence that earlier depression predicts later anxiety among youth (consistent with the Pathway 3; Costello, Mustillo, Erkanli, Keeler, & Angold, 2003), the bulk of the data indicate that the onset of anxiety most often occurs before the onset of depression (consistent with Pathway 1; e.g., Avenevoli et al., 2001; Fichter et al., 2010; Kovacs et al., 1989). Further, comorbid anxiety (in particular, GAD and SoP) appears to be more prevalent among depressed youth with an earlier onset of depression (i.e., before age 15; Hammen, Brennan, Keenan-Miller, & Herr, 2008).

As our review makes salient, anxiety disorders are not unitary, and there is variation in the onset of specific anxiety disorders. Lewinsohn, Holm-Denoma, Small, Seeley, and Joiner (1997) found that specific phobia, SAD, overanxious disorder (currently GAD), and SoP more often preceded diagnosis of MDD, but that obsessive-compulsive disorder (OCD) and

²Given that anxiety disorders in youth are highly comorbid (Kendall et al., 2010), the pathways are not mutually exclusive. It is possible, for example, that a child may have a shared diathesis for GAD and MDD and the risk for MDD is exacerbated by the onset of SoP as the child approaches adolescence, as anxiety-related impairment confers more risk for a depressive episode.

panic disorder were more likely to occur after the onset of depression. Essau (2003) reported that SoP and specific phobias most often preceded depression but that agoraphobia, anxiety disorder not otherwise specified (NOS), and GAD occurred first only 50% of the time in their adolescent sample. Consistent with Pathway 1, SoP, in particular, has been found to precede depression for the majority of comorbidly anxious and depressed patients, with childhood and adolescent (versus adult) onset of SoP (based on retrospective report) associated with greater severity of depression (Dalrymple & Zimmerman, 2011). Childhood (versus adolescent) SoP onset was associated with a shorter time to MDD onset. Social anxiety in youth often goes along with poor social skills, low self-esteem, loneliness, and helplessness (Messer & Beidel, 1994; Rubin & Burgess, 2001) as well as cognitive vulnerabilities such as hopelessness (Gibb & Alloy, 2006), which predict later depression. Additionally, anxious adolescents have been found to engage in risky behavior (e.g., substance abuse or misconduct; possibly to gain acceptance from peers) that is associated with later depressive symptoms (Sears & Armstrong, 1998).

Anxiety that occurs first may leave the child more susceptible to depression (e.g., Avenevoli et al., 2001; Mathew, Pettit, Lewinsohn, Seeley, & Roberts, 2011). At the same time, research does not indicate a direct causal path from early anxiety to later depression among youth (Rice, van den Bree, & Thapar, 2004). Rather, a combination of factors associated with anxiety may lead to later depression. Anxiety's causal relationship to depression may be explained, in part, by cognitive models (i.e., Nolen-Hoeksema, 2000; Starr & Davila, 2012). Additionally, physiological models suggest that heightened arousal from sustained levels of anxiety may eventually cause the body to "shut down," or become depressed (Zahn-Waxler, Klimes-Dougan, & Slattery, 2000). In short, it is likely that a combination of biological, environmental, and cognitive factors associated with anxiety can contribute to later depression. Most longitudinal studies of community adolescents suggest that anxiety and depression are separate but related disorders. Among community adolescents, those identified as at risk for anxiety disorder (based on first-year anxiety symptoms) with high severity of depression or anxiety, were at risk for high severity of the other type of disorder (this did not hold for the low-risk group; Hale, Raaijmakers, Muris, van Hoof, & Meeus, 2009). In a community sample, high rates of self- and parent-reported anxiety predicted self- and parent-reported depression over time (Cole, Peeke, Martin, Truglio, & Seroczynski, 1998). However, the reverse was not true; in fact, parents who reported that their child exhibited elevated depressive symptoms later reported decreased anxiety.

A longitudinal study of non-referred girls suggested that *symptoms* of depression, SoP, and SAD were relatively stable and non-predictive of each other from year to year. However, increases in levels of SoP in childhood did predict depressive *disorders* in early adolescence. Depressive symptoms were the strongest predictors of later depression, again suggesting that anxiety and depression can be separate but related (Keenan, Feng, Hipwell, & Klostermann, 2009). Olino, Klein, Lewinsohn, Rohde, and Seeley (2010) identified six distinct trajectories of anxiety and depressive symptoms among a community sample of adolescents followed until age 30, with each trajectory demonstrating a distinct relationship between anxiety and depression over time. Trajectories characterized by depressive disorders showed relatively low probabilities of anxiety disorders, whereas trajectories characterized by anxiety

disorders showed relatively high probabilities of depressive disorders. Interestingly, depressive disorders that followed anxiety disorders tended to be less persistent than other forms of depression characterized in the study. It is important to note that this study followed individuals with relatively low rates of anxiety disorders, and changes in depressive/anxiety disorders were followed from adolescence (versus childhood) to adulthood.

Finally, retrospective reporting of childhood sexual and physical abuse was associated with more severe anxiety symptoms and more frequent depressive comorbidity in an adult anxiety-disordered sample (Mancini, Van Amerigen, & Macmillian, 1995). Childhood trauma (i.e., retrospective reports of abuse or neglect) and recent life stressors were associated with the development of subsequent comorbidity (including depression) among anxious adults (de Graaf, Bijl, ten Have, Beekman, & Vollebergh, 2004). However, comorbidity was relatively low (11%) over the three-year period. In a longitudinal study of 816 youth, the combination of early exposure to stressors and a history of an anxiety disorder predicted increased depressive symptoms in response to low levels of current stress. The authors hypothesized that these variables interact to create a sensitivity/reactivity to stress, suggesting that anxiety disorder and stress sensitivity are markers of a vulnerability to depression that results from early exposure to adversity (Espejo, Hammen, Connolly, Brennan, Najman, & Bor, 2007). Hopelessness, on the other hand, may interact with stress to specifically predict depression (Gibb & Alloy, 2006; Hankin, 2008a).

It may be that depression and anxiety share a genetic pathway that is expressed differently depending on environmental stressors (Williamson et al., 2005). For example, anxiety disorders in youth are more strongly associated with parental overprotection and control, whereas depression in youth is more strongly associated with parental rejection and lack of warmth (Beesdo, Pine, Lieb, & Wittchen, 2010; Rapee, 1997). Additionally, stressful life events are often more closely linked to depression than anxiety (e.g., Pine, Cohen, Johnson, & Brook, 2002; Newman & Bland, 1994). Factors related to family and peers have also been studied in anxious and depressed youth, although the extent to which such interpersonal difficulties are causes versus consequences of these disorders remains unclear.

Specific Anxiety Disorders

Brady and Kendall (1992) did not encounter studies examining the relationship of depression to specific anxiety disorders in youth, but this area of research has greatly expanded since then, likely driven by the consensus that anxiety disorders are heterogeneous. In general, the number of types of fears experienced is associated with lifetime depression rates (Choy, Fyer, & Goodwin, 2007). Although co-occurring depressive symptoms are common across the anxiety disorders, the etiology of these relationships may differ by anxiety disorder. The research described already suggests mechanisms by which anxiety and depression could be related. It is possible that some anxiety disorders lead to increased rates of depressive disorders through their impact on the youth's environment (Pathway 1). For instance, avoidance of feared stimuli can lead to decreased engagement in pleasant activities and poorer interpersonal relationships, resulting in depression. At the same time, depression and other anxiety disorders may be associated through overlapping

characteristics, such as cognitive style (Pathway 2). Finally, one or more third variables (e.g., childhood adversity; genetics) could present a shared vulnerability to both depression and anxiety. These vulnerabilities interact with risk factors for depression related to anxiety-related impairment (or vice versa, Pathways 1 and 3), or they lead to the simultaneous comorbidity of anxiety and depression (Pathway 2). We suggest that each of these mechanisms varies by specific anxiety disorder, as research since the 1992 review indicates that depression-anxiety comorbidity varies depending on the specific anxiety disorder.

SAD and depression—Relatively little research has been devoted to the relationship between SAD and depression, perhaps because depression is more commonly comorbid with GAD and SoP (Verduin & Kendall, 2003). Some work suggests that persistent SAD can be a precursor to panic (Perugi et al., 1988; Savino et al., 1993), with which it may share a common genetic diathesis (Roberson-Nay, Eaves, Hettema, Kendler, & Silberg, 2012). In turn, panic disorder is associated with depression in youth and adults (Goodwin & Sotlib, 2004; Kessler, Stang, Wittchen, Ustun, Roy-Byrne, & Walters, 1998; Roy-Byrne, Stang, Wittchen, Walters, & Kessler, 2000). Thus, children with SAD may be at risk for depression.

However, several studies with varying methodologies present mixed findings. A 7.4-year-follow-up of children with SAD showed that it was associated with later anxiety but not panic disorder/MDD specifically (Aschenbrand, Kendall, Webb, Safford, & Flannery-Schroeder, 2003). A study that used retrospective ratings of SAD also did not support a significant relationship with depression after adjusting for the effects of prior panic attacks (Hayward, Killen, Kramer, & Taylor, 2000). Foley, Pickles, Maes, Silberg, and Eaves (2004) reported that children with persistent SAD had a higher prevalence of depression at 18-month follow-up compared with children with transient SAD, after controlling for the presence of comorbid disorders. In another study, childhood SAD was a risk factor for depression within one year, but otherwise did not predict depressive symptoms/disorders (Keenan, Feng, Hipwell, & Klostermann, 2009). In line with this finding, Pine, Cohen, Gurley, Brook, and Ma (1998) found that SAD in adolescence was not significantly associated with depression in adulthood.

In contrast, Lewinsohn, Holm-Denoma, Small, Seeley, and Joiner (2008) found that adults who reported childhood SAD were more likely to have panic disorder and depressive disorders but not other anxiety disorders by age 30, after controlling for other disorders through age 19 (Lewinsohn et al., 2008). A study that followed offspring of adults with and without panic disorder and MDD found that childhood SAD increased risk for developing MDD (odds ratio = 3.2) but far less than it increased risk for developing panic disorder (odds ratio = 9.2) and agoraphobia (odds ratio = 9.1; Beiderman et al., 2007). Inconsistencies in the findings may be due to the method and timing of assessments (e.g., relative to risk period for developing SAD or depression) and whether or not panic disorder is controlled.

Overall, SAD may be associated with increased risk for later depression (consistent with Pathway 1) but to a lesser degree than the other anxiety disorders. It is possible that increased risk for depression among youth with SAD is greatest in the short-term (i.e., closer

in time to SAD). Consistent with Pathway 1, children with more severe forms of SAD are at greater risk for later depression based on SAD-related impairment (e.g., strain on peer and familial relationships, not participating in school and other activities). Future longitudinal research could examine whether or not panic symptoms mediate the relationship between SAD and depression. Additionally, studies finding that successful treatment of SAD prevents the onset of subsequent depression would be consistent with Pathway 1. Risk factors for depression that stem from SAD-related impairment include social isolation and withdrawal from activities, academic difficulties, and conflicted familial relationships. Studies that specifically test these risk factors would be informative and beneficial.

SoP and depression—In contrast to SAD, depression appears to be particularly linked to childhood SoP, especially the generalized subtype, both at the level of disorder (Chavira, Stein, Bailey, & Stein, 2004; O’Neil et al., 2010; Ranta, Kaltiala-Heino, Rantanen, & Marttunen, 2009a) and symptoms (O’Neil et al., 2010; Tillfors, El-Khoury, Stein, & Trost, 2009). In a twin study, familial aggregation and common genetic factors were observed for major depressive disorder (MDD) and SoP (Mosing et al., 2009). Although shyness has not been related to increased levels of MDD among adolescents (Burnstein, Ameli-Grillon, & Merikangas, 2011), SoP in adolescence has predicted depression (i.e., onset in adolescence or early adulthood; Beesdo et al., 2007; Stein, Fuetsch, Muller, Hofler, Lief, & Wittchen, 2001). Childhood-onset SoP may be associated with earlier onset of depression than adolescence-onset SoP (based on retrospective, self-report in treatment-seeking samples: Alpert et al., 1999; Dalrymple & Zimmerman, 2011). Likewise, childhood-onset MDD showed higher associations with comorbid SoP than adult-onset MDD (Alpert et al. 1999).

The co-occurrence of older age, severity, SoP, and depressed state was associated with lower rate of remission in the Child/Adolescent Anxiety Multimodal Study (CAMS; Ginsburg et al., 2011), and other studies have also linked comorbid mood problems and age to less favorable cognitive-behavioral therapy (CBT) outcomes among youth with SoP (Crawley, Beidas, Benjamin, Martin, & Kendall, 2008). It may be that depressed mood decreases motivation for change and/or makes it difficult to engage youth in treatment. Another possibility is that depression affects how youth with SoP cognitively process feedback during or following exposure to anxiety-provoking social situations, which appears to be a critical element of CBT (e.g., Peris et al., in press). If depression increases negative post-event processing (i.e., negatively valenced review of social situations in which inadequacies, mistakes, imperfections, and negative perceptions of the interaction are exaggerated; Rachman, Grater-Andrew, & Shafran, 2000), exposure tasks may be less effective in producing new learning.

Among children followed longitudinally, those identified by their peers as anxious-solitary (i.e., interested in interacting with others but refrain due to anxiety) were likely to receive future diagnoses of SoP, dysthymic disorder, and MDD (Gazelle, Workman, & Allan, 2010). Interpersonal variables appear to play an important role in both disorders, and may be a key link between depression and SoP in youth, particularly adolescents. Peer variables are salient in SoP, whereas family variables may be more salient to depression (Starr & Davilla, 2008; Hutcherson & Epkins, 2009; Johnson et al., 2005). At the same time, comorbid symptoms of SoP and depression among adolescent girls from a community sample were

associated with increased peer and family alienation compared to girls with only symptoms of SoP or depression, although findings may have been affected by relatively low levels of psychopathology among participants (Starr & Davilla, 2008). Girls' and mothers' reports of lower maternal acceptance and parental support were related to girls' depression but not SoP (controlling for depression) and girls' and mothers' reports of lower peer acceptance were related to girls' social anxiety but not depression (controlling for social anxiety; Hutcherson & Epkins, 2009). Peers can play a central role: early onset of depression can lead to poor social interactions and under-developed social skills (Rudolph, Hammen, & Burge, 1994), a path to SoP (Pathway 3). SoP has been found to be associated with peer victimization among adolescents (Ranta et al., 2009a), and youth with comorbid symptoms of depression and SoP experience peer victimization at even greater rates (Ranta, Kaltiala-Heino, Pelkonen, & Marttunen, 2009b).

Cognitive biases, interpersonal styles, and coping styles link SoP and depression. Comorbid depression amplifies biases that are common in SoP (i.e., negative social events reflect negative self-characteristics; negative social events have long-term implications), whereas SoP alone has biases concerning negative evaluation by others (Wilson & Rapee, 2005). A study of late adolescents (undergraduates) found that interpersonal dependency, avoidance of expressing emotion, and lack of assertion were associated with symptoms of SoP, but only avoidance of expressing emotion was associated with depressive symptoms one year later (Grant, Beck, Farrow, & Davila, 2007).

Do coping strategies differentiate SoP and depression in youth? Within a community sample of school-aged children, six coping strategies were identified (Wright, Banerjee, Hoek, Rieffe, & Novin, 2010). Elevated depression symptoms were associated with decreased problem-solving, distraction, and social support seeking, and increased externalizing (e.g., yelling or throwing something) over time. In contrast, elevated social anxiety symptoms were associated with increased social support seeking, distraction, and internalizing (e.g., worrying or feeling sorry for oneself), and decreased externalizing over time. Although, importantly, individual coping strategies did not predict later depression and/or anxiety, the findings allude to differential patterns of coping strategies in depression versus SoP.

The theoretical models can be applied to the links between SoP and depression. BIS/BAS theory suggests that behavioral inhibition (linked with social withdrawal; Rubin, Coplan, & Bowker, 2009) is more strongly related to social anxiety than to the other anxiety disorders (Chronis-Tuscano et al., 2009; Hirshfield-Becker, 2010; Hirshfield-Beck et al., 2007) and depression (Caspi et al., 1996). Tests of the Tripartite Model suggests that low PA is related to SoP in addition to depression (Clark & Watson, 2008; Chorpita, Plummer, & Moffitt, 2000; Dougherty et al., 2011), although more research is needed with youth (Epkins & Heckler, 2011). SoP most often precedes depression in youth (Pathway 1). The less common instance of depression preceding SoP may be attributed to poorly-developed social skills due to early onset of depression and decreased motivation for social activities (Pathway 3). Future studies should examine interpersonal risk factors for depression as they relate to SoP. Based on data to date, interpersonal risk factors, namely peer victimization, social withdrawal (due to anxiety), poor friendship quality, and maladaptive coping strategies are relevant to SoP as a precursor to depression (Pathway 1).

Appropriately, Epkins and Heckler (2011) used interpersonal risk as a model for the co-occurrence of social anxiety and depression in youth. Core risk factors (i.e., temperament; genetics; parental psychopathology) were proposed to interact with interpersonal risk factors centering on parents and peers (e.g., loneliness; maladaptive parenting; peer victimization) leading to depression. By emphasizing interpersonal variables as a pathway between SoP and depression, the model fits for a specific anxiety disorder. Even so, research linking core and interpersonal risk factors to SoP specifically (and not just anxiety in general) is lacking. Our Pathway 1 is consistent with the Epkins and Heckler (2011) findings. As with SAD, finding that successful treatment of SoP protects against onset of depression would be consistent with Pathway 1. Additionally, Pathway 1 suggests that youth with the situational subtype of SoP (who may be likely to demonstrate less impairment in interpersonal relationships than youth with generalized SoP) are considerably less likely to develop subsequent depression. Longitudinal studies of youth with risk factors for both depression and SoP would inform our understanding of the relationship of SoP and depression relative to Pathways 1 and 3.

GAD and MDD—Attention has been paid to whether or not GAD and MDD are separate disorders given the symptom overlap (i.e., insomnia; fatigue; difficulty concentrating). Longitudinal data suggest that GAD and MDD cross-predict each other more strongly than each disorder predicts itself over time (Copeland, Shanahan, Costello, & Angold, 2009; Moffitt et al., 2007; Pine et al., 1998). However, the pattern may not be consistent across developmental stages. In Copeland et al. (2009), only childhood depression predicted young adult GAD and only adolescent GAD predicted later depression. Further, childhood and adolescent GAD and MDD predicted different adult disorders, and young adult GAD and MDD were predicted by different childhood and adolescent disorders. The National Comorbidity Survey (N = 8098 respondents, ages 15–54 years) found that nearly one-third of all non-chance co-occurrences of GAD and a major depressive episode involved both disorders starting in the same year (Kessler et al., 2008). Within this study, the odds ratio for secondary major depression among individuals with GAD did not become higher with the passage of time since onset of GAD, contradicting the theory that MDD results from exhaustion in response to unremitting anxiety (Akiskal, 1985). According to Kessler et al. (2008), the cross-lagged associations between GAD and major depression are likely due to common causes and/or the effects of one disorder on the other. A recent study of the symptoms of adults with comorbid GAD-MDD versus MDD alone suggests that the high comorbidity rates are partly an artifact of the diagnostic system (Zbozinek et al., 2012).

According to meta-analyses by Hettema, Neale, and Kendler (2001) and Sullivan, Neale, and Kendler (2000), MDD and GAD each show modest familial aggregation and heritability. Family studies (Skre, Onstad, Edvardsen, Torgersen, & Kringlen, 1994; Mendlewicz, Papdimitriou, & Wilmotte, 1993; Reich, 1995; Kendler, Davis, & Kessler, 1997), twin studies (Kendler, Gardner, Gatz, & Pedersen, 2007; Kendler, 1996; Kendler, Neale, Kessler, Heath, & Eaves, 1992; Roy, Neale, Pedersen, Mathe, & Kendler, 1995), and transmission studies (which estimate prevalence rates in children whose parents are probands; Lieb, Isensee, Hoffer, Pfister, & Wittchen, 2002) indicate that MDD shares genetic risk factors with GAD, to a greater extent than with other anxiety disorders

(Hettema, 2008). Using twin data, Kendler, Prescott, Myers, and Neale (2003) provided evidence that genetic risk pertains to internalizing and externalizing factors, with the internalizing factor further divided into “anxiety-misery” and “fear” factors. Anxiety-misery loads most strongly on GAD and MDD and “fear” loads most strongly on animal and situational phobias, with panic disorder falling between but closer to GAD and MDD.

