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Review

An update on the debated association between ADHD and bipolar disorder across the lifespan

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ABSTRACT

Diagnostic formulations for attention deficit hyperactivity disorder (ADHD) and bipolar disorder (BD) both include symptoms of distractibility, psychomotor agitation and talkativeness, alongside associated emotional features (irritability and emotional lability). Treatment studies suggest the importance of accurate delineation of ADHD and BD. However, boundaries between the two disorders are blurred by the introduction of broader conceptualisations of BD. This review attempts to elucidate whether associations between ADHD and BD are likely to be driven by superficial symptomatological similarities or by a more meaningful etiological relationship between the disorders. This is achieved by outlining findings on comorbidity, temporal progression of the disorders, familial co-variation, and neurobiology in ADHD and BD across the lifespan. Longitudinal studies fail to consistently show developmental trajectories between ADHD and BD. Comparative research investigating neurobiology is in its infancy, and although some similarities are seen between ADHD and BD, studies also emphasise differences between the two disorders. However, comorbidity and family studies appear to show that the two disorders occur together and aggregate in families at higher than expected rates. Furthermore close inspection of results from population studies reveals heightened co-occurrence of ADHD and BD even in the context of high comorbidity commonly noted in psychopathology. These results point towards a meaningful association between ADHD and BD, going beyond symptomatic similarities. However, future research needs to account for heterogeneity of BD, making clear distinctions between classical episodic forms of BD, and broader conceptualisations of the disorder characterised by irritability and emotional lability, when evaluating the relationship with ADHD.

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1. Introduction

There is a longstanding debate regarding the diagnostic differentiation of mania, the distinctive feature of bipolar disorder (BD), from attention deficit hyperactivity disorder (ADHD). The crux of the debate centres on the presentation of ADHD-like symptoms alongside chronic irritability, aggression and mood lability. Whether this represents ADHD, BD, their co-occurrence, or a distinct psychiatric disorder, remains controversial even amongst clinical experts.

Current psychiatric nosology aims to demarcate syndromes, defined by distinct clusters of signs and symptoms, and predictive of clinical parameters such as course, outcome and treatment response (Farmer et al., 2002). However, in practise there are often similarities between symptoms and syndromes across diagnostic boundaries. For example, Caron and Rutter (1991), note that non-specific symptoms such as poor concentration, restlessness, anxiety and depressed mood are also hallmarks of specific diagnostic entities. High comorbidity rates are a widespread phenomenon in psychiatric research, even in non-referred community samples (De Graaf et al., 2012; Kessler et al., 1994, 2005b; Weich et al., 2011). In the context of symptomatology that does not differentiate between one disorder and another, this raises the question of whether associations between any two psychiatric disorders are likely to be meaningful, or whether they reflect more general problems such as poor diagnostic delineation or common risk factors for psychiatric illness.

The purpose of this paper is to evaluate the available evidence on the association between ADHD and BD. To provide a framework for delineating between ADHD and BD, we adopt classical diagnostic validators (Robins and Guze, 1970), including: (i) clinical description, (ii) delimitation from other disorders, (iii) longitudinal course, (iv) family clinical characteristics, and (v) laboratory study of the underlying biology (including aspects of neurobiology, chemical, physiological and anatomical findings and cognitive tests).

We begin by presenting a detailed account of the main clinical features of both disorders, outlining the diagnostic similarities between ADHD and mania, considering the implications for treatment, and describing alternative approaches to the diagnostic criteria and their implications. We then attempt to elucidate whether the relationship seen between ADHD and BD is an artifactual one, driven by overlap in operationally defined clinical symptom checklists, or whether it reflects a meaningful relationship between the diagnostic entities. This is guided by the framework outlined above and is achieved by considering: (i) clinical features which are common to, or distinct features of BD and ADHD (ii) rates of comorbidity and comparison of comorbidity rates with other common psychiatric conditions, (iii) longitudinal course, (iv) evidence for the familial covariation of ADHD and BD, and (v) neurobiological research carried out comparing ADHD and BD.

As noted by Vella et al. (2000, p. 25) comorbidity should be defined as "two or more diseases, with distinct aetiopathogenesis (or, if the etiology is unknown, with distinct pathophysiology of organ or system), that are present in the same individual in a defined period of time." The important consideration in the assessment of comorbidity, or other syndromatic relationships, is therefore that each 'disease' must make a *distinct* contribution to the clinical presentation of the individual. Although, a breadth of literature is reviewed here, we base our conclusions on contrasts between ADHD and more conservatively defined BD, specifically BD-I, where episodicity of symptoms are most extreme, and clearest distinctions can be made between the two disorders. To promote consistency this review focuses on the DSM-IV criteria for BD and ADHD, while taking into account alternative definitions of BD.

2. Clinical features of ADHD and BD

ADHD is a childhood onset disorder, characterised by developmentally inappropriate and impairing levels of overactivity, impulsivity and inattention. Worldwide prevalence of childhood ADHD is approximately 5% (Polanczyk et al., 2007). Meta-analysis of longitudinal studies of children with ADHD confirms the continuity of ADHD symptoms and impairment into adulthood in around two-thirds of cases (Faraone et al., 2006). Prevalence of DSM-IV ADHD in adults is currently estimated at 2.5–4.3% (Kessler et al., 2006; Simon et al., 2009).

BD is traditionally conceptualised as a disorder of adulthood, with a lifetime prevalence of approximately 2% (Merikangas et al., 2007, 2011). Individuals with typical BD experience episodes of mania (e.g. abnormally expansive, elated or irritable mood) and depression (e.g. pervasive and persistent low mood and/or a profound loss of interest and pleasure), with the first manic episode in BD occurring by age 25 years in around 50% of cases, as measured by retrospective report (Kessler et al., 2005a). However, BD is now relatively frequently diagnosed in childhood and adolescence (Moreno et al., 2007). It should be