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The co-occurrence of attention-deficit/hyperactivity disorder and unipolar depression in children and adolescents: A meta-analytic review

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HIGHLIGHTS

- ADHD and depression were positively related, but substantial variability existed across the studies.
- Few studies have examined potential mediators of the association between ADHD and depression.
- Clinicians should routinely screen for depressive symptoms among individuals with a history of ADHD.
- Tailored depression preventive efforts for ADHD youth and maintenance treatment of ADHD may reduce the risk of depression.

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ABSTRACT

This paper reviews the empirical literature on the association between attention-deficit/hyperactivity disorder (ADHD) and depression (i.e., unipolar depressive disorders and symptoms) among children and adolescents. Findings from cross-sectional and longitudinal studies published on the co-occurrence of ADHD and depression were summarized and subjected to a meta-analysis. Results ($k = 29$, $N = 8755$; rbar $= 0.22$) indicated that ADHD and depression were positively related, but substantial variability existed across the studies. Subgroup analyses indicated medium positive effects for cross-sectional studies, studies that operationalized ADHD based on *DSM-III* or *DSM-IV* diagnostic criteria, and studies that did not include teacher report in the assessment of ADHD. Subgroup analyses showed a large positive effect for studies that operationalized ADHD based on *DSM-III-R* criteria and studies using clinic referred samples. In contrast, subgroup analyses indicated a small negative and/or unreliable association between ADHD and depression for longitudinal studies, studies using *DSM-II* diagnostic criteria for hyperkinetic reaction of childhood or used a dichotomous motor hyperactivity criterion, studies that used nonreferred samples, and studies including teacher report in the assessment of ADHD. When studies that used *DSM-II* diagnostic criteria were removed, a reliable medium effect was found for studies that included teacher report. Similarly when the study that used idiosyncratic methods of diagnosing ADHD was excluded, a reliable medium effect was found for studies that used nonreferred samples. Potential explanations for the findings are discussed, including explanations based on sampling and base rates, artifacts of diagnostic criteria, inaccurate diagnostic boundaries, and etiological relationships. Directions for future research and clinical implications are discussed.

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1. Introduction

Attention deficit/hyperactivity disorder (ADHD) affects up to 9% of children (Centers for Disease Control, 2010). Although ADHD was once considered to be a disorder limited to childhood, research indicates that approximately 70% of children diagnosed with ADHD continue to meet diagnostic criteria into adolescence and an additional 17% display substantial impairment without meeting full criteria for a diagnosis of ADHD (Biederman, Petty, Clarke, Lomedico, & Faraone, 2011; Mannuzza, Klein, Bessler, Malloy, & Lapadula, 1993; Sibley et al., 2012). The impairment and risks associated with persistent ADHD are evident in high rates of academic failure, delinquency, substance abuse, automobile accidents, and risky sexual behavior (Flory, Molina, Pelham, Gnagy, & Smith, 2006; Kuriyan et al., 2013; Lee, Humphreys, Flory, Liu, & Glass, 2011; Sibley et al., 2011; Thompson, Molina, Pelham, & Gnagy, 2007). Children with ADHD also display higher rates of co-occurring psychiatric disorders, including unipolar depressive disorders, than would be expected by chance (Blackman, Ostrander, & Herman, 2005; Busch et al., 2002). In the remainder of this review, the term "depression" is used in reference to unipolar depressive disorders or subthreshold depressive symptoms, not bipolar disorders.