Supporting the notion of separate disorders, GAD and MDD have been found to show neuroanatomical differences and distinct disruptions to neuroendocrine and neuropeptide systems (Martin & Nemeroff, 2010). Although both disorders respond to SSRIs, GAD but not MDD generally responds to anxiolytics (e.g., Schatzberg & Cole, 1987). There has been less research on environmental contributions to MDD and GAD specifically (versus anxiety disorders generally). Stressful life events in adolescence predict adult MDD but not GAD (e.g., Pine, Cohen, Johnson, & Brook, 2002). Adult studies suggest that stressful life events are related to both disorders but more strongly to MDD (e.g., Newman & Bland, 1994), with only partial overlap in the types of events preceding the onset of each disorder (e.g., Kendler, Hettema, Butera, Gardner, & Prescott, 2003).

Overall, findings support MDD as separate but more closely related to GAD than other anxiety disorders. Given that the median age of onset is much earlier for anxiety than depression (e.g., Kessler et al., 2005), it makes sense to think of these disorders as distinct in youth, although GAD typically does not precede depression in comorbid youth (e.g., Essau, 2003). We consider GAD/MDD comorbidity as exemplary of Pathway 2. In assessing GAD/MDD comorbidity, future studies need to attend to overlap in the diagnostic criteria. There are shared symptoms, but are there qualitative differences? For example, individuals with these diagnoses report difficulties with sleep and concentration, but are they experienced as different by GAD versus depressed individuals? Sleep interruptions may be due to worry in GAD versus restlessness in MDD. Diagnostic instruments lack detail, and may need revision to address such symptom distinctions.

Gender Differences

Boy-girl differences, not reviewed in 1992 due to a dearth of published reports, have since received substantial attention. Not until early adolescence, when rates of depression in girls increase drastically, are gender differences in depression evident. At this time, depression occurs two to three times more often in girls than in boys (Hankin, 2009; Zahn-Waxler, Crick, Shirtcliff, & Woods, 2006). Teen girls report higher levels of depression than boys, a finding that is amplified in clinical samples (i.e., Compas et al., 1997; De Bolle et al., 2010). Data on Age X Gender interactions for anxiety in youth are much less clear. Anxiety has been found to be more prevalent among girls in some community samples (Aune & Stiles, 2009; Angold et al., 1999; Axelson & Birmaher, 2001; Costello et al., 1996; Leikanger, Ingul, & Larsson, 2012) but not in diagnosed samples (i.e., Kendall et al., 2010). Girls report more fears than boys (Gullone, 2000), but they do not have higher rates of anxiety disorders (e.g., Kendall, Hudson, Gosch, Flannery-Schroeder, & Suveg, 2008; Kendall et al., 2010). There is some evidence of gender differences in temperamental fear as early as infancy (e.g., Halpern, Brand, & Malone, 2001). Although a meta-analysis suggested that these gender differences are negligible (Else-Quest, Hyde, Hill Goldsmith, & Van Hulle, 2006), most of

the studies had modest sample sizes and relied on parent-report measures of temperament. More recent studies using multiple informants have consistently shown significant gender differences in fear. Across three independent samples of preschool- and early elementary school-aged children, girls exhibited higher levels of fear than boys across maternal- and paternal-report measures as well as behavioral observations of temperament (Olino, Durbin, Klein, Hayden, & Dyson, 2013). In a twin study that used the same methods of assessment, girls showed higher levels of shyness than boys (Gagne, Miller, & Goldsmith, 2013). Evidence from the adult literature suggests that, compared with men, women are more likely to have comorbid anxiety-mood disorders (e.g., Angst, Merikangas, & Preisig, 1997).

Theories regarding gender discrepancies in anxiety and depression have been reviewed (Bell, Foster, & Mash, 2005; Hankin & Abramson, 2001; Hankin, Wetter, Cheely, & Oppenheimer, 2008; Rutter, Caspi, & Moffitt, 2003; Zahn-Waxler et al., 2006), and gender differences offer hints about the etiology of comorbid anxiety and depression. For instance, cognitive vulnerabilities such as rumination (more common among females) are common to depression and anxiety. McLaughlin and Nolen-Hoeksema (2011) found that rumination accounted for a large portion of the overlap between self-reported depression and anxiety symptoms among adolescents (and adults), and was also associated with elevated risk for the development of comorbid anxiety/depression symptoms over time. Co-rumination (excessive negative discussion of problems within a close relationship) is also common among adolescent girls (Rose, 2002) and is positively associated with symptoms of both depression and anxiety (Rose, Carlson, & Waller, 2007; Tompkins, Hockett, Abraibesh, & Witt, 2011), although negatively associated with social anxiety (Starr & Davila, 2009). Gender differences in relationship processes and interpersonal stressors, particularly in adolescence, may be linked with depression and anxiety, and warrant research (Rudolph, 2002).

Hankin (2009) supported a cognitive vulnerability-transactional stress model (Hankin & Abramson, 2001) among community youth: sex differences in depression and anxiety symptoms were partially explained by risk mechanisms, including rumination and a negative cognitive style, and exposure to stressors. Given that anxiety generally precedes depression, sex differences in anxiety have been hypothesized as a potential reason for sex differences in later depression (Zahn-Waxler, Shirtcliff, & Marceau, 2008). However, two retrospective reports (Parker & Hadzi-Pavlovic, 2004; Parker & Hadzi-Pavlovic, 2001) suggested that female gender was independently related to subsequent depression when accounting for prior anxiety, although prior anxiety made a stronger contribution than gender (Parker & Hadzi-Pavlovic, 2001). Other studies suggest that the gender difference may be attributed to variations in the expression of depression. The “anxious” subtype of depression (i.e., high anxiety during mood episodes, negative self-evaluation, poor concentration) and “somatic” subtype of depression (i.e., sleep disturbance, pain symptoms) may be more prevalent among adult females than adult males (Halbreich & Kahn, 2007; Silverstein, 1999), but this finding has little support with youth (i.e., Nilzon & Palmerus, 1997).

Anxious boys, in some research, were more prone to developing later depression than girls (Gallerani, Garber & Martin, 2010; Väänänen et al., 2011). Anxiety may be less socially

acceptable for boys than girls, contributing to decreased social support and increased feelings of rejection.

Overall, the literature indicates that there are higher rates of anxiety, depression, and anxious-depressive comorbidity among community samples of girls, particularly in adolescence. Boys and girls have comparable rates of anxiety disorders, but girls are more prone to common risk factors for anxiety and depression. Further research is needed to better understand biological (e.g., pubertal) as well as psychosocial factors that contribute to anxious-depressive comorbidity and gender differences over time. Within Pathways 1 and 3, gender differences can interact with risk factors associated with anxiety and depression comorbidity. Pathway 2 involves an anxious type of depression (two disorders are highly related), more often observed in females.

Suicidality

Youth suicide rates are a worldwide concern (Goldsmith, Pellmar, Kleinman, & Bunney, 2002). An increased rate of suicidality in depression, particularly MDD, has been well established (i.e., Liu et al., 2006). In contrast, the results of studies of the relationship between anxiety disorders and suicidality have been mixed, and not reviewed in 1992 due to the absence of data. In a recent study (O'Neil-Rodriguez & Kendall, 2012), 58% of youth diagnosed with an anxiety disorder reported suicidal ideation. Some studies have uncovered an association between anxiety and suicidality independent of depression (Boden, Fergusson, & Horwood, 2007; Foley, Goldston, Costello, & Angold, 2006; Ghaziuddin, King, Naylor, & Ghaziuddin, 2000; Goldston et al., 2009; Liu et al., 2006; Masi, Mucci, et al., 2001; O'Neil, Puleo, Benjamin, Podell, & Kendall, 2012; O'Neil-Rodriguez & Kendall, 2012) whereas a few others have not (Barbe et al., 2005; Esposito & Clum, 2002; Greene, Chorpita, & Aukahi, 2009; Ryan et al., 1987; Strauss et al., 2000). It may be that emotion dysregulation (Southam-Gerow & Kendall, 2000; Garber, Braafladt, & Weiss, 1995; Keenan, Hipwell, Hinze, & Babinski, 2009; Silk, Steinberg, & Morris, 2003; Suveg, Hoffman, Zeman, & Thomassin, 2009) and distress tolerance (Ellis, Fischer, & Beevers, 2010; Huang, Szabó, & Han, 2009; Keough, Riccardi, Timpano, Mitchell, & Schmidt, 2010; Daughters et al., 2009) constructs related to both depression and anxiety, drive their associations with suicidality (Zlotnick, Donaldson, Spirito, & Pearlstein, 1997; Tamas et al., 2007; Nock & Mendes, 2008; Anestis, Bagge, Tulle, & Joiner, 2011). However, operational definitions of emotion dysregulation and distress intolerance have been inconsistent.

Why are the findings regarding the relationship between anxiety and suicidality mixed? One explanation has to do with severity of the disorder (e.g., in community versus hospitalized youth), type of anxiety disorder, and the operational definition of suicidality (O'Neil-Rodriguez & Kendall, 2012). Although few studies have been adequately powered to examine suicidality in relation to each individual anxiety disorder, studies have supported specific relationships with GAD (Foley et al., 2006; Goldston et al., 2009; Masi, Mucci et al., 2001) and SAD (Liu et al., 2006; Masi, Mucci et al., 2001). The operational definition of suicidality (e.g., ideation; intent; capability of acting on intent) is especially relevant. For example, it is plausible that youth with an anxiety disorder show heightened suicidality because they experience and/or report *intrusive* thoughts about suicide, yet are not likely to

experience suicidal intent. The content of suicidal thoughts experienced by depressed youth may differ and have associations with suicidal intent/behavior. Given the low base rate of suicidal behavior, large samples, as well as clear definitions of suicidality, are needed for this research.

It has been suggested that youth with both an anxiety disorder and a recent onset of a depressive episode are at particularly high risk for suicide attempts (Pawlak, Pascual-Sanchez, Raë, Fischer, & Ladame, 1999). Studies with youth have not distinguished among the anxiety disorders in examining their relationship to suicidality, but research with adults links generalized anxiety and social phobia, in particular, to high risk patterns of self-harm and suicide attempts (Chartrand, Sareen, Toews, & Bolton, 2012). Given the public concern that suicidality poses (Heron, 2007), research is need, but anxiety needs to be examined in terms of specific anxiety disorders rather than as a unitary disorder.

Assessment

To understand the pathways to anxiety and depression among youth, it is important to have accurate assessments. Brady and Kendall (1992) reviewed measures specific to anxiety or depression, relevant subscales of more general behavioral ratings scales, and structured interviews. At that time, anxiety and depression measures were highly correlated and lacked discriminant validity. We discuss discriminant validity and highlight the emergence of relevant symptom measures.³ We emphasize that the purpose of assessment should guide the decision to measure symptoms versus disorders (Kraemer, Noda, & O'Harra, 2004), as well as the selection of specific symptom measures.⁴

Discriminant Validity of Anxiety and Depression Measures

Numerous clinician-rated, child self-report, and parent-report instruments are available (see Myers & Winters, 2002; Silverman & Ollendick, 2005). However, findings regarding the ability of the available measures to discriminate between anxiety and depression have been mixed. There is evidence that three measures, the Multidimensional Anxiety Scale for Children (MASC; March et al., 1997), the Screen for Anxiety and Related Disorders (SCARED; Birmaher et al., 1999), and the Pediatric Anxiety Rating Scale (PARS; RUPP, 2002), tap depression less than other anxiety measures (e.g., Dierker et al., 2001; Wood et al., 2002; Birmaher et al., 1997; 1999), although this has not been studied extensively. Total scores on the Revised Children's Manifest Anxiety Scale (RCMAS; Reynolds & Richmond, 1985) do not appear to discriminate between anxiety and affective disorders (see meta-analysis by Seligman, Ollendick, Langley, & Baldacci, 2004), but the Worry/Oversensitivity subscale of the RCMAS performs better (Lonigan, Carey, & Finch, 1994).

³Although not yet a focus for assessing anxiety and depression in youth, item response theory (IRT) merits consideration and application. IRT may be especially useful because it includes methods for scoring questionnaires that tap (a) the strength of a relationship of specific item responses to an underlying construct and (b) the degree to which a collection of questions measure one coherent construct (see Steinberg & Thissen, 2013). For example, one IRT study found that psychomotor agitation/retardation was more likely to be endorsed by adolescents with depression only than depressed adolescents with comorbid internalizing problems (Small et al., 2008).

⁴For example, there is some evidence based on item response modeling that the Beck Depression Inventory (BDI; Beck & Steer, 1993; Beck et al., 1961) assesses a larger range of depression symptom severity among adolescents than the Center for Epidemiologic Studies – Depression Scale (Radloff, 1977), providing more information at higher severity levels (Olino et al., 2012).

The Beck Depression Inventory (BDI; Beck & Steer, 1993; Beck et al., 1961) has discriminated between anxiety and depression in adults (Barrera & Garrison-Jones, 1988; Marton et al., 1991) and two of four factors, Negative Self-Attitude and Performance Difficulty, have discriminated depressed from anxious teenagers (Bennett et al., 1997). There is relatively little evidence supporting discriminative validity of other measures, such as the Children's Depression Inventory (CDI; Kovacs, 1985; 1992), the Reynolds Adolescent Depression Scale (RADS; Reynolds & Mazza, 1998), the Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960; Warren, 1997). The Child Behavior Checklist (CBCL) does not differentiate between depression and anxiety, as the Anxious/Depressed subscale assesses negative affect more globally (Chorpita, Albano, & Barlow, 1998; Chorpita & Daleiden, 2002).

Measures Based on the Tripartite Model

Since Brady and Kendall's (1992) review, measures consistent with the Tripartite Model have been developed for youth.⁵ These include the Revised Child Anxiety and Depression Scale (RCADS; Chorpita, Yim, Moffitt, Umemoto, & Francis, 2000), the Positive and Negative Affect Scale for Children (PANAS-C; Laurent et al., 1999), the Physiological Hyperarousal Scale for Children (PH-C; Laurent, Catanzaro, & Joiner, 2004), the Negative Affectivity Self-Statement Questionnaire (NASSQ; Ronan, Kendall, & Rowe, 1994), and the Affect and Arousal Scale (AFARS; Chorpita, Daleiden, Moffitt, Yim, & Umemoto, 2000; Daleiden, Chorpita, & Lu, 2000). According to Silverman and Ollendick (2005), these measures have discriminated between anxiety and depression better than scales designed to target one or the other specifically. Considering the multiple pathways model, it is important to use measures of specific anxiety disorders that discriminate between depression and specific forms of anxiety, while also documenting any overlap of the two conditions. Although categorical assessments (i.e., structured diagnostic interviews) are required to document comorbidity (i.e., the presence of two disorders) and may be useful for research, they decrease power for hypothesis testing. Dimensional assessments (levels of severity) that tap risk for the comorbid condition may be preferred. To the extent that predictors of disorders may be different from predictors of symptoms (e.g., Gotlib, Lewinsohn, & Seeley, 1995), a combined approach to assessment is ideal for understanding comorbidity.

⁵The 47-item RCADS (Chorpita, Yim et al., 2000) assesses SAD, SoP, GAD, panic disorder, OCD, and MDD in youth 6 to 19 years of age. Internal consistency estimates for the diagnoses range from .71 (SoP) to .83 (GAD) and retest reliability estimates range from .65 (OCD) to .80 (SoP). There is a parent version (RCADS-P) (Ebesutani et al., 2010). Confirmatory factor analyses using clinic-referred and community/school samples have not supported combining MDD and GAD scales (Ebesutani et al., 2010, 2011; Watts & Weems, 2006; Weems, Zakem, Costa, Cannon, & Watts, 2005).

The 27-item PANAS-C assesses sensitivity to positive and negative stimuli over the past two weeks in children 8 to 14 years old. Fifteen items load on the NA subscale (alpha = .92) and 12 items load on the PA subscale (alpha = .97). The PANAS-C scales have demonstrated convergent and discriminant validity with scores on child self-reports of depression and anxiety (Laurent et al., 1999). The 18-item PH-C assesses bodily manifestations of autonomic arousal in youth ages 12 to 17 over the past two weeks. The PH-C is internally consistent (alpha = .97). Three factors emerged representing PA, NA, and physiological arousal, and their intercorrelations were generally consistent with the Tripartite Model. Regression analyses showed that the PH-C added significantly to the prediction of anxiety after accounting for positive and negative affect.

The 27-item AFARS (Chorpita, Daleiden, et al., 2000), for use with 8–19 year-olds, has three subscales: NA, PA, and PH. Internal consistency estimates range from .77 to .81. Factor analyses identified NA and PA as relatively orthogonal while physiological arousal was positively associated with negative affect.

Treatment Response

The impact of comorbid anxiety and depression on treatment outcome among youth was identified as a “major concern yet to be addressed” (p. 253) in the 1992 review. Although treatment response does not confirm or disconfirm an initial pretreatment diagnosis or causal hypothesis, it is of interest to consider the distinct and/or overlapping treatment effects with regard to anxiety and depression in youth. Since Brady and Kendall (1992), studies have examined the effect of comorbidity on response to treatment of the target disorder(s). Identifying treatment moderators (e.g., comorbidities), or determining which children respond to which treatments, could greatly improve short- and long-term outcomes (Emslie, Mayes, Laptook, & Batt, 2003). If comorbid depression-anxiety predicts a poorer response to treatment for either disorder separately, then we are challenged to both (1) understand why/how comorbidity interferes with a favorable treatment outcome, and (2) enhance current or develop new interventions to meet the unmet needs. The majority of anxiety treatment studies have targeted multiple disorders: to the extent that the pathways to comorbidity are differentially related to specific anxiety disorders, larger and/or single-disorder samples would be needed to evaluate the impact of comorbid depression within the context of the proposed model.

Medication Treatment

Anxiety and depression have been reported to respond to selective-serotonin reuptake inhibitors (SSRIs; i.e., Walkup et al., 2008; Brent et al., 2008; Hughes et al., 2007), and studies suggest that anxiety and depression have overlapping functional and structural brain pathology (Nutt & Stein, 2006; see review by Cameron, Abelson, & Young, 2004). Research regarding the neurobiology of anxiety and depression is outside the current scope, but interested readers are referred to other articles (Beesdo et al., 2009; Hettema, 2008; Lau et al., 2009; Morilak & Frazer, 2004; Thibodeau, Jorgensen, & Kim, 2006).

There is a small literature on medication response in youth with comorbid mood and anxiety disorders. For example, although studied in adults (Dunlop & Davis, 2008), few studies have examined benzodiazepine use in youth and the available findings are mixed (Strawn, Sakolsky, & Rynn, 2012). Guidelines for benzodiazepine use, even for adults, cannot be established until further research is available (Sekula, DeSantis, & Gianetti, 2003).

SSRIs are frequently prescribed for child/adolescent anxiety disorders (Baldwin et al., 2005) and depression (Birmaher & Brent, 2002). Of interest, comorbid disorders (including anxiety) were not associated with fluoxetine outcomes among youth in three large trials (Cheung et al., 2010; Tao et al., 2009). The Research Units on Pediatric Psychopharmacology Anxiety Study Group found that depressive symptoms predicted poorer response to fluvoxamine among anxious youth, but none of the youth in the sample met criteria for MDD (Walkup et al., 2003). In sum, SSRIs may be effective in reducing comorbid anxiety and mood symptoms but the current state of the research is too limited for a strong conclusion. At this juncture, if medication is pursued as a treatment option for anxious and depressed youth, combined treatment (CBT + medication) is the best option (Walkup et al., 2008; TADS Team, 2004).

Psychosocial Treatment

The most frequently studied psychosocial intervention for anxiety and/or depression in youth is CBT. Since Brady and Kendall (1992), gains have been made in three broad areas: (1) the differential effects of CBT on depression versus anxiety, (2) the impact of comorbidity on CBT outcomes, and (3) the impact of CBT for the principal disorder on comorbid symptoms.

The effects of CBT on depression versus anxiety—Based on the treatment literature, Chu and Harrison (2007) concluded that CBT has been comparably effective in producing symptom change in both anxiety and depression. However, relative to CBT for depression, CBT for anxiety has resulted in greater behavioral change and improved coping. Few studies examined physiological processes (although studies examining fMRI changes are underway), and studies are needed to examine whether CBT affects change through similar or different mediational pathways for anxiety versus depression. Many previous studies neglected to test mediation (Prins & Ollendick, 2003), but there are data indicating that anxiety and depression treatment outcomes are both at least partially mediated by changes in self-talk (e.g., Kaufman, Rohde, Seeley, Clark, & Stice, 2005; Kendall & Treadwell, 2007). That is, reduced negative self-talk mediates positive treatment outcomes, although temporal precedence has yet to be established. Corresponding to this, studies have supported the content specificity of negative self-statements, with anxious self-talk involving future-oriented questioning about harm, and depressive self-talk focused on loss and personal failure (e.g., Schniering & Rapee, 2004). Consistent with the Tripartite Model, which posits level of negative but not positive affect as common to anxiety and depression, change in negative but not positive self-talk has been implicated in anxiety reduction (Kendall & Treadwell, 2007). As Garber and Weersing (2010) noted, improved understanding of the mechanisms by which anxiety and depression are linked can be invaluable for identifying optimal treatment targets.

The impact of comorbidity on CBT outcomes—The impact of comorbid depression on CBT for anxiety (and vice versa) has been explored but findings are mixed. Several studies found that comorbid anxiety predicted poorer outcomes of depression treatment (Curry et al., 2006; Vostanis, Feehan, & Grattan, 1998; Young, Mufson, & Davies, 2006). Findings from a depression prevention program for adolescents (Interpersonal Psychotherapy-Adolescent Skills Training; Young & Mufson, 2003) showed that higher levels of comorbid anxiety symptoms were associated with slower rates of change in depressive symptoms. Upon further exploration, the authors determined that the effect of anxiety symptoms was apparent in the early weeks of treatment, but by postintervention, comorbid anxiety symptoms had no impact on depression outcomes. Perhaps, the presence of anxiety merely “delayed” intervention effects (Young et al., 2012). Similarly, there was largely no impact of comorbid anxiety on psychoeducational therapy for mood disorders (Cummings & Fristad, 2012), a school-based universal prevention program (Pössel, Seeman, & Hautzinger, 2008), or combined medication and psychotherapy for treatment resistant depression (Asarnow et al., 2009).

The presence of anxiety has predicted a more positive response to depression treatment for youth. Brent and colleagues (1998) reported that comorbid anxiety predicted end-of-treatment level of depression, and that comorbidly anxious youth responded better to CBT than to a family therapy and a nondirective supportive therapy. Perhaps, as the authors suggested, this finding is related to the fact that youth with comorbid anxiety and depression share cognitive distortions (both targeted in CBT). Comorbid anxiety has also been associated with better treatment outcome for group and multifamily CBT for mood disorders (Cummings & Fristad, 2012; Rohde et al., 2001), but findings may be due to the comorbidly anxious patients' higher pretreatment depression scores, which provided greater opportunity for change. It is also possible that anxiety magnifies treatment effects among depressed youth due to the perfectionistic and social evaluation concerns that are part of anxiety contributing to child involvement and adherence.

What about the role of comorbid depressive symptoms on treatments for anxiety? Few studies have been sufficiently powered to answer this question, although some have examined the impact of non-anxiety comorbidity broadly (see Ollendick, Jarrett, Grills-Taquechel, Hovey, & Wolff, 2008). Two studies found that comorbid depressive symptoms and diagnoses were associated with poorer response to CBT for anxiety disorders generally (Berman, Weems, Silverman, & Kurtines, 2000) whereas another study did not replicate this finding (Southam-Gerow, Kendall, & Weersing, 2001; Rapee et al., 2013). Few studies have examined the impact of comorbid depression on the treatment of specific anxiety disorders. However, depressive symptoms have not predicted response to group CBT for SoP in youth (Kley, Heinrichs, Bender, & Tuschen-Caffier, 2012), nor have they moderated outcomes of social effectiveness therapy for children with SoP (Alfano et al., 2009). In some anxiety-treatment study designs, such as comparisons to medications where the medication arm may actually target both disorders, depressive disorders are an appropriate exclusion criterion (e.g., Walkup et al., 2008). Even so, excluding MDD cases limits conclusions regarding the role of depressive disorders on anxiety treatment outcomes.

The impact of CBT on comorbid symptoms—Although cases of diagnosed depression may not have been included, evidence from treatment-outcome studies indicates that CBT for anxiety often results in decreased depressive symptoms (e.g., Barrett, Dadds, & Rapee, 1996; Kendall et al., 1997; Kendall et al., 2008; Kendall, Safford, Flannery-Schroeder, & Webb, 2004; Manassis et al., 2002; Mendlowitz et al., 1999; Silverman et al., 1999). In terms of school-based interventions, a meta-analysis found that anxiety interventions did not yield significantly greater reductions in depressive symptoms than controls, but only five studies have been reported (Mychailyszyn, Brodman, Read, & Kendall, 2012). The effect of depression treatments on anxiety symptoms has not been consistent. One meta-analysis, by Weisz, McCarty, and Valeri (2006), indicated that interventions for depression in children yielded significant reductions in anxiety symptoms (effect size = 0.39), though smaller in magnitude than reductions in depressive symptoms (effect size = 0.57). Interpersonal therapy has been associated with fewer panic/somatic and generalized anxiety symptoms, but not social anxiety symptoms compared to treatment as usual (Young et al., 2012). No reduction in comorbid anxiety symptoms was found in a study of treatment for mood-disordered youth (Cummings & Fristad, 2012).

It seems reasonable that youth with comorbid anxiety need treatments that specifically target fears through exposure tasks (Bouchard, Mendlowitz, Coles, & Franklin., 2004; Kendall et al., 1997; Kendall et al., 2005). Given evidence that the onset of anxiety typically precedes the onset of depression, randomized clinical trials with extended follow-up assessments are needed to determine if treating anxiety prevents depression. The only study to date did not support this possibility (Benjamin, Harrison, Settiani, Brodman & Kendall, 2013). Successful treatment of childhood anxiety was associated with reduced likelihood of substance use problems but not depressive disorders at 16-year follow-up. Enhancing anxiety treatment with strategies specific to the prevention of depression may prove beneficial.

Treating Comorbid Anxiety and Depression

Findings regarding both comorbidity and CBT outcomes have led investigators to directly address comorbid symptoms. Chu, Merson, Zandberg, and Areizaga (2012) proposed three approaches: the flexible implementation of single-target interventions, modular-based treatment, and transdiagnostic therapy. Interventions that target principal disorders can be implemented flexibly (e.g., Hudson, Krain & Kendall, 2001; Manassis & Monga, 2001) to address related comorbidities. For example, “flexibility within fidelity” (Kendall & Beidas, 2007) involves adapting an empirically supported manual to suit a particular child while adhering to the treatment goals/approach (Kendall, Gosch et al., 2008; see also Kendall, Kortlander, Chanksy, & Brady, 1992). Modular-based CBT includes core and supplemental modules that are selected to fit client needs based on decision-making algorithms (Chorpita et al., 2004; Chorpita & Weisz, 2009). Finally, transdiagnostic therapy focuses on commonalities between the co-diagnosed disorders (Kendall et al., in press).

Twenty years ago, Brady and Kendall (1992) raised the question of whether depression and anxiety benefit from similar treatment approaches or require differential intervention. At that time, transdiagnostic treatment approaches (e.g., Barlow, Allen, & Choate, 2004) had not been introduced. Presently, the Unified Protocol for the Treatment of Emotional Disorders in Youth (UP-Y; Ehrenreich et al., 2008; Ehrenreich, Goldstein, Wright, & Barlow, 2009) and Group Behavioral Activation Therapy (GBAT) for Anxious and Depressed Youth (Chu, Colognori, Weissman, & Bannon, 2009) are two examples. By combining target problems, both UP-Y and GBAT hope to minimize the burden associated with training and supervision in community settings.

UP-Y, adapted from a transdiagnostic treatment for emotional disorders in adults (Barlow et al., 2004), focuses on ways in which youth experience and respond to multiple emotions. UP-Y has eight sections, five of which are required. Preliminary data support the feasibility of UP-Y (Bilek & Ehrenreich-May, 2012). GBAT, also referred to as the SKILLS Program, was adapted from adult protocols (Addis & Martell, 2004; Martell et al., 2001) for use with adolescents in school settings. The program is based on the idea that behavioral activation is involved in the treatment of both anxiety and depression. The program consists of ten weekly sessions, after which clients identify functional domains they would like to optimize. Pilot data suggest that the program is feasible and acceptable, but, as with the range of transdiagnostic approaches, randomized clinical trials are needed establish treatment

efficacy. Additionally, evaluations of transdiagnostic prevention programs are needed. For example, EMOTION (Kendall, Stark, Martinsen, O'Neil, & Aroras, 2013), is a 20-session indicated prevention program, implemented in a group format, that integrates core components of empirically supported treatments for anxiety and depression in youth (*Coping Cat*, Kendall & Hedtke, 2006a; 2006b; *ACTION*, Stark, Schnoebelen, Simpson, Hargave, & Glenn, 2007, respectively).

Do the multiple pathways warrant differential treatment? For instance, we hypothesize that Pathway 2 comorbidity, with greater symptom overlap and simultaneous presentation of anxiety-depression, calls for concurrent treatment of anxiety and depression (e.g., a transdiagnostic approach). Pathway 1, with principal anxiety problem and depression as a complicating factor, may be best addressed with a flexible implementation of an anxiety treatment. Pathway 3 implicates a flexible implementation of a depression treatment, with residual anxiety addressed pending successful treatment of depression.

Conclusions and Future Directions

Research since the 1992 review has advanced our knowledge about comorbid anxiety and depression in youth (see Table 1). Although Brady and Kendall's (1992) conclusion that depression and anxiety were distinct but related disorders has been supported by the updated review, progress has been made delineating the overlapping and distinctive features of anxiety and depression. Further progress has been made describing the heterogeneity of the anxiety disorders (SoP, SAD, and GAD) and the unique relationship of each to depression.

Several studies suggest developmental trajectories of depression-anxiety comorbidity in youth and these trajectories appear to vary depending on the subtype and onset of the disorders. Of the anxiety disorders, GAD demonstrates the most overlap with depression in terms of symptoms and risk factors. Although these two disorders have shared genetic risk and cross-predict each other, we must ask, "How much of the relationship is linked to symptom overlap between the two diagnoses?" Some researchers (e.g., Watson, 2005) suggest that GAD and depression be considered within a general category of "distress disorders," but we suggest that variations in the age of onset indicate that they are best considered distinct (but highly related) disorders in youth.

SAD and SoP are fear-related anxiety disorders (Watson, 2005), and demonstrate different associations with depression than GAD. In some instances, anxiety puts individuals at risk for depression, likely a result of interpersonal and cognitive processes. There is some indication that depression secondary to anxiety may be a less severe form of depression (Olinio et al., 2010), perhaps different from more severe depression that occurs as a result of biological processes. SAD and depression may share risk factors (e.g., parental depression), or depression may onset following SAD-related impairment. Youth with SoP are more likely to become depressed, perhaps resulting from social isolation, low self-esteem, and potential peer victimization. However, the developmental pathway to depression from SoP is complex (Epkins & Heckler, 2011) and depression can precede SoP. Additional longitudinal studies beginning in early childhood, *with consideration given to the specific anxiety disorder*, will clarify the relationship between depression and anxiety and could have strong implications

for the early identification of youth at risk for either disorder. Gender differences in depression and in anxiety, separately, have been studied, but less attention has been paid to gender and comorbidity. Data from community samples suggest that anxiety-depression comorbidity is more common in girls than boys. Some data suggest that suggest that anxious boys are prone to developing later depression. Future exploration of gender differences in the anxiety-depression comorbidity is warranted.

Theoretical models help explain the frequent co-comorbidity between anxiety and depression. Several models have been proposed, such as the Tripartite (Clark & Watson, 1991) and BIS/BAS (Gray, 1982) theories, yet findings have indicated shortcomings with both. For instance, the relationships between anxiety-depression and PA and PH are less straightforward than hypothesized. The role of the BIS/BAS and co-occurring depression-anxiety merits further study. Behavioral inhibition serves as an early marker of anxiety (and perhaps depression), a finding with important implications for prevention and early intervention (Hirshfeld-Becker et al., 2010). The models offer guidance and have merit but there are research needs related to developmental change. Essential to advancements, future research must consider the heterogeneity among anxiety disorders when considering the co-occurrence/comorbidity of anxiety and depression: anxiety disorders are not all the same!

The multiple pathways model builds on previous models by emphasizing the heterogeneity of the anxiety disorders and their degree of overlap with depression, as well the developmental sequence of anxiety and depression. Consistent with the reported findings, we propose that anxiety-depression comorbidity is heterogeneous, not singular, and emerges from multiple pathways. Pathway 1 describes depressive presentations secondary to a principal anxiety disorder. The literature is consistent with Pathway 1 applying to SoP and SAD, both of which often precede the onset of a comorbid depression disorder (e.g., Fichter et al., 2010). Findings that depression secondary to anxiety is milder in presentation (Olinio et al., 2010) also support Pathway 1. Pathway 2 involves depression and anxiety as co-primary, having the highest degree of overlap between the two conditions, and best fits the comorbidity of GAD and depression. In support of this pathway, the order of onset of these two disorders in comorbid youth is not consistent (Essau, 2003), and many studies have found that GAD may be more similar to depression than to the other anxiety disorders (e.g., Watson, 2005). Pathway 3 describes principal depression, with anxiety secondary. Pathway 3 includes SoP secondary to a more severe depression. This pathway has the least empirical support and may occur less frequently than Pathway 1 or Pathway 2. We cannot yet determine the extent to which Pathway 3 describes chance comorbidity of anxiety and depression (Klein & Riso, 1993), or whether undetected anxiety symptoms are present primary to the onset of a depressive disorder. The pathways all require empirical testing to further inform the interplay between depression and anxiety symptoms and disorders in youth.

The goal is for models of anxiety-depression comorbidity to be applied in a way that improves current assessment and intervention for comorbid anxiety-depression. Knowledge has advanced since 1992 regarding the impact of anxiety-depression comorbidity on treatment outcome, with some indications of secondary benefits for the non-targeted disorder. Transdiagnostic treatment (geared to anxiety and depression) has gathered interest

and offers promise. Given the overlapping features of anxiety and depression, and the effects of one on the other, there may be cases where the successful treatment of one disorder (i.e., social anxiety) prevents or reduces the progression of the other disorder (Kessler & Price, 1993). The effective treatment of comorbid anxiety-depression depends on the relationship between them, with Pathways 1 and 3 calling for treatment of the principal disorder. Pathway 2, on the other hand, suggests the need for a transdiagnostic treatment.

We highlight specific areas for future research regarding the multiple trajectories of anxiety-depression among youth. For one, we need to further evaluate the risk factors. There are high-quality studies that examine the trajectories of anxiety/depression from adolescence to depression (e.g., Olino et al., 2010), but longitudinal studies beginning in early childhood are needed. These longitudinal studies could include analysis at the level of symptoms, as well as disorders, as otherwise undetected symptoms of one disorder may predict a diagnosis of another. Second, we highlight that anxiety disorders are heterogeneous, and that advances are linked to specific anxiety disorders. Depression, too, can be heterogeneous (e.g., Davidson, Pizzagalli, Nitschke, & Putnam, 2002; Small et al., 2008) and future work would be wise to consider such variation. For instance, it is possible to meet criteria for MDD through several symptoms (i.e., only five of nine MDD symptoms need be present). Diagnosed youth may exhibit varying symptom combinations, and future research should examine differing depressive profiles and how they are associated with anxiety in youth.

Thirdly, development can inform us about the protective factors, and future research should examine depressed or anxious youth who do not develop comorbidity. These protective factors have preventative implications, especially in instances where comorbidity arises as a result of impairment from the primary diagnosis. Fourth, research addressing transdiagnostic factors (e.g., rumination, negative affectivity, neuroticism) of anxiety and depression is needed, as well as features that distinguish them (e.g., anhedonia). Fifth, research identifying specific genes (Frani et al., 2010), such as the serotonin transporter (5-HTTT; Verhagen et al., 2009) and dopamine receptor genes (DRD2; Hayden et al., 2010), would benefit from precise assessment of depression and anxiety and their comorbidity, as well as any direct and indirect influences on the expression of anxiety and depression (i.e. gene-environment interactions; Silberg, Rutter, Neale, & Eaves, 2001).

Finally, multiple pathways need to take into account other comorbidities (e.g., externalizing disorders) and comorbidity within the anxiety disorders. As the field shifts toward classification schemes that promote rapid translation of basic neurobiological and behavioral research to improved understanding of psychopathology and advances in treatment (e.g., Sanislow et al., 2010), integration of categorical and dimensional approaches to comorbidity will be critical. One can readily anticipate that the next twenty years will further advance our understanding of these impairing conditions, as well as inform intervention efforts, reducing the impact of anxiety and depression on society and those affected.

Acknowledgments

Preparation of this review was facilitated by research grants from the National Institute of Mental Health (MH063747; MH086438) awarded to Philip C. Kendall.

References

- Addis, M.; Martell, C. *Overcoming depression one step at a time: The new behavioral activation approach to getting your life back*. Oakland, CA: New Harbinger; 2004.
- Akiskal, HS. Anxiety: Definition, relationship to depression, and proposal for an integrative model. In: Tuma, AH.; Maser, JD., editors. *Anxiety and the Anxiety Disorders*. Hillsdale, NJ: Lawrence Erlbaum Associates; 1985. p. 787-797.
- Alfano CA, Pina AA, Villalta IK, Beidel DC, Ammerman RT, Crosby LE. Mediators and moderators of outcome in the behavioral treatment of childhood social phobia. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2009; 48(9):945–953. [PubMed: 19625981]
- Alloy LB. Depression and anxiety: disorders of emotion or cognition. *Psychological Inquiry*. 1991; 2:72–74.10.1207/s15327965pli0201_16
- Alloy, LB.; Kelly, KA.; Mineka, S.; Clements, CM. Comorbidity in anxiety and depressive disorders: A helplessness-hopelessness perspective. In: Maser, JD.; Cloninger, CR., editors. *Comorbidity of mood and anxiety disorders*. Washington, DC: American Psychiatric Press; 1990. p. 499-543.
- Alpert JE, Fava M, Uebelacker LA, Nierenberg AA, Pava JA, Worthington JJ, Rosenbaum JF. Patterns of axis I comorbidity in early-onset versus late-onset major depressive disorder. *Biological Psychiatry*. 1999; 46:202–11.10.1016/S006-3223(99)00017-7 [PubMed: 10418695]
- American Psychiatric Association.. *Diagnostic and statistical manual of mental disorders*. 3. Washington, DC: American Psychiatric Association; 1987. revision
- American Psychiatric Association.. *Diagnostic and statistical manual of mental disorders*. 4. Washington, DC: American Psychiatric Association; 2000. text revision
- American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. 5. Arlington, VA: American Psychiatric Publishing; 2013.
- Anderson ER, Hope DA. A review of the tripartite model for understanding the link between anxiety and depression in youth. *Clinical Psychology Review*. 2008; 28:275–87.10.1016/j.cpr.2007.05.004 [PubMed: 17582665]
- Anderson ER, Veed GJ, Inderbitzen-Nolan HM, Hansen DJ. An evaluation of the applicability of the tripartite constructs to social anxiety in adolescents. *Journal of Clinical Child and Adolescent Psychology*. 2010; 39:195–207.10.1080/15374410903532643 [PubMed: 20390811]
- Anderson JC, Williams SM, McGee R, Silva PA. DSM-III disorders in preadolescent children: Prevalence in a large sample from the general population. *Archives of General Psychiatry*. 1987; 44:69–76.10.1001/archpsyc.1987.01800130081010 [PubMed: 2432848]
- Angold A, Costello EJ, Erkanli A. Comorbidity. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*. 1999; 40:57–87.10.1111/1469-7610.00424
- Angst J, Merikangas KR, Preisig M. Subthreshold syndromes of depression and anxiety in the community. *Journal of Clinical Psychiatry*. 1997; 58:6–10. [PubMed: 9236729]
- Anestis MD, Bagge CL, Tull MT, Joiner TE. Clarifying the role of emotion dysregulation in the interpersonal-psychological theory of suicidal behavior in an undergraduate sample. *Journal of Psychiatric Research*. 2011; 45:603–611.10.1016/j.jpsychires.2010.10.013 [PubMed: 21092986]
- Asarnow JR, Emslie G, Clarke G, Wagner KD, Spirito A, Vitiello B, Brent D. Treatment of selective serotonin reuptake inhibitor—resistant depression in adolescents: Predictors and moderators of treatment response. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2009; 48:330–339.10.1097/CHI.0b013e3181977476 [PubMed: 19182688]
- Aschenbrand SG, Kendall PC, Webb A, Safford SM, Flannery-Schroeder E. Is childhood separation anxiety disorder a predictor of adult panic disorder and agoraphobia? A seven-year longitudinal study. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2003; 42:1478–85.10.1097/00004583-200312000-00015 [PubMed: 14627883]
- Aune T, Stiles TC. The effects of depression and stressful life events on the development and maintenance of syndromal social anxiety: Sex and age differences. *Journal of Clinical Child and Adolescent Psychology*. 2009; 38:501–512.10.1080/15374410902976304 [PubMed: 20183637]
- Avenevoli S, Stolar M, Li J, Dierker L, Merikangas K. Comorbidity of depression in children and adolescents: Models and evidence from a prospective high-risk family study. *Biological Psychiatry*. 2001; 49:1071–81.10.1016/S0006-3223(01)01142-8 [PubMed: 11430849]