Unipolar depression, including major depressive disorder (MDD), affects approximately 1–2% of children (Costello et al., 1996; Kashani & Simonds, 1979) and 4–24% of adolescents (Lewinsohn, Hops, Roberts, Seeley, & Andrews, 1993; Whitaker et al., 1990). Depression in childhood and adolescence is associated with high rates of co-occurring anxiety disorders, disruptive behavior disorders, and substance use disorders (Lewinsohn et al., 1993; Simonoff et al., 1997) and with impairments in academic performance, peer relationships, and family relationships (Garber & Horowitz, 2002). Depression during childhood and adolescence also predicts negative outcomes in adulthood including stressful life events, low social support, and low life satisfaction (Franko et al., 2005; Gotlib, Lewinsohn, & Seeley, 1998; Rao et al., 1995). Children and adolescents with co-occurring ADHD and depression experience more impairment than individuals with either disorder in isolation (Biederman, Mick, & Faraone, 1998; Biederman, Newcorn, & Sprich, 1991; Biederman et al., 2008; Chronis-Tuscano et al., 2010).

A large number of empirical studies on the co-occurrence of ADHD and depression in children and adolescents have been published. These studies have used different sampling strategies and methodologies and have reported mixed findings on the association between ADHD and depression. For example, studies have used longitudinal (e.g., Biederman et al., 2008) or cross-sectional (e.g., Ostrander, Crystal, & August, 2006) designs, clinic referred (e.g., Busch et al., 2002) or community (e.g., Fergusson, Boden, & Horwood, 2010) samples, and diagnostic interviews (Chronis-Tuscano et al., 2010) or dimensional parent rating scales (e.g., Fischer, Barkley, Smallish, & Fletcher, 2002) to assess ADHD. Findings have ranged from no significant association between measures of ADHD and depression (e.g., Mannuzza, Klein, Bessler, Malloy, & LaPadula, 1998) to significant small (e.g., Fergusson et al., 2010), medium (e.g., Smalley et al., 2007), or large (Biederman et al., 2008) associations between measures of ADHD and depression. The heterogeneity of methodologies and findings from past studies makes it challenging to draw conclusions about the associations between ADHD and depression.

To our knowledge, two relevant previous reviews have been published. Biederman et al. (1991) provided a narrative review on the co-occurrence of ADHD, mood disorders, anxiety disorders, oppositional defiant disorder, conduct disorder, and learning disorders. They concluded that a majority of studies using clinical samples reported statistically significant associations between ADHD and mood disorders and that these associations were not artifactual. Daviss (2008) provided a narrative review of pharmacological treatment studies among adolescents with co-occurring ADHD and depression. Many studies on the co-occurrence of ADHD and depression have been published since the Biederman et al. (1991) review. Further, we are aware of no published quantitative or meta-analytic review of the association between ADHD and depression in children and adolescence.

In an effort to bring clarity to this complicated literature, we conducted the first meta-analysis on the association between ADHD and depression in children and adolescents, including their co-occurrence on a diagnostic level and their covariance on a symptom severity level. We first evaluated the size of the association between ADHD and depression. We then conducted subgroup analyses to examine the size of the association between ADHD and depression for specific domains, including studies using cross-sectional designs and longitudinal designs, studies operationalizing ADHD and depression using different editions of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*), studies that used teacher report of ADHD and studies that did not, and studies using clinic referred samples and nonreferred samples.

Studies were dichotomized by study design (i.e., cross-sectional or longitudinal) to evaluate the size of the concurrent association and the prospective association between ADHD and depression. Given the diverse methodology for measuring ADHD and the differences between diagnostic criteria across editions of the *DSM*, ADHD diagnostic criteria were also chosen as a variable for subgroup analyses. Studies were dichotomized by the sample type (i.e., clinic referred or non-referred) to examine the size of the relationship between ADHD and depression in referred samples (in which comorbidity estimates tend to be inflated) and non-referred samples. Lastly, studies were categorized based on diagnostic complexity (i.e., whether or not they included teacher report of symptoms in the assessment of ADHD). This subgroup analysis was chosen to determine whether number and setting of informant sources for assessing ADHD influenced effect sizes. We hypothesized an overall positive association between ADHD and depression, and similar positive effects for all subgroup analyses with the exception of subgroups that used early editions of the *DSM* to diagnose ADHD

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