- Axelson DA, Birmaher B. Relation between anxiety and depressive disorders in childhood and adolescence. *Depression and Anxiety*. 2001; 14:67–78.10.1002/da.1048 [PubMed: 11668659]
- Baldwin DS, Anderson IM, Nutt DJ, Bandelow B, Bond A, Davidson JRT, Wittchen HU. Evidence-based guidelines for the pharmacological treatment of anxiety disorders: Recommendations from the British Association for Psychopharmacology. *Journal of Psychopharmacology*. 2005; 19:567–96.10.1177/0269881105059253 [PubMed: 16272179]
- Barbe RP, Williamson DE, Bridge JA, Birmaher B, Dahl RE, Axelson DA, Ryan ND. Clinical differences between suicidal and nonsuicidal depressed children and adolescents. *The Journal of Clinical Psychiatry*. 2005; 66:492–8.10.4088/JCP.v66n0412 [PubMed: 15816792]
- Barlow, DH. The nature of anxiety: Anxiety, depression, and emotional disorders. In: Rapee, RM.; Barlow, DH., editors. *Chronic anxiety: Generalized anxiety disorder and mixed anxiety-depression*. New York, NY: Guilford Press; 1991. p. 1-28.
- Barlow DH, Allen LB, Choate ML. Toward a unified treatment for emotional disorders. *Behavior Therapy*. 2004; 35:205–30.10.1016/S0005-7894(04)80036-4
- Barlow, DH.; Chorpita, BF.; Turovsky, J. Fear, panic, anxiety, and disorders of emotion. In: Hope, DA., editor. *Nebraska Symposium on Motivation, 1995: Perspectives on anxiety, panic, and fear*. Lincoln, NE: University of Nebraska Press; 1996. p. 251-328.
- Barrera M, Garrison-Jones CV. Properties of the Beck Depression Inventory as a screening instrument for adolescent depression. *Journal of Abnormal Child Psychology*. 1988; 16:263–73.10.1007/BF00913799 [PubMed: 3403810]
- Barrett PM, Dadds MR, Rapee RM. Family treatment of childhood anxiety: A controlled trial. *Journal of Consulting and Clinical Psychology*. 1996; 64:333–342.10.1037/0022-006X.64.2.333 [PubMed: 8871418]
- Beck, AT.; Steer, RA. *Beck Depression Inventory manual*. San Antonio, TX: Psychological Corporation; 1993.
- Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Archives of General Psychiatry*. 1961; 4:561–571.10.1001/archpsyc.1961.01710120031004 [PubMed: 13688369]
- Beevers CG, Meyer B. Lack of positive experiences and positive expectancies mediate the relationship between BAS responsiveness and depression. *Cognition and Emotion*. 2002; 16:549–564.10.1080/02699930143000365
- Beesdo K, Bittner A, Pine DS, Stein MB, Höfler M, Lieb R, Wittchen HU. Incidence of social anxiety disorder and the consistent risk for secondary depression in the first three decades of life. *Archives of General Psychiatry*. 2007; 64:903–12.10.1001/archpsyc.64.8.903 [PubMed: 17679635]
- Beesdo K, Knappe S, Pine DS. Anxiety and anxiety disorders in children and adolescents: Developmental issues and implications for DSM-V. *Psychiatric Clinics of North America*. 2009; 32:483–542.10.1016/j.psc.2009.06.002 [PubMed: 19716988]
- Beesdo K, Lau JY, Guyer AE, McClure-Tone EB, Monk CS, Nelson EE, ...Pine DS. Common and distinct amygdala-function perturbations in depressed versus anxious adolescents. *Archives of General Psychiatry*. 2009; 66:275–85.10.1001/archgenpsychiatry.2008.545 [PubMed: 19255377]
- Beesdo K, Pine DS, Lieb R, Wittchen H. Incidence and risk patterns of anxiety and depressive disorders and categorization of Generalized Anxiety Disorder. *Archives of General Psychiatry*. 2010; 67:1–16.10.1001/archgenpsychiatry.2009.177
- Beidel DC, Turner SM. At risk for anxiety: I. Psychopathology in the offspring of anxious parents. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1997; 36:918–24.10.1097/00004583-199707000-00013 [PubMed: 9204669]
- Bell, DJ.; Foster, SL.; Mash, EJ. Understanding behavioral and emotional problems in girls. In: Bell, DJ.; Foster, SL.; Mash, EJ., editors. *Handbook of Behavioral and Emotional Problems in Girls*. NY: Kluwer Academic/Plenum Publishers; 2005. p. 1-24.
- Belzer K, Schneier FR. Comorbidity of anxiety and depressive disorders: Issues in conceptualization, assessment, and treatment. *Journal of Psychiatric Practice*. 2004; 10:296–306.10.1097/00131746-200409000-00003 [PubMed: 15361744]

- Benjamin C, Beidas R, Comer J, Puliafico A, Kendall PC. Generalized Anxiety Disorder in youth: diagnostic considerations. *Depression and Anxiety*. 2011; 28:173–182.10.1002/da.20747 [PubMed: 21284071]
- Benjamin CL, Harrison JP, Settiani CA, Brodman DM, Kendall PC. Mental health outcomes in young adults 16 years after receiving treatment for child anxiety. 2012 Manuscript submitted for publication.
- Bennett DS, Ambrosini PJ, Bianchi M, Barnett D, Metz C, Rabinovich H. Relationship of Beck Depression Inventory factors to depression among adolescents. *Journal of Affective Disorders*. 1997; 45:127–134.10.1016/S0165-0327(97)00045-1 [PubMed: 9298425]
- Berman SL, Weems CF, Silverman WK, Kurtines WM. Predictors of outcome in exposure-based cognitive and behavioral treatments for phobic and anxiety disorders in children. *Behavior Therapy*. 2000; 31:713–731.10.1016/S0005-7894(00)80040-4
- Bernstein GA, Garfinkel BD. School phobia: The overlap of affective and anxiety disorders. *Journal of the American Academy of Child Psychiatry*. 1986; 25:235–241.10.1016/S0002-7138(09)60231-4 [PubMed: 3700911]
- Biederman J, Petty CR, Hirshfeld-Becker DR, Henin A, Faraone SV, Fraire M, Rosenbaum JF. Developmental trajectories of anxiety disorders in offspring at high risk for panic disorder and major depression. *Psychiatry Research*. 2007; 153:245–252.10.1017/S0033291706007781 [PubMed: 17764753]
- Bilek EL, Ehrenreich-May J. An open trial investigation of a transdiagnostic group treatment for children with anxiety and depressive symptoms. *Behavior Therapy*. 2012; 43:887–897.10.1016/j.beth.2012.04.007 [PubMed: 23046789]
- Bijttebier P, Beck I, Claes L, Vandereycken W. Gray's Reinforcement Sensitivity Theory as a framework for research on personality-psychopathology associations. *Clinical Psychology Review*. 2009; 29:421–30.10.1016/j.cpr.2009.04.002 [PubMed: 19403216]
- Birmaher, B.; Brent, D. Pharmacotherapy for depression in children and adolescents. In: Shaffer, D.; Waslick, BD., editors. *The Many Faces of Depression in Children and Adolescents*. Washington, DC: American Psychiatric Publishing, Inc; 2002. p. 309-330.
- Birmaher B, Brent DA, Chiappetta L, Bridge J, Monga S, Baugher M. Psychometric properties of the Screen for Child Anxiety Related Emotional Disorders (SCARED): A replication study. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1999; 38:1230–1236.10.1097/00004583-199910000-00011 [PubMed: 10517055]
- Birmaher B, Khetarpal S, Brent D, Cully M, Balach L, Kaufman J, Neer SM. The Screen for Child Anxiety Related Emotional Disorders (SCARED): Scale construction and psychometric characteristics. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1997; 36:545–553.10.1097/00004583-199704000-00018 [PubMed: 9100430]
- Boden JM, Fergusson DM, Horwood LJ. Anxiety disorders and suicidal behaviours in adolescence and young adulthood: Findings from a longitudinal study. *Psychological Medicine*. 2007; 37:431–40.10.1017/S0033291706009147 [PubMed: 17109776]
- Bouchard S, Mendlowitz SL, Coles ME, Franklin M. Considerations in the use of exposure with children. *Cognitive and Behavioral Practice*. 2004; 11:56–65.10.1016/S1077-7229(04)80007-5
- Boylan KR, Miller JL, Vaillancourt T, Szatmari P. Confirmatory factor structure of anxiety and depression: Evidence of item variance across childhood. *International Journal of Methods in Psychiatric Research*. 2011; 20:194–202.10.1002/mpr [PubMed: 22009887]
- Brady EU, Kendall PC. Comorbidity of anxiety and depression in children and adolescents. *Psychological Bulletin*. 1992; 111:244–55.10.1037/0033-2909.111.2.244 [PubMed: 1557475]
- Brent DA, Kolko DJ, Birmaher B, Baugher M, Bridge J, Roth C, Holder D. Predictors of treatment efficacy in a clinical trial of three psychosocial treatments for adolescent depression. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1998; 37:906–914.10.1097/00004583-199809000-00010 [PubMed: 9735610]
- Brent D, Emslie G, Clarke G, Wagner KD, Asarnow JR, Keller M, Zelazny J. Switching to another SSRI or to venlafaxine with or without cognitive behavioral therapy for adolescents with SSRI-resistant depression. *Journal of the American Medical Association*. 2008; 4:1–16.10.1001/jama.299.8.901

- Brown TA, Chorpita BF, Barlow DH. Structural relationships among dimensions of the DSM-IV anxiety and mood disorders and dimensions of negative affect, positive affect, and autonomic arousal. *Journal of Abnormal Psychology*. 1998; 107:179–92.10.1037/0021-843X.107.2.179 [PubMed: 9604548]
- Bubier JL, Drabick DG. Co-occurring anxiety and disruptive behavior disorders: The roles of anxious symptoms, reactive aggression, and shared risk processes. *Clinical Psychology Review*. 2009; 29:658–669.10.1016/j.cpr.2009.08.005 [PubMed: 19729235]
- Burstein M, Ameli-Grillon L, Merikangas KR. Shyness versus social phobia in US youth. *Pediatrics*. 2011; 128:917–25.10.1542/peds.2011-1434 [PubMed: 22007009]
- Cameron OG, Abelson JL, Young EA. Anxious and depressive disorders and their comorbidity: Effect on central nervous system noradrenergic function. *Biological Psychiatry*. 2004; 56:875–83.10.1016/j.biopsych.2004.08.007 [PubMed: 15576065]
- Campbell-Sills L, Liverant GI, Brown TA. Psychometric evaluation of the Behavioral Inhibition/Behavioral Activation Scales in a large sample of outpatients with anxiety and mood disorders. *Psychological Assessment*. 2004; 16:244–254.10.1037/1040-3590.16.3.244 [PubMed: 15456380]
- Cannon MF, Weems CF. Do anxiety and depression cluster into distinct groups? A test of tripartite model predictions in a community sample of youth. *Depression and Anxiety*. 2006; 23:453–60.10.1002/da [PubMed: 16845650]
- Carey, MP.; Finch, AJ.; Imm, P. Differentiating depressive and anxiety disorders from other child psychiatric disorders: The role of overt behavior, cognition, and emotions. Paper presented at the Association for the Advancement of Behavior Therapy; Washington, DC. 1989 Nov.
- Caspi A, Moffitt TE, Newman DL, Silva PA. Behavioral observations at age 3 years predict adult psychiatric disorders: Longitudinal evidence from a birth cohort. *Archives of General Psychiatry*. 1996; 53:1033–1039. [PubMed: 8911226]
- Chartrand H, Sareen J, Toews M, Bolton JM. Suicide attempts versus nonsuicidal self-injury among individuals with anxiety disorders in a nationally representative sample. *Depression and Anxiety*. 2012; 29:172–179.10.1002/da.20882 [PubMed: 21948315]
- Chavira DA, Stein MB, Bailey K, Stein MT. Comorbidity of generalized social anxiety disorder and depression in a pediatric primary care sample. *Journal of Affective Disorders*. 2004; 80:163–71.10.1016/S0165-0327(03)00103-4 [PubMed: 15207929]
- Cheung A, Mayes T, Levitt A, Schaffer A, Michalak E, Kiss A, Emslie G. Anxiety as a predictor of treatment outcome in children and adolescents with depression. *Journal of Child and Adolescent Psychopharmacology*. 2010; 20:211–216.10.1089/cap.2010.0006 [PubMed: 20578934]
- Chorpita BF, Albano AM, Barlow DH. The structure of negative emotions in a clinical sample of children and adolescents. *Journal of Abnormal Psychology*. 1998; 107:74–85.10.1037/0021-843X.107.1.74 [PubMed: 9505040]
- Chorpita BF, Daleiden EL. Tripartite dimensions of emotion in a child clinical sample: Measurement strategies and implications for clinical utility. *Journal of Consulting and Clinical Psychology*. 2002; 70:1150–1160.10.1037/0022-006X.70.5.1150 [PubMed: 12362965]
- Chorpita BF, Daleiden EL, Moffitt C, Yim L, Umemoto LA. Assessment of tripartite factors of emotion in children and adolescents I: Structural validity and normative data of an affect and arousal scale. *Journal of Psychopathology and Behavioral Assessment*. 2000; 22:141–160.10.1023/A:1007584423617
- Chorpita BF, Plummer CM, Moffitt CE. Relations of tripartite dimensions of emotion to childhood anxiety and mood disorders. *Journal of Abnormal Child Psychology*. 2000; 28:299–310.10.1023/A:1005152505888 [PubMed: 10885687]
- Chorpita BF, Taylor AA, Francis SE, Moffitt C, Austin AA. Efficacy of modular cognitive behavior therapy for childhood anxiety disorders. *Behavior Therapy*. 2004; 35:263–287.10.1016/S0005-7894(04)80039-X
- Chorpita BF, Weisz JR. MATCH-ADTC: Modular approach to therapy for children with anxiety, depression, trauma, or conduct problems. PracticeWise. 2009
- Chorpita BF, Yim L, Moffitt C, Umemoto LA, Francis SE. Assessment of symptoms of DSM-IV anxiety and depression in children: A revised child anxiety and depression scale. *Behaviour Research and Therapy*. 2000; 38:835–55.10.1016/S0005-7967(99)00130-8 [PubMed: 10937431]

- Chorpita, Bruce F. The tripartite model and dimensions of anxiety and depression: An examination of structure in a large school sample. *Journal of Abnormal Child Psychology*. 2002; 30:177–190.10.1023/A:1014709417132 [PubMed: 12002397]
- Choy Y, Fyer AJ, Goodwin RD. Specific phobia and comorbid depression: A closer look at the National Comorbidity Survey data. *Comprehensive Psychiatry*. 2007; 48:132–136.10.1016/j.comppsy.2006.10.010 [PubMed: 17292703]
- Chronis-Tuscano A, Degnan K, Pine DS, Perez-Edgar K, Henderson HA, Diaz Y, Fox NA. Stable early maternal report of behavioral inhibition predicts lifetime social anxiety disorder in adolescence. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2009; 48:928–935.10.1097/CHI.0b013e3181ae09df [PubMed: 19625982]
- Chu BC, Colognori D, Weissman AS, Bannon K. An initial description and pilot of group behavioral activation therapy for anxious and depressed youth. *Cognitive and Behavioral Practice*. 2009; 16:408–419.10.1016/j.cbpra.2009.04.003
- Chu BC, Harrison TL. Disorder-specific effects of CBT for anxious and depressed youth: A meta-analysis of candidate mediators of change. *Clinical Child and Family Psychology Review*. 2007; 10:352–372.10.1007/s10567-007-0028-2 [PubMed: 17985239]
- Chu BC, Merson RA, Zandberg LJ, Areizaga M. Calibrating for comorbidity: Clinical decision-making in youth depression and anxiety. *Cognitive and Behavioral Practice*. 2012; 19:5–16.10.1016/j.cbpra.2010.10.005
- Cicchetti D, Toth SL. The past achievements and future promises of developmental psychopathology: The coming of age of a discipline. *Journal of Child Psychology and Psychiatry*. 2009; 50:16–25.10.1111/j.1469-7610.2008.01979.x [PubMed: 19175810]
- Clark LA, Watson D. Tripartite model of anxiety and depression: Psychometric evidence and taxonomic implications. *Journal of Abnormal Psychology*. 1991; 100:316–336.10.1037/0021-843X.100.3.316 [PubMed: 1918611]
- Clark L, Watson D. Distress and fear disorders: An alternative empirically based taxonomy of the ‘mood’ and ‘anxiety’ disorders. *The British Journal of Psychiatry*. 2006; 189:481–483.10.1192/bjp.bp.106.03825 [PubMed: 17139030]
- Clark, L.; Watson, D. Temperament: An organizing paradigm for trait psychology. In: John, OP.; Robins, RW.; Pervin, LA., editors. *Handbook of personality: Theory and research*. 3. New York, NY: Guilford Press; 2008. p. 265-286.
- Cohen P, Cohen J, Brook JS. An epidemiological study of disorders in late childhood and adolescence: II. Persistence of disorders. *Journal of Child Psychology and Psychiatry*. 1993; 34:869–877.10.1111/j.1469-7610.1993.tb01095.x [PubMed: 8408372]
- Cole DA, Peeke LG, Martin JM, Truglio R, Seroczynski AD. A longitudinal look at the relation between depression and anxiety in children and adolescents. *Journal of Consulting and Clinical Psychology*. 1998; 66:451–60.10.1037/0022-006X.66.3.451 [PubMed: 9642883]
- Cole DA, Truglio R, Peeke L. Relation between symptoms of anxiety and depression in children: A multitrait-multimethod-multigroup assessment. *Journal of Consulting and Clinical Psychology*. 1997; 65:110–119.10.1037/0022-006X.65.1.110 [PubMed: 9103740]
- Compas BE, Oppedisano G, Connor JK, Gerhardt CA, Hinden BR, Achenbach TM, Hammen C. Gender differences in depressive symptoms in adolescence: Comparison of national samples of clinically referred and nonreferred youths. *Journal of Consulting and Clinical Psychology*. 1997; 65:617–26.10.1037/0022-006X.65.4.617 [PubMed: 9256563]
- Copeland WE, Shanahan L, Costello EJ, Angold A. Childhood and adolescent psychiatric disorders as predictors of young adult disorders. *Archives of General Psychiatry*. 2009; 66:764–72.10.1001/archgenpsychiatry.2009.85 [PubMed: 19581568]
- Coplan RJ, Wilson J, Frohlick SL, Zelenski J. A person-oriented analysis of behavioral inhibition and behavioral activation in children. *Personality and Individual Differences*. 2006; 41:917–927.10.1016/j.paid.2006.02.019
- Corr PJ. J. A. Gray’s reinforcement sensitivity theory: Tests of the joint subsystems hypothesis of anxiety and impulsivity. *Personality and Individual Differences*. 2002; 33:511–532.10.1016/S0191-8869(01)00170-2

- Corr, PJ. Reinforcement Sensitivity Theory (RST): Introduction. In: Corr, PJ., editor. *The reinforcement sensitivity theory of personality*. New York, NY US: Cambridge University Press; 2008. p. 1-43.
- Costello EJ, Angold A, Burns BJ, Stangl DK, Tweed DL, Erkanli A, Worthman CM. The Great Smoky Mountains Study of youth: Goals, design, methods, and the prevalence of DSM-III-R Disorders. *Archives of General Psychiatry*. 1996; 53:1129–1136.10.1001/archpsyc.1996.01830120067012 [PubMed: 8956679]
- Costello EJ, Costello AJ, Edelbrock C, Burns BJ, Dulcan MK, Brent D, Janiszewski S. Psychiatric disorders in pediatric primary care. *Archives of General Psychiatry*. 1988; 45:1107–1116. [PubMed: 3264146]
- Costello EJ, Mustillo S, Erkanli A, Keeler G, Angold A. Prevalence and development of psychiatric disorders in childhood and adolescence. *Archives of General Psychiatry*. 2003; 60:837–844.10.1001/archpsyc.60.8.837 [PubMed: 12912767]
- Crawley SA, Beidas RS, Benjamin CL, Martin E, Kendall PC. Treating socially phobic youth with CBT: Differential outcomes and treatment considerations. *Behavioural and Cognitive Psychotherapy*. 2008; 36:379–389.10.1017/S1352465808004542
- Cummings, E.; Davies, PT.; Campbell, SB. *Developmental psychopathology and family process: Theory, research, and clinical implications*. New York: Guilford Press; 2000.
- Cummings CM, Fristad MA. Anxiety in children with mood disorders: A treatment help or hindrance? *Journal of Abnormal Child Psychology*. 2012; 40:339–351.10.1007/s10802-011-9568-5 [PubMed: 21912843]
- Curry J, Rohde P, Simons A, Silva S, Vitiello B, Kratochvil C, March J. Predictors and moderators of acute outcome in the Treatment for Adolescents with Depression Study (TADS). *Journal of the American Academy of Child & Adolescent Psychiatry*. 2006; 45:1427–1439.10.1097/01.chi.0000240838.78984.e2 [PubMed: 17135988]
- Daleiden E, Chorpita BF, Lu W. Assessment of tripartite factors of emotion in children and adolescents II: Concurrent validity of the affect and arousal scales for children. *Behavioral Assessment*. 2000; 22:161–82.10.1023/A:1007536507687
- Dalrymple KL, Zimmerman M. Age of onset of social anxiety disorder in depressed outpatients. *Journal of Anxiety Disorders*. 2011; 25:131–137.10.1016/j.janxdis.2010.08.012 [PubMed: 20832989]
- Daughters SB, Reynolds EK, MacPherson L, Kahler CW, Danielson CK, Zvolensky M, Lejuez CW. Distress tolerance and early adolescent externalizing and internalizing symptoms: The moderating role of gender and ethnicity. *Behaviour Research and Therapy*. 2009; 47:198–205.10.1016/j.brat.2008.12.001 [PubMed: 19135649]
- Davidson RJ. Affective style and affective disorders: Perspectives from affective neuroscience. *Cognition and Emotion*. 1998; 12:307–331.10.1080/026999398379628
- Davidson RJ, Pizzagalli D, Nitschke JB, Putnam K. Depression: Perspectives from affective neuroscience. *Annual Review of Psychology*. 2002; 53:545–574.10.1146/annurev.psych.53.100901.135148
- De Bolle M, Decuyper M, De Clercq B, De Fruyt F. Relevance of the tripartite dimensions of affect for anxiety and depression in youth: Examining sex and psychopathology status. *Journal of Abnormal Child Psychology*. 2010; 38:935–948.10.1007/s10802-010-9413-2 [PubMed: 20369378]
- de Graaf R, Bijl RV, Ten Have M, Beekman ATF, Vollebergh WAM. Pathways to comorbidity: The transition of pure mood, anxiety and substance use disorders into comorbid conditions in a longitudinal population-based study. *Journal of Affective Disorders*. 2004; 82:461–467.10.1016/j.jad.2004.03.001 [PubMed: 15555699]
- Dieleman GC, van der Ende J, Verhulst FC, Huizink AC. Perceived and physiological arousal during a stress task: Can they differentiate between anxiety and depression? *Psychoneuroendocrinology*. 2010; 35:1223–1234.10.1016/j.psyneuen.2010.02.012 [PubMed: 20219286]
- Dierker LC, Albano AM, Clarke GN, Heimberg RG, Kendall PC, Merikangas K, Kupfer DJ. Screening for anxiety and depression in early adolescence. *Journal of the American Academy of*

- Child and Adolescent Psychiatry. 2001; 40:929–36.10.1097/00004583-200108000-00015 [PubMed: 11501693]
- Dougherty LR, Bufferd SJ, Carlson GA, Dyson M, Olinio TM, Durbin C, Klein DN. Preschoolers' observed temperament and psychiatric disorders assessed with a parent diagnostic interview. *Journal of Clinical Child and Adolescent Psychology*. 2011; 40:295–306.10.1080/15374416.2011.546046 [PubMed: 21391025]
- Dunlop BW, Davis PG. Combination treatment with benzodiazepines and SSRIs for comorbid anxiety and depression: A review. *Primary Care Companion to the Journal of Clinical Psychiatry*. 2008; 10:222–8.
- Ebesutani C, Bernstein A, Nakamura BJ, Chorpita BF, Higa-McMillan CK, Weisz JR. Concurrent validity of the Child Behavior Checklist DSM-oriented scales: Correspondence with DSM diagnoses and comparison to syndrome scales. *Journal of Psychopathology and Behavioral Assessment*. 2010; 32:373–84.10.1007/s10862-009-9174-9 [PubMed: 20700377]
- Ebesutani C, Okamura K, Higa-McMillan C, Chorpita BF. A psychometric analysis of the Positive and Negative Affect Schedule for Children–Parent Version in a school sample. *Psychological Assessment*. 2011; 23:406–416.10.1037/a0022057 [PubMed: 21381834]
- Ehrenreich, JT.; Buzzella, BA.; Trosper, SE.; Bennett, SM.; Wright, LR.; Barlow, DH. The unified protocol for treatment of emotional disorders in adolescents. Boston University; 2008. Unpublished manuscript
- Ehrenreich JT, Goldstein CR, Wright LR, Barlow DH. Development of a unified protocol for the treatment of emotional disorders in youth. *Child & Family Behavior Therapy*. 2009; 31:20–37.10.1080/07317100802701228 [PubMed: 19617930]
- Eley TC, Stevenson J. Using genetic analyses to clarify the distinction between depressive and anxious symptoms in children. *Journal of Abnormal Child Psychology*. 1999; 27:105–14.10.1023/A:1021947113860 [PubMed: 10400057]
- Ellis AJ, Fischer KM, Beevers CG. Is dysphoria about being red and blue? Potentiation of anger and reduced distress tolerance among dysphoric individuals. *Cognition and Emotion*. 2010; 24:596–608.10.1080/13803390902851176
- Else-Quest NM, Hyde J, Goldsmith H, Van Hulle CA. Gender differences in temperament: A meta-analysis. *Psychological Bulletin*. 2006; 132:33–72.10.1037/0033-2909.132.1.33 [PubMed: 16435957]
- Emslie GJ, Mayes TL, Laptook RS, Batt M. Predictors of response to treatment in children and adolescents with mood disorders. *Psychiatric Clinics of North America*. 2003; 26:435–456.10.1016/S0193-953X(02)00110-7 [PubMed: 12778842]
- Epkins CC, Heckler DR. Integrating etiological models of social anxiety and depression in youth: Evidence for a cumulative interpersonal risk model. *Clinical Child and Family Psychology Review*. 2011; 14:329–76.10.1007/s10567-011-0101-8 [PubMed: 22080334]
- Espejo EP, Hammen CL, Connolly NP, Brennan PA, Najman JM, Bor W. Stress sensitization and adolescent depressive severity as a function of childhood adversity: A link to anxiety disorders. *Journal of Abnormal Child Psychology*. 2007; 35:287–99.10.1007/s10802-006-9090-3 [PubMed: 17195949]
- Esposito CL, Clum GA. Psychiatric symptoms and their relationship to suicidal ideation in a high-risk adolescent community sample. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2002; 41:44–51.10.1097/00004583-200201000-00010 [PubMed: 11800204]
- Essau CA. Comorbidity of anxiety disorders in adolescents. *Depression and Anxiety*. 2003; 18:1–6.10.1002/da.10107 [PubMed: 12900947]
- Essau CA. Comorbidity of depressive disorders among adolescents in community and clinical settings. *Psychiatry Research*. 2008; 158:35–42.10.1016/j.psychres.2007.09.007 [PubMed: 18164075]
- Essau CA, Conradt J, Petermann F. Frequency and comorbidity of social phobia and social fears in adolescents. *Behaviour Research and Therapy*. 1999; 37:831–843.10.1016/S0005-7967(98)00179-X [PubMed: 10458047]
- Ferdinand RF, de Nijs PFA, van Lier P, Verhulst FC. Latent class analysis of anxiety and depressive symptoms in referred adolescents. *Journal of Affective Disorders*. 2005; 88:299–306.10.1016/j.jad.2005.08.004 [PubMed: 16182373]

- Fichter MM, Quadflieg NN, Fischer UC, Kohlboeck GG. Twenty-five-year course and outcome in anxiety and depression in the Upper Bavarian Longitudinal Community Study. *Acta Psychiatrica Scandinavica*. 2010; 122:75–85.10.1111/j.1600-0447.2009.01512.x [PubMed: 19922523]
- Finch, AR.; Lipovsky, JA.; Casat, CD. Anxiety and depression in children and adolescents: Negative affectivity or separate constructs?. In: Kendall, PC.; Watson, D., editors. *Anxiety and depression: Distinctive and overlapping features*. San Diego, CA: Academic Press; 1989. p. 171-202.
- Fleming JE, Offord DR. Epidemiology of childhood depressive disorders: A critical review. *Journal of the American Academy Of Child & Adolescent Psychiatry*. 1990; 29:571–80.10.1097/00004583-199007000-00010 [PubMed: 2201675]
- Foley DL, Goldston DB, Costello EJ, Angold A. Proximal risk factors for suicidality in youth: The Great Smoky Mountains Study. *Archives of General Psychiatry*. 2006; 63:1017–24.10.1001/archpsyc.63.9.1017 [PubMed: 16953004]
- Foley DL, Pickles A, Maes HM, Silberg JL, Eaves LJ. Course and short-term outcomes of separation anxiety disorder in a community sample of twins. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2004; 43:1107–1114.10.1097/01.chi.0000131138.16734.f4 [PubMed: 15322414]
- Franco X, Saavedra LM, Silverman WK. External validation of comorbid patterns of anxiety disorders in children and adolescents. *Journal of Anxiety Disorders*. 2007; 21:717–729.10.1016/j.janxdis.2006.10.002 [PubMed: 17095184]
- Frani S, Middeldorp CM, Dolan CV, Ligthart L, Boomsma DI. Childhood and adolescent anxiety and depression: Beyond heritability. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2010; 49:820–829.10.1016/j.jaac.2010.05.013 [PubMed: 20643315]
- Gagne JR, Miller MM, Goldsmith HH. Early—but modest—gender differences in focal aspects of childhood temperament. *Personality and Individual Differences*. 2013; 55:95–100.
- Gallerani CM, Garber J, Martin NC. The temporal relation between depression and comorbid psychopathology in adolescents at varied risk for depression. *Journal of Child Psychology and Psychiatry*. 2010; 51:242–9.10.1111/j.1469-7610.2009.02155.x [PubMed: 19874429]
- Garber J, Braafladt N, Weiss B. Affect regulation in depressed and nondepressed children and young adolescents. *Development and Psychopathology*. 1995; 7:93–115.10.1017/S0954579400006362
- Garber J, Weersing VR. Comorbidity of anxiety and depression in youth: Implications for treatment and prevention. *Clinical Psychology*. 2010; 17:293–306.10.1111/j.1468-2850.2010.01221.x [PubMed: 21499544]
- Gaylord-Harden NK, Elmore CA, Campbell CL, Wethington A. An examination of the tripartite model of depressive and anxiety symptoms in African American youth: Stressors and coping strategies as common and specific correlates. *Journal of Clinical Child and Adolescent Psychology*. 2011; 40:360–74.10.1080/15374416.2011.563467 [PubMed: 21534048]
- Gazelle H, Workman JO, Allan W. Anxious solitude and clinical disorder in middle childhood: Bridging developmental and clinical approaches to childhood social anxiety. *Journal of Abnormal Child Psychology*. 2010; 38:1–17.10.1007/s10802-009-9343-z [PubMed: 19707867]
- Ghaziuddin N, King CA, Naylor MW, Ghaziuddin M. Anxiety contributes to suicidality in depressed adolescents. *Depression and Anxiety*. 2000; 11:134–138. [PubMed: 10875056]
- Gibb BE, Alloy LB. A prospective test of the hopelessness theory of depression in children. *Journal of Clinical Child and Adolescent Psychology*. 2006; 35:264–274.10.1207/s15374424jccp3502_10 [PubMed: 16597222]
- Ginsburg GS, Kendall PC, Sakolsky D, Compton SN, Piacentini J, Albano AM, March J. Remission after acute treatment in children and adolescents with anxiety disorders: Findings from the CAMS. *Journal of Consulting and Clinical Psychology*. 2011; 79:806–13.10.1037/a0025933 [PubMed: 22122292]
- Goldsmith, SK.; Pellmar, TC.; Kleinman, AM.; Bunney, WE. *Reducing suicide: A national imperative*. Washington, D.C: National Academies Press; 2002.
- Goldston DB, Daniel SS, Erkanli A, Reboussin BA, Mayfield A, Frazier PH, Treadway SL. Psychiatric diagnoses as contemporaneous risk factors for suicide attempts among adolescents and young adults: Developmental changes. *Journal of Consulting and Clinical Psychology*. 2009; 77:281–290.10.1037/a0014732 [PubMed: 19309187]

- Goodwin RD, Gotlib IH. Panic attacks and psychopathology among youth. *Acta Psychiatrica Scandinavica*. 2004; 109:216–221.10.1046/j.1600-0447.2003.00255.x [PubMed: 14984394]
- Grant DM, Beck GJ, Farrow SM, Davila J. Do interpersonal features of social anxiety influence the development of depressive symptoms? *Cognition and Emotion*. 2007; 21:646–663.10.1080/02699930600713036
- Gray, JA. *The neuropsychology of anxiety: An enquiry into the functions of the septo-hippocampal system*. 1. Oxford: Oxford University Press; 1982.
- Gray, JA. *The psychology of fear and stress*. Cambridge, England: Cambridge University Press; 1987.
- Gray, JA. Neural systems of motivation, emotion, and affect. In: Madden, J., editor. *Neurobiology of Learning, Emotion, and Affect*. New York: Raven Press; 1991. p. 273-306.
- Gray, JA.; McNaughton, N. *The neuropsychology of anxiety: An inquiry into the functions of the septo-hippocampal system*. Oxford: Oxford University Press; 2000.
- Greaves-Lord K, Ferdinand RF, Sondejker FEPL, Dietrich A, Oldehinkel AJ, Rosmalen JGM, Verhulst FC. Testing the tripartite model in young adolescents: is hyperarousal specific for anxiety and not depression? *Journal of Affective Disorders*. 2007; 102:55–63.10.1016/j.jad.2006.12.009 [PubMed: 17234274]
- Greene FN, Chorpita BF, Aukahi AA. Examining youth anxiety symptoms and suicidal ideation in the context of the tripartite model of emotion. *Journal of Psychopathology and Behavioral Assessment*. 2009; 31:405–11.10.1007/s10862-009-9129-1
- Griffith JW, Zinbarg RE, Craske MG, Mineka S, Rose RD, Waters AM, Sutton JM. Neuroticism as a common dimension in the internalizing disorders. *Psychological Medicine*. 2010; 40:1125–1136.10.1017/S0033291709991449 [PubMed: 19903363]
- Guberman CG, Manassis K. Symptomatology and family functioning in children and adolescents with comorbid anxiety and depression. *Journal of the Canadian Academy of Child and Adolescent Psychiatry*. 2011; 20:186–95. [PubMed: 21804847]
- Gullone E. The development of normal fear: A century of research. *Clinical Psychology Review*. 2000; 20:429–451.10.1016/S0272-7358(99)00034-3 [PubMed: 10832548]
- Hale W, Raaijmakers QW, Muris P, van Hoof A, Meeus WJ. One factor or two parallel processes? Comorbidity and development of adolescent anxiety and depressive disorder symptoms. *Journal of Child Psychiatry and Psychology*. 2009; 10:1218–26.10.1111/j.1469-7610.2009.02115.x
- Halbreich U, Kahn LS. Atypical depression, somatic depression and anxious depression in women: Are they gender-preferred phenotypes? *Journal of Affective Disorders*. 2007; 102:245–258.10.1016/j.jad.2006.09.023 [PubMed: 17092565]
- Halpern LF, Brand KL, Malone AF. Parenting stress in mothers of very-low-birth-weight (VLBW) and full-term infants: A function of infant behavioral characteristics and child-rearing attitudes. *Journal of Pediatric Psychology*. 2001; 26:93–104.10.1093/jpepsy/26.2.93 [PubMed: 11181885]
- Hamilton M. A rating scale for depression. *Journal of Neurology, Neurosurgery, and Psychiatry*. 1960; 23:56–62.
- Hammen C, Brennan PA, Keenan-Miller D, Herr NR. Early onset recurrent subtype of adolescent depression: Clinical and psychosocial correlates. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*. 2008; 49:433–40.10.1111/j.1469-7610.2007.01850.x
- Hankin BL. Cognitive vulnerability-stress model of depression during adolescence: Investigating depressive symptom specificity in a multi-wave prospective study. *Journal of Abnormal Child Psychology*. 2008a; 36:999–1014.10.1007/s10802-008-9228-6 [PubMed: 18437551]
- Hankin BL. Rumination and depression in adolescence: Investigating symptom specificity in a multiwave prospective study. *Journal of Clinical Child and Adolescent Psychology*. 2008b; 37:701–13.10.1080/15374410802359627 [PubMed: 18991122]
- Hankin BL. Development of sex differences in depressive and co-occurring anxious symptoms during adolescence: Descriptive trajectories and potential explanations in a multiwave prospective study. *Journal of Clinical Child and Adolescent Psychology*. 2009; 38:460–472.10.1080/15374410902976288 [PubMed: 20183634]
- Hankin BL, Abramson LY. Development of gender differences in depression: An elaborated cognitive vulnerability-transactional stress theory. *Psychological Bulletin*. 2001; 127:773–796.10.1037/0033-2909.127.6.773 [PubMed: 11726071]

- Hankin BL, Wetter E, Cheely C, Oppenheimer CW. Beck's cognitive theory of depression in adolescence: Specific prediction of depressive symptoms and reciprocal influences in a multi-wave prospective study. *International Journal of Cognitive Therapy*. 2008; 1:313–332.10.1521/ijct.2008.1.4.313
- Hayden EP, Klein DN, Dougherty LR, Olino TM, Lipton RS, Dyson MW, Singh SM. The dopamine D2 receptor gene and depressive and anxious symptoms in childhood: Associations and evidence for gene-environment correlation and gene-environment interaction. *Psychiatric Genetics*. 2010; 20:304–310.10.1097/YPG.0b013e32833adccb [PubMed: 20526230]
- Hayward C, Killen JD, Kraemer HC, Taylor CB. Predictors of panic attacks in adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2000; 39:207–214.10.1097/00004583-200002000-00021 [PubMed: 10673832]
- Heron M. Deaths: Leading causes for 2004. *National Vital Statistics Reports*. 2007; 56:1–96. [PubMed: 18092547]
- Hettema JM. What is the genetic relationship between anxiety and depression? *American Journal of Medical Genetics. Part C, Seminars in Medical Genetics*. 2008; 148C:140–6.10.1002/ajmg.c.30171
- Hettema JM, Neale MC, Ph D, Kendler KS. A review and meta-analysis of the genetic epidemiology of anxiety disorders. *American Journal of Psychiatry*. 2001; 158:1568–1578.10.1176/appi.ajp.158.10.1568 [PubMed: 11578982]
- Hirshfeld-Becker DR. Familial and temperamental risk factors for social anxiety disorder. *New Directions for Child and Adolescent Development*. 2010; 127:51–65.10.1002/cd.262 [PubMed: 20205183]
- Hirshfeld-Becker DR, Biederman J, Henin A, Faraone SV, Davis S, Harrington K, Rosenbaum JF. Behavioral inhibition in preschool children at risk is a specific predictor of middle childhood social anxiety: A five-year follow-up. *Journal of Developmental and Behavioral Pediatrics*. 2007; 28:225–233.10.1097/01.DBP.0000268559.34463.d0 [PubMed: 17565290]
- Hirshfeld-Becker DR, Masek B, Henin A, Blakely L, Pollock-Wurman RA, McQuade J, Biederman J. Cognitive behavioral therapy for 4- to 7-year-old children with anxiety disorders: A randomized clinical trial. *Journal of Consulting and Clinical Psychology*. 2010; 78:498–510.10.1037/a0019055 [PubMed: 20658807]
- Hofmann SG, Moscovitch DA, Litz BT, Kim H, Davis LL, Pizzagalli DA. The worried mind: Autonomic and prefrontal activation during worrying. *Emotion*. 2005; 5:464–475.10.1037/1528-3542.5.4.464 [PubMed: 16366750]
- Huang K, Szabó M, Han J. The relationship of low distress tolerance to excessive worrying and cognitive avoidance. *Behaviour Change*. 2009; 26:223–234.10.1375/bech.26.4.223
- Hudson JL, Krain AL, Kendall PC. Expanding horizons: Adapting manual-based treatments for anxious children with comorbid diagnoses. *Cognitive and Behavioral Practice*. 2001; 8:338–346.10.1016/S1077-7229(01)80007-9
- Hughes CW, Emslie GJ, Crismon ML, Posner K, Birmaher B, Ryan N, Trivedi MH. Texas Children's Medication Algorithm Project: Update from Texas Consensus Conference Panel on Medication Treatment of Childhood Major Depressive Disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2007; 46:667–686.10.1097/chi.0b013e31804a859b [PubMed: 17513980]
- Hundt NE, Nelson-Gray RO, Kimbrel NA, Mitchell JT, Kwapił TR. The interaction of reinforcement sensitivity and life events in the prediction of anhedonic depression and mixed anxiety-depression symptoms. *Personality and Individual Differences*. 2007; 43:1001–1012.10.1016/j.paid.2007.02.021
- Hutcherson ST, Epkins CC. Differentiating parent- and peer-related interpersonal correlates of depressive symptoms and social anxiety in preadolescent girls. *Journal of Social and Personal Relationships*. 2009; 26:875–897.10.1177/0265407509345654
- Hyde J, Mezulis AH, Abramson LY. The ABCs of depression: Integrating affective, biological, and cognitive models to explain the emergence of the gender difference. *Psychological Review*. 2008; 115:291–313.10.1037/0033-295X.115.2.291 [PubMed: 18426291]

- Issler CK, Sant'Anna MK, Kapczinski F, Lafer B. Anxiety disorders comorbidity in bipolar disorder. *Revista Brasileira de Psiquiatria*. 2004; 26:31–6.10.1590/S1516-44462004000700008 [PubMed: 15597137]
- Jacques HAK, Mash EJ. A test of the tripartite model of anxiety and depression in elementary and high school boys and girls. *Journal of Abnormal Child Psychology*. 2004; 32:13–25.10.1023/B:JACP.0000007577.38802.18 [PubMed: 14998108]
- Johnson HS, Inderbitzen-Nolan HM, Schapman AM. A comparison between socially anxious and depressive symptomatology in youth: A focus on perceived family environment. *Journal of Anxiety Disorders*. 2005; 19:423–442.10.1016/j.janxdis.2004.04.004 [PubMed: 15721573]
- Johnson SL, Turner RJ, Iwata N. BIS / BAS levels and psychiatric disorder: An epidemiological study. *Journal of Psychopathology and Behavioral Assessment*. 2003; 25:25–36.10.1023/A:1022247919288
- Jorm AF, Christensen HH, Henderson AS, Jacomb PA, Korten AE, Rodgers BB. Using the BIS/BAS scales to measure behavioural inhibition and behavioural activation: Factor structure, validity and norms in a large community sample. *Personality and Individual Differences*. 1999; 26:49–58.10.1016/S0191-8869(98)00143-3
- Joiner TE, Catanzaro SJ, Laurent J. Tripartite structure of positive and negative affect, depression, and anxiety in child and adolescent psychiatric inpatients. *Journal of Abnormal Psychology*. 1996; 105:401–409.10.1037/0021-843X.105.3.401 [PubMed: 8772010]
- Kagan J, Reznick JS, Snidman N. The physiology and psychology of behavioral inhibition in children. *Child Development*. 1987; 58:1459–1473. [PubMed: 3691195]
- Karlsson L, Pelkonen M, Ruutu T, Kiviruusu O, Heilä H, Holi M, Marttunen JM. Current comorbidity among consecutive adolescent psychiatric outpatients with DSM-IV mood disorders. *European Child & Adolescent Psychiatry*. 2006; 15:220–231.10.1007/s00787-006-0526-7 [PubMed: 16502209]
- Kasch KL, Rottenberg J, Arnow BA, Gotlib IH. Behavioral activation and inhibition systems and the severity and course of depression. *Journal of Abnormal Psychology*. 2002; 111:589–597.10.1037/0021-843X.111.4.589 [PubMed: 12428772]
- Kaufman NK, Rohde P, Seeley JR, Clarke GN, Stice E. Potential mediators of cognitive-behavioral therapy for adolescents with comorbid major depression and conduct disorder. *Journal of Consulting and Clinical Psychology*. 2005; 73:38–46.10.1037/0022-006X.73.1.38 [PubMed: 15709830]
- Keenan K, Feng X, Hipwell A, Klostermann S. Depression begets depression: Comparing the predictive utility of depression and anxiety symptoms to later depression. *Journal of Child Psychology and Psychiatry*. 2009; 50:1167–1175.10.1111/j.1469-7610.2009.02080.x [PubMed: 19344385]
- Keenan K, Hipwell A, Hinze A, Babinski D. Equanimity to excess: Inhibiting the expression of negative emotion is associated with depression symptoms in girls. *Journal of Abnormal Child Psychology*. 2009; 37:739–747.10.1007/s10802-009-9301-9 [PubMed: 19184401]
- Kendall PC, Beidas RS. Smoothing the trail for dissemination of evidence-based practices for youth: Flexibility within fidelity. *Professional Psychology: Research and Practice*. 2007; 38:13–20.10.1037/0735-7028.38.1.13
- Kendall PC, Compton SN, Walkup JT, Birmaher B, Albano AM, Sherrill J, ...Piacentini J. Clinical characteristics of anxiety disordered youth. *Journal of Anxiety Disorders*. 2010; 24:360–365.10.1016/j.janxdis.2010.01.009 [PubMed: 20206470]
- Kendall PC, Flannery-Schroeder E, Panichelli-Mindel S, Southam-Gerow M, Henin A, Warman M. Therapy for youth with anxiety disorders: A second randomized clinical trial. *Journal of Consulting and Clinical Psychology*. 1997; 65:366–380.10.1037/0022-006X.65.3.366 [PubMed: 9170760]
- Kendall PC, Gosch E, Furr JM, Sood E. Flexibility within fidelity. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2008; 47:987–993. [PubMed: 18714195]
- Kendall, PC.; Hedtke, KA. *Cognitive-behavioral therapy for anxious children: Therapist manual*. 3. Ardmore, PA: Workbook Publishing; 2006a. www.WorkbookPublishing.com

- Kendall, PC.; Hedtke, K. Coping Cat workbook. 2. Ardmore, PA: Workbook Publishing; 2006b. www.WorkbookPublishing.com
- Kendall PC, Hudson JL, Gosch E, Flannery-Schroeder E, Suveg C. Cognitive-behavioral therapy for anxiety disordered youth: A randomized clinical trial evaluating child and family modalities. *Journal of Consulting and Clinical Psychology*. 2008; 76:282–297.10.1037/0022-006X.76.2.282 [PubMed: 18377124]
- Kendall PC, Kortlander E, Chansky TE, Brady EU. Comorbidity of anxiety and depression in youth: Treatment implications. *Journal of Consulting and Clinical Psychology*. 1992; 60:869–880.10.1037/0022-006X.60.6.869 [PubMed: 1360989]
- Kendall, PC.; O’Neil, K.; Villabø, M.; Martinsen, K.; Stark, K.; Banneyer, K. Therapy with children and adolescents: Cognitive-behavioral therapy offers a transdiagnostic perspective. In: Ehrenreich-May, J.; Chu, B., editors. *Transdiagnostic mechanisms and treatment for youth psychopathology*. New York: NY: Guilford; in press
- Kendall PC, Robin JA, Hedtke KA, Suveg C, Flannery-Schroeder E, Gosch E. Considering CBT with anxious youth? Think exposures. *Cognitive and Behavioral Practice*. 2005; 12:136–150.10.1016/S1077-7229(05)80048-3
- Kendall PC, Safford S, Flannery-Schroeder E, Webb A. Child anxiety treatment: outcomes in adolescence and impact on substance use and depression at 7.4-year follow-up. *Journal of Consulting and Clinical Psychology*. 2004; 72:276–287.10.1037/0022-006X.72.2.276 [PubMed: 15065961]
- Kendall, PC.; Stark, K.; Martinsen, K.; O’Neil, K.; Arora, P. EMOTION: “Coping Kids” Managing Anxiety and Depression. Ardmore, PA: Workbook Publishing; 2013.
- Kendall PC, Treadwell KR. The role of self-statements as a mediator in treatment for youth with anxiety disorders. *Journal of Consulting and Clinical Psychology*. 2007; 75:380–389.10.1037/0022-006X.75.3.380 [PubMed: 17563155]
- Kendler KS. Major depression and generalized anxiety disorder same genes, (Partly) different environments—Revisited. *British Journal of Psychiatry*. 1996; 168(Suppl 30):68–75. [PubMed: 8770431]
- Kendler KS, Davis CG, Kessler RC. The familial aggregation of common psychiatric and substance use disorders in the National Comorbidity Survey: A family history study. *The British Journal of Psychiatry*. 1997; 170:541–548.10.1192/bjp.170.6.541 [PubMed: 9330021]
- Kendler KS, Gardner CO, Gatz M, Pedersen NL. The sources of co-morbidity between major depression and generalized anxiety disorder in a Swedish national twin sample. *Psychological Medicine*. 2007; 37:453–462.10.1017/S0033291707002012 [PubMed: 17121688]
- Kendler KS, Hettema JM, Butera F, Gardner CO, Prescott CA. Life event dimensions of loss, humiliation, entrapment, and danger in the prediction of onsets of major depression and generalized anxiety. *Archives of General Psychiatry*. 2003; 60:789–796.10.1001/archpsyc.60.8.789 [PubMed: 12912762]
- Kendler KS, Prescott CA, Myers J, Neale MC. The structure of genetic and environmental risk factors for common psychiatric and substance use disorders in men and women. *Archives of General Psychiatry*. 2003; 60:929–937.10.1001/archpsyc.60.9.929 [PubMed: 12963675]
- Kendler KS, Neale MC, Kessler RC, Heath AC, Eaves LJ. Major depression and generalized anxiety disorder: same genes, (partly) different environments? *Archives of General Psychiatry*. 1992; 49:716–722.10.1001/archpsyc.1992.01820090044008 [PubMed: 1514877]
- Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry*. 2005; 62:593–602.10.1001/archpsyc.62.6.593 [PubMed: 15939837]
- Kessler RC, Gruber M, Hettema JM, Hwang I, Sampson N, Yonkers KA. Co-morbid major depression and generalized anxiety disorders in the National Comorbidity Survey follow-up. *Psychological Medicine*. 2008; 38:365–374.10.1017/S0033291707002012 [PubMed: 18047766]
- Kessler RC, Price RH. Primary prevention of secondary disorders: A proposal and agenda. *American Journal of Community Psychology*. 1993; 21:607–633.10.1007/BF00942174 [PubMed: 8192124]

- Kessler RC, Stang PE, Wittchen HU, Ustun TB, Roy-Byrne PP, Walters EE. Lifetime panic-depression comorbidity in the National Comorbidity Survey. *Archives of General Psychiatry*. 1998; 55:801–808.10.1001/archpsyc.55.9.801 [PubMed: 9736006]
- Keough ME, Riccardi CJ, Timpano KR, Mitchell MA, Schmidt NB. Anxiety symptomatology: The association with distress tolerance and anxiety sensitivity. *Behavior Therapy*. 2010; 41:567–574.10.1016/j.beth.2010.04.002 [PubMed: 21035619]
- Kimbrel NA. A model of the development and maintenance of generalized social phobia. *Clinical Psychology Review*. 2008; 28:592–612.10.1016/j.cpr.2007.08.003 [PubMed: 17959288]
- Klein DN, Lewinsohn PM, Rohde P, Seeley JR, Shankman SA. Family study of co-morbidity between major depressive disorder and anxiety disorders. *Psychological Medicine*. 2003; 33:703–714.10.1017/S0033291703007487 [PubMed: 12785472]
- Klein, DN.; Riso, LP. Psychiatric disorders: Problems of boundaries and comorbidity. In: Costello, CG., editor. *Basic Issues in Psychopathology*. New York: Guilford Press; 1993.
- Kley H, Heinrichs N, Bender C, Tuschen-Caffier B. Predictors of outcome in a cognitive-behavioral group program for children and adolescents with social anxiety disorder. *Journal of anxiety disorders*. 2012; 26(1):79–87. [PubMed: 21975266]
- Kovacs M. The Children's Depression Inventory (CDI). *Psychopharmacology Bulletin*. 1985; 21:995–998. [PubMed: 4089116]
- Kovacs, M. *Manual for Children's Depression Inventory*. North Tonawanda, NY: Multi-Health Systems, Inc; 1992.
- Kovacs M, Gatsonis C, Paulauskas SL, Richards C. Depressive disorders in childhood: IV. A longitudinal study of comorbidity with and risk for anxiety disorders. *Archives of General Psychiatry*. 1989; 46:776–782. [PubMed: 2774847]
- Kraemer HC. Statistical issues in assessing comorbidity. *Statistics in Medicine*. 1995; 14:721–733.10.1002/sim.4780140803 [PubMed: 7644854]
- Kraemer H, Wilson KA, Hayward C. Lifetime prevalence and pseudocomorbidity in psychiatric research. *Archives of General Psychiatry*. 2006; 63:604–608.10.1001/archpsyc.63.6.604 [PubMed: 16754833]
- Lahey BB, Rathouz PJ, Van Hulle C, Urbano RC, Krueger RF, Applegate B, Garriock HA, Waldman ID. Testing structural models of DSM-IV symptoms of common forms of child and adolescent psychopathology. *Journal of Abnormal Child Psychology*. 2008; 36:187–206.10.1007/s10802-007-9169-5 [PubMed: 17912624]
- Lambert SF, McCreary BT, Joiner TE, Schmidt NB, Ialongo NS. Structure of anxiety and depression in urban youth: An examination of the tripartite model. *Journal of Consulting and Clinical Psychology*. 2004; 72:904–908.10.1037/0022-006X.72.5.904 [PubMed: 15482049]
- Lau JYF, Goldman D, Buzas B, Fromm SJ, Guyer AE, Hodgkinson C, Ernst M. Amygdala function and 5-HTT gene variants in adolescent anxiety and major depressive disorder. *Biological Psychiatry*. 2009; 65:349–355.10.1016/j.biopsych.2008.08.037 [PubMed: 18950748]
- Laurent J, Catanzaro SJ, Joiner TE. Development and preliminary validation of the physiological hyperarousal scale for children. *Psychological Assessment*. 2004; 16:373–380.10.1037/1040-3590.16.4.373 [PubMed: 15584796]
- Laurent J, Catanzaro SJ, Joiner TE, Rudolph KD, Potter KI, Lambert S, Gathright T. A measure of positive and negative affect for children: Scale development and preliminary validation. *Psychological Assessment*. 1999; 11:326–338.10.1037/1040-3590.11.3.326
- Lee LC, Rebok GW. Anxiety and depression in children: A test of the positive-negative affect model. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2002; 41:419–426.10.1097/00004583-200204000-00014 [PubMed: 11931598]
- Leikanger E, Ingul JM, Larsson B. Sex and age-related anxiety in a community sample of Norwegian adolescents. *Personality and Social Psychology*. 2012; 53:150–157.10.1111/j.1467-9450.2011.00915.x
- Lewinsohn PM, Zinbarg R, Seeley JR, Lewinsohn M, Sack WH. Lifetime comorbidity among anxiety disorders and between anxiety disorders and other mental disorders in adolescents. *Journal of Anxiety Disorders*. 1997; 11:377–394.10.1016/S0887-6185(97)0017-0 [PubMed: 9276783]

- Lewinsohn PM, Holm-Denoma JM, Small JW, Seeley JR, Joiner TE. Separation anxiety disorder in childhood as a risk factor for future mental illness. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2008; 47:548–555.10.1097/CHI.0b013e31816765e7 [PubMed: 18356763]
- Lewinsohn, Peter M.; Rohde, P.; Seeley, JR. Adolescent psychopathology: III. The clinical consequences of comorbidity. *Journal of the American Academy of Child & Adolescent Psychiatry*. 1995; 34:510–9.10.1097/00004583-199504000-00018 [PubMed: 7751265]
- Lieb R, Isensee B, Hofler M, Pfister H, Wittchen HU. Parental major depression and the risk of depression and other mental disorders in offspring: A prospective-longitudinal community study. *Archives of General Psychiatry*. 2002; 59:365–374.10.1001/archpsyc.59.4.365 [PubMed: 11926937]
- Liu X, Gentzler AL, Tepper P, Kiss E, Kothencné VO, Tamás Z, Kovacs M. Clinical features of depressed children and adolescents with various forms of suicidality. *Journal of Clinical Psychiatry*. 2006; 67:1442–1450.10.4088/JCP.v67n0917 [PubMed: 17017833]
- Lonigan CJ, Carey MP, Finch AJ. Anxiety and depression in children and adolescents: Negative affectivity and the utility of self-reports. *Journal of Consulting and Clinical Psychology*. 1994; 62:1000–1008.10.1037/0022-006X.62.5.1000 [PubMed: 7806708]
- Lonigan CJ, Phillips BM, Hooe ES. Relations of positive and negative affectivity to anxiety and depression in children: Evidence from a latent variable longitudinal study. *Journal of Consulting and Clinical Psychology*. 2003; 71:465–481.10.1037/0022-006X.71.3.465 [PubMed: 12795571]
- Lopez B, Turner RJ, Saavedra LM. Anxiety and risk for substance dependence among late adolescents/young adults. *Journal of Anxiety Disorders*. 2005; 19:275–294.10.1016/j.janxdis.2004.03.001 [PubMed: 15686857]
- Mahoney AJ, McEvoy PM. A transdiagnostic examination of intolerance of uncertainty across anxiety and depressive disorders. *Cognitive Behaviour Therapy*. 2012; 41:212–222.10.1080/16506073.2011.622130 [PubMed: 22032195]
- Manassis K, Mendlowitz SL, Scapillato D, Avery D, Fiksenbaum L, Freire M, Owens M. Group and individual cognitive-behavioral therapy for childhood anxiety disorders: A randomized trial. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2002; 41:1423–1430.10.1097/00004583-200212000-0013 [PubMed: 12447028]
- Manassis K, Monga S. A therapeutic approach to children and adolescents with anxiety disorders and associated comorbid conditions. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2001; 40:115–117.10.1097/00004583-200101000-00024 [PubMed: 11195553]
- Mancini C, Van Amerigen M, Macmillian H. Relationship of child sexual and physical abuse to anxiety disorders. *The Journal of Nervous and Mental Disease*. 1995; 183:5.10.1097/00005053-199505000-00006
- March JS, Parker JD, Sullivan K, Stallings P, Conners CK. The Multidimensional Anxiety Scale for Children (MASC): Factor structure, reliability, and validity. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1997; 36:554–565.10.1097/00004583-199704000-00019 [PubMed: 9100431]
- Markon KE. How things fall apart: Understanding the nature of internalizing through its relationship with impairment. *Journal of Abnormal Psychology*. 2010; 119:447–458.10.1037/a0019707 [PubMed: 20677834]
- Martell, CR.; Addis, ME.; Jacobson, NS. *Depression in context*. New York, NY: W.W. Norton; 2001.
- Martin, EL.; Nemeroff, CB. The biology of generalized anxiety disorder and major depressive disorder: Commonalities and distinguishing features. In: Goldberg, D.; Kendler, KS.; Sirovatka, PJ., editors. *Diagnostic issues in depression and generalized anxiety disorder: Refining the research agenda for DSM-V*. Washington, DC: American Psychiatric Association; 2010. p. 45-70.
- Marton P, Churchard M, Kutcher S, Korenblum M. Diagnostic utility of the Beck Depression Inventory with adolescent psychiatric outpatients and inpatients. *The Canadian Journal of Psychiatry*. 1991; 36:428–431.
- Masi G, Favilla L, Mucci M, Millepiedi S. Depressive comorbidity in children and adolescents with generalized anxiety disorder. *Child Psychiatry and Human Development*. 2000; 30:205–15.10.1023/A:1021351722364 [PubMed: 10851794]

- Masi G, Mucci M, Favilla L, Millepiedi S. Anxiety comorbidity in referred children and adolescents with dysthymic disorder. *Psychopathology*. 2001; 34:253–258.10.1159/000049318 [PubMed: 11799320]
- Mathew AR, Pettit JW, Lewinsohn PM, Seeley JR, Roberts RE. Co-morbidity between major depressive disorder and anxiety disorders: Shared etiology or direct causation? *Psychological Medicine*. 2011; 41:2023–34.10.1017/S0033291711000407 [PubMed: 21439108]
- McFarland BR, Shankman SA, Tenke CE, Bruder GE, Klein DN. Behavioral activation system deficits predict the six-month course of depression. *Journal of Affective Disorders*. 2006; 91:229–234.10.1016/j.jad.2006.01.012 [PubMed: 16487598]
- McLaughlin KA, Nolen-Hoeksema S. Rumination as a transdiagnostic factor in depression and anxiety. *Behaviour Research and Therapy*. 2011; 49:186–193.10.1016/j.brat.2010.12.006 [PubMed: 21238951]
- Mendlewicz JJ, Papdimitriou GG, Wilmotte JJ. Family study of panic disorder: Comparison with generalized anxiety disorder, major depression and normal subjects. *Psychiatric Genetics*. 1993; 3:73–78.10.1097/00041444-199322000-00002
- Mendlowitz SL, Manassis K, Bradley S, Scapillato D, Miezitis S, Shaw BF. Cognitive-behavioral group treatments in childhood anxiety disorders: The role of parental involvement. *Journal of the American Academy Of Child & Adolescent Psychiatry*. 1999; 38:1223–1229.10.1097/00004583-199910000-00010 [PubMed: 10517054]
- Merikangas KR, Swendsen JD, Preisig MA, Chazan RZ. Psychopathology and temperament in parents and offspring: Results of a family study. *Journal of Affective Disorders*. 1998; 51:63–74.10.1016/S0165-0327(98)00157-8 [PubMed: 9879804]
- Messer SC, Beidel DC. Psychosocial correlates of childhood anxiety disorders. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1994; 33:975–983.10.1097/00004583-199409000-00007 [PubMed: 7961353]
- Middeldorp CM, Cath DC, Van Dyck R, Boomsma DI. The co-morbidity of anxiety and depression in the perspective of genetic epidemiology: A review of twin and family studies. *Psychological Medicine*. 2005; 35:611–624.10.1017/S003329170400412X [PubMed: 15918338]
- Mineka S, Watson D, Clark LA. Comorbidity of anxiety and unipolar mood disorders. *Annual Review of Psychology*. 1998; 49:377–412.10.1146/annurev.psych.49.1.377
- Mitchell JR, McCauley E, Burke PM, Moss SJ. Phenomenology of depression in children and adolescents. *Journal of the American Academy of Child & Adolescent Psychiatry*. 1988; 27:12–20.10.1097/00004583-198801000-00004 [PubMed: 3343195]
- Moffitt TE, Caspi A, Harrington H, Milne BJ, Melchior M, Goldberg D, Poulton R. Generalized anxiety disorder and depression: Childhood risk factors in a birth cohort followed to age 32. *Psychological Medicine*. 2007; 37:441–452.10.1017/S0033291706009640 [PubMed: 17201999]
- Moffitt TE, Harrington H, Caspi A, Kim-Cohen J, Goldberg D, Gregory AM, Poulton R. Depression and generalized anxiety disorder: Cumulative and sequential comorbidity in a birth cohort followed prospectively to age 32 years. *Archives of General Psychiatry*. 2007; 64:651–660.10.1001/archpsyc.64.6.651 [PubMed: 17548747]
- Morilak DA, Frazer A. Antidepressants and brain monoaminergic systems: A dimensional approach to understanding their behavioural effects in depression and anxiety disorders. *International Journal of Neuropsychopharmacology*. 2004; 7:193–218.10.1017/S1461145704004080 [PubMed: 15003145]
- Mosing MA, Gordon SD, Medland SE, Statham DJ, Nelson EC, Heath AC, Wray NR. Genetic and environmental influences on the co-morbidity between depression, panic disorder, agoraphobia, and social phobia: A twin study. *Depression and Anxiety*. 2009; 26:1004–1011.10.1002/da.20611 [PubMed: 19750555]
- Muris P, Meesters C, de Kanter E, Timmerman PE. Behavioural inhibition and behavioural activation system scales for children: Relationships with Eysenck's personality traits and psychopathological symptoms. *Personality and Individual Differences*. 2005; 38:831–841.10.1016/j.paid.2004.06.007

- Murphy DA, Marelich WD, Hoffman D. Assessment of anxiety and depression in young children: Support for two separate constructs. *Journal of Clinical Child Psychology*. 2000; 29:383–91.10.1207/S15374424JCCP2903_9 [PubMed: 10969422]
- Mychailyszyn MP, Brodman DM, Read KL, Kendall PC. Cognitive-behavioral school-based interventions for anxious and depressed youth: A meta-analysis of outcomes. *Clinical Psychology: Science and Practice*. 2012; 19:129–153.10.1111/j.1468-2850.2012.01279.x
- Myers K, Winters NC. Ten-year review of rating scales. II: Scales for internalizing disorders. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2002; 41:634–659.10.1097/00004583-200206000-00004 [PubMed: 12049439]
- Newman DL, Moffitt TE, Caspi A, Silva PA. Comorbid mental disorders: Implications for treatment and sample selection. *Journal of Abnormal Psychology*. 1998; 107:305–311.10.1037/0021-843X.107.2.305 [PubMed: 9604559]
- Newman SC, Bland RC. Life events and the 1-year prevalence of major depressive episode, generalized anxiety disorder, and panic disorder in a community sample. *Comprehensive Psychiatry*. 1994; 35:76–82.10.1016/0010-440X(94)90173-2 [PubMed: 8149733]
- Nilzon KR, Palmerus K. Anxiety in depressed school children. *School Psychology International*. 1997; 18:165–177.10.1177/0143034397182005
- Nock MK, Mendes W. Physiological arousal, distress tolerance, and social problem-solving deficits among adolescent self-injurers. *Journal of Consulting and Clinical Psychology*. 2008; 76:28–38.10.1037/0022-006X.76.1.28 [PubMed: 18229980]
- Nolen-Hoeksema S. The role of rumination in depressive disorders and mixed anxiety/depressive symptoms. *Journal of Abnormal Psychology*. 2000; 109:504–511.10.1037/0021-843X.109.3.504 [PubMed: 11016119]
- Nutt DJ, Stein DJ. Understanding the neurobiology of comorbidity in anxiety disorders. *CNS Spectrums*. 2006; 11:13–20. [PubMed: 17008826]
- Olino TM, Durbin CE, Klein DN, Hayden EP, Dyson MW. Gender differences in young children's temperament traits: Comparisons across observational and parent-report methods. *Journal of Personality*. 2013; 81:119–129. [PubMed: 22924826]
- Olino TM, Klein DN, Lewinsohn PM, Rohde P, Seeley JR. Longitudinal associations between depressive and anxiety disorders: A comparison of two trait models. *Psychological Medicine*. 2008; 38:353–363.10.1017/S0033291707001341 [PubMed: 17803836]
- Olino TM, Klein DN, Lewinsohn PM, Rohde P, Seeley JR. Latent trajectory classes of depressive and anxiety disorders from adolescence to adulthood: Descriptions of classes and associations with risk factors. *Comprehensive Psychiatry*. 2010; 51:224–235.10.1016/j.comppsy.2009.07.002 [PubMed: 20399331]
- Olino TM, Yu L, Klein DN, Rohde P, Seeley JR, Pilkonis PA, Lewinsohn PM. Measuring depression using item response theory: an examination of three measures of depressive symptomatology. *International Journal of Methods in Psychiatric Research*. 2012; 21(1):76–85.10.1002/mpr.1348 [PubMed: 22290656]
- Ollendick TH, Jarrett MA, Grills-Taquechel AE, Hovey LD, Wolff JC. Comorbidity as a predictor and moderator of treatment outcome in youth with anxiety, affective, attention deficit/hyperactivity disorder, and oppositional/conduct disorders. *Clinical Psychology Review*. 2008; 28:1447–71.10.1016/j.cpr.2008.09.003 [PubMed: 18973971]
- Ollendick TH, Seligman LD, Goza AB, Byrd DA, Singh K. Anxiety and depression in children and adolescents: A factor-analytic examination of the tripartite model. *Journal of Child and Family Studies*. 2003; 12:157–70.10.1023/A:1022806731527
- O'Neil KA, Podell JL, Benjamin CL, Kendall PC. Comorbid depressive disorders in anxiety-disordered youth: Demographic, clinical, and family characteristics. *Child Psychiatry and Human Development*. 2010; 41:330–341.10.1007/s10578-009-0170-9
- O'Neil KA, Puleo CM, Benjamin CL, Podell JL, Kendall PC. Suicidal ideation in anxiety-disordered youth. *Suicide & Life-Threatening Behavior*. 2012; 42:305–317.10.1111/j.1943-278X.2012.00091.x [PubMed: 22509976]
- O'Neil-Rodriguez K, Kendall PC. Suicidal ideation in anxiety-disordered youth: Identifying predictors of risk. 2012 Manuscript in preparation.

- Parker G, Hadzi-Pavlovic D. Is any female preponderance in depression secondary to a primary female preponderance in anxiety disorders? *Acta Psychiatrica Scandinavica*. 2001; 103:252–256.10.1034/j.1600-0447.2001.00375.x [PubMed: 11328237]
- Parker G, Hadzi-Pavlovic D. Is the female preponderance in major depression secondary to a gender difference in specific anxiety disorders? *Psychological Medicine*. 2004; 34:461–470.10.1017/S0033291703001181 [PubMed: 15259831]
- Pawlak C, Pascual-Sanchez T, Raë P, Fischer W, Ladame F. Anxiety disorders, comorbidity, and suicide attempts in adolescence: A preliminary investigation. *European Psychiatry*. 1999; 14:132–136.10.1016/S0924-9338(99)80730-5 [PubMed: 10572337]
- Peris T, Compton S, Piacentini J. and the CAMS author list. Trajectories of change in cognitive behavior therapy for childhood anxiety. 2013 Manuscript submitted for publication.
- Perugi G, Deltito J, Soriani A, Musetti L, Petracca A, Nisita C, Maremmanni I, et al. Relationships between panic disorder and separation anxiety with school phobia. *Comprehensive Psychiatry*. 1988; 29:98–107.10.1016/0010-440X(88)90003-X [PubMed: 3370974]
- Pickering, AD.; Gray, JA. The neuroscience of personality. In: Pervin, LA.; John, OP., editors. *Handbook of personality: Theory and research*. 2. New York, NY US: Guilford Press; 1999. p. 277-299.
- Pine DS, Cohen P, Gurley D, Brook J, Ma Y. The risk for early-adulthood anxiety and depressive disorders in adolescents with anxiety and depressive disorders. *Archives of General Psychiatry*. 1998; 55:56–64. [PubMed: 9435761]
- Pine DS, Cohen P, Johnson JG, Brook JS. Adolescent life events as predictors of adult depression. *Journal of Affective Disorders*. 2002; 68:49–57.10.1001/archpsyc.55.1.56 [PubMed: 11869782]
- Pizzagalli DA, Jahn AL, O’Shea JP. Toward an objective characterization of an anhedonic phenotype: A signal-detection approach. *Biological Psychiatry*. 2005; 57:319–327.10.1016/j.biopsych.2004.11.026 [PubMed: 15705346]
- Pössel P, Seemann S, Hautzinger M. Impact of comorbidity in prevention of adolescent depressive symptoms. *Journal of Counseling Psychology*. 2008; 55:106–117.10.1037/0022-0167.55.1.106
- Prins PJ, Ollendick TH. Cognitive change and enhanced coping: Missing mediational links in cognitive behavior therapy with anxiety-disordered children. *Clinical Child and Family Psychology Review*. 2003; 6:87–105.10.1023/A:1023730526716 [PubMed: 12836579]
- Quay HC. Inhibition and attention deficit hyperactivity disorder. *Journal of Abnormal Child Psychology*. 1997; 25:7–13.10.1023/A:1025799122529 [PubMed: 9093895]
- Rachman S, Grüter-Andrew J, Shafran R. Post-event processing in social anxiety. *Behaviour Research and Therapy*. 2000; 38(6):611–617.10.1016/S0005-7967(99)00089-3 [PubMed: 10846809]
- Ranta K, Kaltiala-Heino R, Pelkonen M, Marttunen M. Associations between peer victimization, self-reported depression and social phobia among adolescents: The role of comorbidity. *Journal of Adolescence*. 2009; 32:77–93.10.1016/j.adolescence.2007.11.005 [PubMed: 18191998]
- Ranta K, Kaltiala-Heino R, Rantanen P, Marttunen M. Social phobia in Finnish general adolescent population: Prevalence, comorbidity, individual and family correlates, and service use. *Depression and Anxiety*. 2009; 26:528–536.10.1002/da.20422 [PubMed: 19170089]
- Rapee RM. Potential role of childrearing practices in the development of anxiety and depression. *Clinical Psychology Review*. 1997; 17:47–67. [PubMed: 9125367]
- Rapee RM, Lyneham HJ, Hudson JL, Kangas M, Wuthrich VM, Schniering CA. Effect of comorbidity on treatment of anxious children and adolescents: Results from a large, combined sample. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2013; 53:47–56.10.1016/j.jaac.2012.10.002 [PubMed: 24342385]
- Reardon LE, Leen-Feldner EW, Hayward C. A critical review of the empirical literature on the relation between anxiety and puberty. *Clinical Psychology Review*. 2009; 29:1–23.10.1016/j.cpr.2008.09.005 [PubMed: 19019513]
- Reich J. Family psychiatric histories in male patients with generalized anxiety disorder and major depressive disorder. *Annals of Clinical Psychiatry*. 1995; 7:71–78.10.3109/10401239509149030 [PubMed: 8556096]
- Reynolds, CR.; Richmond, BO. *Revised Children’s Manifest Anxiety Scale: Manual*. Los Angeles: Western Psychological Services; 1985.

- Reynolds WM, Mazza JJ. Reliability and validity of the Reynolds Adolescent Depression Scale with young adolescents. *Journal of School Psychology*. 1998; 36:295–312.10.1016/S0022-4405(98)00010-7
- Rice F, van den Bree MBM, Thapar A. A population-based study of anxiety as a precursor for depression in childhood and adolescence. *BMC Psychiatry*. 2004; 4:43.10.1186/1471-244X-4-43 [PubMed: 15596007]
- Roberson-Nay R, Eaves LJ, Hettema JM, Kendler KS, Silberg JL. Childhood separation anxiety disorder and adult onset panic attacks share a common genetic diathesis. *Depression and Anxiety*. 2012; 29:320–327.10.1002/da.21931 [PubMed: 22461084]
- Rohde P, Clarke GN, Lewinsohn PM, Seeley JR, Kaufman NK. Impact of comorbidity on a cognitive-behavioral group treatment for adolescent depression. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2001; 40:795–802.10.1097/00004583-200107000-00014 [PubMed: 11437018]
- Ronan KR, Kendall PC, Rowe M. Negative affectivity in children: Development and validation of a self-statement questionnaire. *Cognitive Therapy and Research*. 1994; 18:509–528.10.1007/BF02355666
- Rose AJ. Co-rumination in the friendships of girls and boys. *Child Development*. 2002; 73:1830–1843.10.1111/1467-8624.00509 [PubMed: 12487497]
- Rose AJ, Carlson W, Waller EM. Prospective associations of co-rumination with friendship and emotional adjustment: Considering the socioemotional trade-offs of corumination. *Developmental Psychology*. 2007; 43:1019–1031.10.1037/0012-1649.43.4.1019 [PubMed: 17605532]
- Rotge JY, Grabot D, Aouizerate B, Pélioso A, Lépine JP, Tignol J. Childhood history of behavioral inhibition and comorbidity status in 256 adults with social phobia. *Journal of Affective Disorders*. 2011; 129:338–341.10.1016/j.jad.2010.07.031 [PubMed: 20797795]
- Roy MA, Neale MC, Pedersen NL, Mathe AA, Kendler KS. A twin study of generalized anxiety disorder and major depression. *Psychological Medicine*. 1995; 25:1037–1049.10.1017/S0033291700037533 [PubMed: 8588001]
- Roy-Byrne PP, Stang P, Wittchen H, Ustun B, Walters EE, Kessler RC. Lifetime panic-depression comorbidity in the National Comorbidity Survey: Association with symptoms, impairment, course and help-seeking. *The British Journal of Psychiatry*. 2000; 176:229–235.10.1192/bjp.176.3.229 [PubMed: 10755069]
- Rubin, KH.; Burgess, KB. Social withdrawal and anxiety. In: Vasey, MW.; Dadds, MR., editors. *The developmental psychopathology of anxiety*. New York, NY US: Oxford University Press; 2001. p. 407-434.
- Rubin KH, Coplan RJ, Bowker JC. Social withdrawal in childhood. *Annual Review of Psychology*. 2009; 60:141–171.10.1146/annurev.psych.60.110707.163642
- Rudolph KD. Gender differences in emotional responses to interpersonal stress during adolescence. *Journal of Adolescent Health*. 2002; 30:3–13.10.1016/S1054-139X(01)00383-4 [PubMed: 11943569]
- Rudolph KD, Hammen C, Burge D. Interpersonal functioning and depressive symptoms in childhood: Addressing the issues of specificity and comorbidity. *Journal of Abnormal Child Psychology*. 1994; 22:355–371.10.1007/BF02168079 [PubMed: 8064038]
- RUPP Anxiety Study Group. The Pediatric Anxiety Rating Scale (PARS): Development and psychometric properties. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2002; 41:1061–1069.10.1017/S0033291700037533 [PubMed: 12218427]
- Rutter M, Caspi A, Moffitt TE. Using sex differences in psychopathology to study causal mechanisms: Unifying issues and research. *Journal of Child Psychiatry and Psychology*. 2003; 44:1092–1115.
- Ryan ND, Puig-Antich J, Ambrosini P, Rabinovich H. The clinical picture of major depression in children and adolescents. *Archives of General Psychiatry*. 1987; 44:854–861.10.1001/archpsyc.1987.01800220016003 [PubMed: 3662742]
- Sanislow CA, Pine DS, Quinn KJ, Kozak MJ, Garvey MA, Heihsen RK, Cuthbert BN. Developing constructs for psychopathology research: Research domain criteria. *Journal of Abnormal Psychology*. 2010; 119:631.10.1037/a0020909 [PubMed: 20939653]

- Savino M, Perugi G, Simonini E, Soriani A, Cassano GB, Akiskal HS. Affective comorbidity in panic disorder: Is there a bipolar connection? *Journal of Affective Disorders*. 1993; 28:155–163.10.1016/0165-0327(93)90101-O [PubMed: 8408978]
- Schatzberg AF, Cole JO. Benzodiazepines in depressive disorders. *Archive of General Psychiatry*. 1978; 35:1359–1365.
- Schniering CA, Rapee RM. The relationship between automatic thoughts and negative emotions in youth: A test of the cognitive content-specificity hypothesis. *Journal of Abnormal Psychology*. 2004; 113:464–470.10.1037/0021-843X.113.3.464 [PubMed: 15311991]
- Schofield CA, Coles ME, Gibb BE. Retrospective reports of behavioral inhibition and young adults' current symptoms of social anxiety, depression, and anxious arousal. *Journal of Anxiety Disorders*. 2009; 23:884–90.10.1016/j.janxdis.2009.05.003 [PubMed: 19592214]
- Sears HA, Armstrong VH. A prospective study of adolescents' self-reported depressive symptoms: Are risk behaviours a stronger predictor than anxiety symptoms? *Canadian Journal of Behavioural Science*. 1998; 30:225–233.10.1037/h0087065
- Sekula LK, DeSantis J, Gianetti V. Considerations in the management of the patient with comorbid depression and anxiety. *Journal of the American Academy of Nurse Practitioners*. 2003; 15:23–33. [PubMed: 12613410]
- Seligman LD, Ollendick TH. Comorbidity of anxiety and depression in children and adolescents: An integrative review. *Clinical Child and Family Psychology Review*. 1998; 1:125–144.10.1023/A:1021887712873 [PubMed: 11324302]
- Seligman LD, Ollendick TH, Langley AK, Baldacci HB. The utility of measures of child and adolescent anxiety: A meta-analytic review of the Revised Children's Manifest Anxiety Scale, the State-Trait Anxiety Inventory for Children, and the Child Behavior Checklist. *Journal of Clinical Child and Adolescent Psychology*. 2004; 33:557–565.10.1207/s15374424jccp3303_13 [PubMed: 15271613]
- Silberg J, Rutter M, Neale M, Eaves L. Genetic moderation of environmental risk for depression and anxiety in adolescent girls. *The British Journal of Psychiatry*. 2001; 179:116–121.10.1192/bjp.179.2.116 [PubMed: 11483472]
- Silk JS, Davis S, McMakin DL, Dahl RE, Forbes EE. Why do anxious children become depressed teenagers? The role of social evaluative threat and reward processing. *Psychological Medicine*. 2012; 42:2095–2107.10.1017/S0033291712000207 [PubMed: 22340187]
- Silk JS, Steinberg L, Morris A. Adolescents' emotion regulation in daily life: Links to depressive symptoms and problem behavior. *Child Development*. 2003; 74:1869–1880.10.1046/j.1467-8624.2003.00643.x [PubMed: 14669901]
- Silverman WK, Kurtines WM, Ginsburg GS, Weems CF, Lumpkin PW, Carmichael DH. Treating anxiety disorders in children with group cognitive-behavioral therapy: A randomized clinical trial. *Journal of Consulting and Clinical Psychology*. 1999; 67:995–1103.10.1037/0022-006X.67.6.995 [PubMed: 10596522]
- Silverman WK, Ollendick TH. Evidence-based assessment of anxiety and its disorders in children and adolescents. *Journal of Clinical Child and Adolescent Psychology*. 2005; 34:380–411.10.1207/s15374424jccp3403_2 [PubMed: 16026211]
- Silverstein B. Gender differences in the prevalence of clinical depression: The role played by depression associated with somatic symptoms. *The American Journal of Psychiatry*. 1999; 156:480–82. [PubMed: 10080570]
- Skre I, Onstad S, Edvardsen J, Torgersen S, Kringlen E. A family study of anxiety disorders: Familial transmission and relationship to mood disorder and psychoactive substance use disorder. *Acta Psychiatrica Scandinavica*. 1994; 90:366–374.10.1111/j.1600-0447.1994.tb01608.x [PubMed: 7872042]
- Small DM, Simons AD, Yovanoff P, Silva SG, Lewis CC, Murakami JL, March J. Depressed adolescents and comorbid psychiatric disorders: Are there differences in the presentation of depression? *Journal of Abnormal Child Psychology*. 2008; 36:1015–1028.10.1007/s10802-008-9237-5 [PubMed: 18509755]

- Southam-Gerow MA, Kendall PC. A preliminary study of the emotion understanding of youths referred for treatment of anxiety disorders. *Journal of Clinical Child Psychology*. 2000; 29:319–327.10.1207/S15374424JCCP2903_3 [PubMed: 10969416]
- Southam-Gerow MA, Kendall PC, Weersing VR. Examining outcome variability: Correlates of treatment response in a child and adolescent anxiety clinic. *Journal of Clinical Child Psychology*. 2001; 30:422–436.10.1207/S15374424JCCP3003_13 [PubMed: 11501258]
- Stark, KD.; Schnoebelen, S.; Simpson, J.; Hargrave, J.; Glenn, R. Treating depressed children: Therapist manual for “ACTION”. Ardmore, PA: Workbook Publishing; 2007.
- Starr LR, Davila J. Differentiating interpersonal correlates of depressive symptoms and social anxiety in adolescence: Implications for models of comorbidity. *Journal of Clinical Child and Adolescent Psychology*. 2008; 37:337–349.10.1080/15374410801955854 [PubMed: 18470771]
- Starr LR, Davila J. Clarifying co-rumination: Associations with internalizing symptoms and romantic involvement among adolescent girls. *Journal of Adolescence*. 2009; 32:19–37.10.1016/j.adolescence.2007.12.005 [PubMed: 18241914]
- Starr LR, Davila J. Responding to anxiety with rumination and hopelessness: Mechanism of anxiety-depression symptom co-occurrence? *Cognitive Therapy and Research*. 2012; 36:321–337.10.1007/s10608-011-9363-1 [PubMed: 22865943]
- Steer RA, Clark DA, Kumar G, Beck AT. Common and specific dimensions of self-reported anxiety and depression in adolescent outpatients. *Journal of Psychopathology and Behavioral Assessment*. 2007; 30:163–170.10.1007/s10862-007-9060-2
- Steinberg, L.; Thissen, D. Item response theory. In: Comer, J.; Kendall, PC., editors. *Handbook of Research Strategies for Clinical Psychology*. New York, NY: Oxford University Press; 2013.
- Stein MB, Fuetsch M, Müller N, Höfler M, Lieb R, Wittchen H. Social anxiety disorder and the risk of depression: A prospective community study of adolescents and young adults. *Archives of General Psychiatry*. 2001; 58:251–256.10.1001/archpsyc.58.3.251 [PubMed: 11231832]
- Strauss CC, Last CG, Hersen M, Kazdin AE. Association between anxiety and depression in children and adolescents with anxiety disorders. *Journal of Abnormal Child Psychology*. 1988; 16:57–68.10.1007/BF00910500 [PubMed: 3361030]
- Strauss J, Birmaher B, Bridge J, Axelson D, Chiappetta L, Brent D, Ryan N. Anxiety disorders in suicidal youth. *The Canadian Journal of Psychiatry*. 2000; 45:739–45.
- Strawn JR, Sakolsky DJ, Rynn MA. Psychopharmacologic treatment of children and adolescents with anxiety disorders. *Child and Adolescent Psychiatric Clinics of North America*. 2012; 21:527–539.10.1016/j.chc.2012.05.003 [PubMed: 22800992]
- Sullivan PF, Neale MC, Ph D, Kendler KS. Genetic epidemiology of major depression: Review and meta-analysis. *American Journal of Psychiatry*. 2000; 157:1552–1562.10.1176/appi.ajp.157.10.1552 [PubMed: 11007705]
- Suveg C, Hoffman B, Zeman JL, Thomassin K. Common and specific emotion-related predictors of anxious and depressive symptoms in youth. *Child Psychiatry and Human Development*. 2009; 40:223–239.10.1007/s10578-008-0121-x [PubMed: 19039662]
- Tamás Z, Kovacs M, Gentzler AL, Tepper P, Gáboros J, Kiss E, Vetró Á. The relations of temperament and emotion self-regulation with suicidal behaviors in a clinical sample of depressed children in Hungary. *Journal of Abnormal Child Psychology*. 2007; 35:640–652.10.1007/s10802-007-9119-2 [PubMed: 17530394]
- Tao R, Emslie G, Mayes T, Nakonezny P, Kennard B, Hughes C. Early prediction of acute antidepressant treatment response and remission in pediatric major depressive disorder. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2009; 48:71–78.10.1097/CHI.0b013e318190043e [PubMed: 19057412]
- Thapar A, McGuffin P. Anxiety and depressive symptoms in childhood--a genetic study of comorbidity. *Journal of Child Psychology and Psychiatry*. 1997; 38:651–656.10.1111/j.1469-7610.1997.tb01692.x [PubMed: 9315975]
- Thibodeau R, Jorgensen RS, Kim S. Depression, anxiety, and resting frontal asymmetry: A meta-analytic review. *Journal of Abnormal Psychology*. 2006; 115:715–729.10.1037/0021-843X.115.4.715 [PubMed: 17100529]

- Tillfors M, El-Khoury B, Stein MB, Trost K. Relationships between social anxiety, depressive symptoms, and antisocial behaviors: Evidence from a prospective study of adolescent boys. *Journal of Anxiety Disorders*. 2009; 23:718–724.10.1016/j.janxdis.2009.02.011 [PubMed: 19304451]
- Tompkins TL, Hockett AR, Abraibesh N, Witt JL. A closer look at rumination: Gender, coping, peer functioning and internalizing/externalizing problems. *Journal Of Adolescence*. 2011; 34:801–811.10.1016/j.adolescence.2011.02.005 [PubMed: 21411134]
- Treatment for Adolescents with Depression Study (TADS) Team. Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression: Treatment for Adolescents with Depression Study (TADS) randomized controlled trial. *Journal of the American Medical Association*. 2004; 292:807–820.10.1001/jama.292.7.807 [PubMed: 15315995]
- Trosper SE, Whitton SW, Brown TA, Pincus DB. Understanding the latent structure of the emotional disorders in children and adolescents. *Journal of Abnormal Child Psychology*. 2012; 40:621–632.10.1007/s10802-011-9582-7 [PubMed: 22006349]
- Tully PJ, Zajac IT, Venning AJ. The structure of anxiety and depression in a normative sample of younger and older Australian adolescents. *Journal of Abnormal Child Psychology*. 2009; 37:717–726.10.1007/s10802-009-9306-4 [PubMed: 19238534]
- Turner CM, Barrett PM. Does age play a role in anxiety and depression in children and youths? An investigation of the tripartite model in three age cohorts. *Journal of Consulting and Clinical Psychology*. 2003; 71:826–833.10.1037/0022-006X.71.4.826 [PubMed: 12924688]
- Väänänen J, Fröjd S, Ranta K, Marttunen M, Helminen M, Kaltiala-Heino R. Relationship between social phobia and depression differs between boys and girls in mid-adolescence. *Journal of Affective Disorders*. 2011; 133:97–104.10.1016/j.jad.2011.03.036 [PubMed: 21497912]
- Van Voorhees BW, Melkonian S, Marko M, Humensky J, Fogel J. Adolescents in primary care with subthreshold depressed mood screened for participation in a depression prevention study: Comorbidity and factors associated with depressive symptoms. *The Open Psychiatry Journal*. 2010; 4:10–18.10.2174/1874354401004010010 [PubMed: 23795221]
- Verduin TL, Kendall PC. Differential occurrence of comorbidity within childhood anxiety disorders. *Journal of Clinical Child and Adolescent Psychology*. 2003; 32:290–295.10.1207/S15374424JCCP3202_15 [PubMed: 12679288]
- Verhagen M, van der Meij A, Janzing JGE, Arias-Vásquez A, Buitelaar JK, Franke B. Effect of the 5-HTTLPR polymorphism in the serotonin transporter gene on major depressive disorder and related comorbid disorders. *Psychiatric Genetics*. 2009; 19:39–44.10.1097/YPG.0b013e3283208061 [PubMed: 19125107]
- Vostanis P, Feehan C, Grattan E. Two-year outcome of children treated for depression. *European Child & Adolescent Psychiatry*. 1998; 7:12–18.10.1007/s007870050039 [PubMed: 9563808]
- Walkup JT, Albano A, Piacentini J, Birmaher B, Compton SN, Sherrill JT, Kendall PC. Cognitive behavioral therapy, sertraline, or a combination in childhood anxiety. *The New England Journal of Medicine*. 2008; 359:2753–2766.10.1056/NEJMoa0804633 [PubMed: 18974308]
- Walkup JT, Labellarte MJ, Riddle MA, Pine D, Greenhill L, Klein R, Roper M. Searching for moderators and mediators of pharmacological treatment effects in children and adolescents with anxiety disorders. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2003; 42:13–21.10.1097/00004583-200301000-00006 [PubMed: 12500072]
- Walton KE, Ormel J, Krueger RF. The dimensional nature of externalizing behaviors in adolescence: Evidence from a direct comparison of categorical, dimensional, and hybrid models. *Journal of Abnormal Child Psychology*. 2011; 39:553–561.10.1007/s10802-010-9478-y [PubMed: 21210204]
- Warren BJ. Depression, stressful life events, social support, and self-esteem in middle class African American women. *Archives of Psychiatric Nursing*. 1997; 11:107–117.10.1016/S0883-9417(97)80033-7 [PubMed: 9193115]
- Watson D. Rethinking the mood and anxiety disorders: A quantitative hierarchical model for DSM-V. *Journal of Abnormal Psychology*. 2005; 114:522–36.10.1037/0021-843X.114.4.522 [PubMed: 16351375]

- Watson D. Differentiating the mood and anxiety disorders: A quadripartite model. *Annual Review of Clinical Psychology*. 2009; 5:221–247.10.1146/annurev.clinpsy.032408.153510
- Watson D, Clark LA, Carey G. Positive and negative affectivity and their relation to anxiety and depressive disorders. *Journal of Abnormal Psychology*. 1988; 97:346–353.10.1037/0021-843X.97.3.346 [PubMed: 3192830]
- Watts SE, Weems CF. Associations among selective attention, memory bias, cognitive errors and symptoms of anxiety in youth. *Journal of Abnormal Child Psychology*. 2006; 34:841–852.10.1007/s10802-006-9066-3 [PubMed: 17051435]
- Weems CF, Zakem AH, Costa NM, Cannon MF, Watts SE. Physiological response and childhood anxiety: Association with symptoms of anxiety disorders and cognitive bias. *Journal of Clinical Child and Adolescent Psychology*. 2005; 34:712–723.10.1207/s15374424jccp3404_13 [PubMed: 16232068]
- Weissman MM, Wolk S, Wickramaratne P, Goldstein RB, Adams P, Greenwald S, Steinberg D. Children with prepubertal-onset major depressive disorder and anxiety grown up. *Archives Of General Psychiatry*. 1999; 56:794–801.10.1001/archpsyc.56.9.794 [PubMed: 12884885]
- Weisz JR, McCarty CA, Valeri SM. Effects of psychotherapy for depression in children and adolescents: A meta-analysis. *Psychological Bulletin*. 2006; 132:132–149.10.1037/0033-2909.132.1.132 [PubMed: 16435960]
- Williamson DE, Forbes EE, Dahl RE, Ryan ND. A genetic epidemiologic perspective on comorbidity of depression and anxiety. *Child and Adolescent Psychiatric Clinics of North America*. 2005; 14:707–26.10.1016/j.chc.2005.05.007 [PubMed: 16171699]
- Wilson JK, Rapee RM. The interpretation of negative social events in social phobia with versus without comorbid mood disorder. *Journal of Anxiety Disorders*. 2005; 19:245–274.10.1016/j.janxdis.2004.03.003 [PubMed: 15686856]
- Wood JJ, Piacentini JC, Bergman RL, McCracken J, Barrios V. Concurrent validity of the anxiety disorders section of the Anxiety Disorders Interview Schedule for DSM-IV: Child and parent versions. *Journal of Clinical Child and Adolescent Psychology*. 2002; 31:335–342.10.1207/S15374424JCCP3103_05 [PubMed: 12149971]
- Woodward LJ, Fergusson DM. Life course outcomes of young people with anxiety disorders in adolescence. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2001; 40:1086–1093.10.1097/00004583-200109000-00018 [PubMed: 11556633]
- Wright M, Banerjee R, Hoek W, Rieffe C, Novin S. Depression and social anxiety in children: Differential links with coping strategies. *Journal of Abnormal Child Psychology*. 2010; 38:405–19.10.1007/s10802-009-9375-4 [PubMed: 20012184]
- Yorbik O, Birmaher B, Axelson D, Williamson DE, Ryan ND. Clinical characteristics of depressive symptoms in children and adolescents with major depressive disorder. *Journal of Clinical Psychiatry*. 2004; 65:1654–1659.10.4088/JCP.v65n1210 [PubMed: 15641870]
- Young JF, Makover HB, Cohen JR, Mufson L, Gallop RJ, Benas JS. Interpersonal Psychotherapy-Adolescent Skills Training: Anxiety outcomes and impact of comorbidity. *Journal of Clinical Child and Adolescent Psychology*. 2012; 41:640–653.10.1080/15374416.2012.705843 [PubMed: 22891881]
- Young, JF.; Mufson, L. *Manual for Interpersonal Psychotherapy-Adolescent Skills Training (IPT-AST)*. New York: Columbia University; 2003.
- Young JF, Mufson L, Davies M. Impact of comorbid anxiety in an effectiveness study of interpersonal psychotherapy for depressed adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2006; 45:904–912.10.1097/01.chi.0000222791.23927.5f [PubMed: 16865032]
- Zahn-Waxler, C.; Crick, NR.; Shirtcliff, EA.; Woods, KE. The origins and development of psychopathology in females and males. In: Cicchetti, D.; Cohen, DJ., editors. *Developmental psychopathology, Vol 1: Theory and method. 2*. Hoboken, NJ: John Wiley & Sons Inc; 2006. p. 76-138.
- Zahn-Waxler C, Klimes-Dougan B, Slattery MJ. Internalizing problems of childhood and adolescence: Prospects, pitfalls, and progress in understanding the development of anxiety and depression.

Development and Psychopathology. 2000; 12:443–466.10.1017/S0954579400003102 [PubMed: 11014747]

Zahn-Waxler C, Shirtcliff EA, Marceau K. Disorders of childhood and adolescence: Gender and psychopathology. Annual Review of Clinical Psychology. 2008; 4:275–303.10.1146/annurev.clinpsy.3.022806.091358

Zbozinek TD, Rose RD, Wolitzky-Taylor KB, Sherbourne C, Sullivan G, Stein MB, Craske MG. Diagnostic overlap of generalized anxiety disorder and major depressive disorder in a primary care sample. Depression and Anxiety. 2012; 29:1065–1071.10.1002/da.22026 [PubMed: 23184657]

Zinbarg, RE.; Yoon, K. RST and clinical disorders: Anxiety and depression. In: Corr, P.J., editor. The reinforcement sensitivity theory of personality. New York, NY: Cambridge University Press; 2008. p. 360-397.

Zlotnick C, Donaldson D, Spirito A, Pearlstein T. Affect regulation and suicide attempts in adolescent inpatients. Journal of the American Academy of Child and Adolescent Psychiatry. 1997; 36:793–798.10.1097/00004583-199706000-00016 [PubMed: 9183134]

Table 1

Key Findings and Areas for Future Research Regarding Comorbid Depression and Anxiety in Youth

Topic	Current Theories/Hypotheses/Models	Key Points	Recommended Research Agenda
Nature of comorbidity	Comorbid anxiety-depression is typically worse than anxiety alone but not worse than depression alone	Comorbid depression in anxiety samples is less common than comorbid anxiety in depressed samples Among comorbid youth, severely depressed youth demonstrate severe anxiety whereas severely anxious youth may not necessarily exhibit severe depression Comorbid youth are more impaired than purely anxious youth but no more impaired than purely depressed youth Comorbid depression may interfere with CBT for anxiety but comorbid anxiety does not consistently interfere with CBT for depression	Address the nature of depressive comorbidity across ages, and in specific anxiety disorders
Theoretical models	Tripartite Model: NA is responsible for anxiety-depression comorbidity	Some studies support NA as a shared general distress factor (NA) in anxiety and depression PH and PA may not be specific to anxiety and depression, respectively PH may be linked to panic disorder Support for the Tripartite Model is inconsistent across developmental levels Variance explained by NA differs across anxiety disorders	Examine applicability of NA, PA, and PH across ages, and in specific anxiety disorders
SAD and depression	BIS/BAS: BIS responsible for anxiety-depression comorbidity SAD increases the risk of depression through common vulnerabilities and/or SAD-related impairment	High BIS related to anxiety Low BAS related to depression and may reflect anhedonia, explaining mixed findings BIS may also be related to depression SAD has genetic links to panic, and depression is often present in youth with panic disorder SAD is related to parental depression	Consider prevention informed by behavioral inhibition in young children Longitudinal studies that span the timeframe within which SAD and depression emerge Specifically address and examine panic disorder Determine if SAD is associated with onset of depression in the short run as a result of SAD-related impairment
SoP and depression	SoP-related impairment leads to comorbid depression, particularly in adolescence due to heightened importance of peers	SoP more commonly onsets before depression than vice versa Core risk factors (e.g., genetics) interact with interpersonal risk factors (e.g., loneliness), leading to depression among SoP youth Interpersonal risk factors with research support include peer alienation, peer victimization, avoidance of expressing emotion, and poor friendship quality	Identify SoP before depression, and the potential of secondary prevention Examine symptom levels of both disorders Delineate interpersonal factors that link SoP and depression
GAD and depression	GAD and depression are highly related but separate disorders	GAD and MDD share genetic risk factors to a greater extent than with other anxiety disorders GAD and MDD cross-predict each other more strongly than each disorder predicts itself over time MDD and GAD do not reliably respond to the same medications Stressful life events are more strongly related to MDD than to GAD High GAD-MDD comorbidity may be due to symptom overlap in the diagnostic criteria	Investigate where comorbidity is an artifact of the diagnostic criteria Investigate criteria that distinguish the two disorders Identify and study cases where GAD does not lead to depression and vice versa

Topic	Current Theories/Hypotheses/Models	Key Points	Recommended Research Agenda
Gender differences	Gender differences in cognitive style and relationship processes increase risk for both depression and anxiety Depression symptoms may differ by gender, with girls showing more symptoms (e.g., somatic) that overlap with anxiety	Depression more prevalent among adolescent girls than boys Anxiety is more prevalent among girls than boys in community samples, but comparable in diagnosed samples Rumination is more common among girls than boys and is associated with anxiety, depression, and comorbid anxiety-depression Depression may develop secondary to anxiety in boys	Use multi-informant approaches to lessen the impact of social desirability Given differences, consider gender more specifically in treatment approaches Observational studies to inform hypothesis-driven research
Suicidality	Suicidality in anxious youth is a result of comorbid depressive symptoms	Increased rate of suicidality among depressed youth; findings among anxious youth are mixed Other constructs related to anxiety and depression (e.g., emotion dysregulation, distress tolerance) may explain increased suicidality in anxious youth	Differentiate across components/types of suicidality Examine associations of suicidality with specific anxiety disorders Consider the possibility that suicidality reported by anxious youth without depression may reflect intrusive thoughts

Note: CBT = cognitive behavioral therapy; NA = negative affect; PA = positive affect; PH = physiological hyperarousal; BIS = behavioral inhibition system; BAS = behavioral activation system; MDD = major depressive disorder; SAD = separation anxiety disorder; SoP = social phobia; GAD = generalized anxiety disorder.