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Review

Symptoms and signs of the initial prodrome of bipolar disorder A systematic review

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ABSTRACT

Background: Systematic studies addressing symptoms, signs and temporal aspects of initial bipolar prodrome are reviewed to identify potential clinical targets for early intervention. Methods: The databases PsycINFO, PubMed, EMBASE and British Nursing Index were searched for original studies.

Results: Eight studies were identified. Irritability and aggressiveness, sleep disturbances, depression and mania symptoms/signs, hyperactivity, anxiety, and mood swings are clusters representing common symptoms and signs of the distal prodrome of bipolar disorder (BD). As time to full BD onset decreases, symptoms of mania and depression seem to increase gradually in strength and prevalence. The specificity of prodromal symptoms and signs appears to be low. Not every person who develops BD experiences a prolonged initial prodrome to the full illness. Current data on the mean duration of the prodrome are contradictory, ranging from 1.8 to 7.3 years. No qualitative studies were found.

Limitations: Because of the scarcity of data, studies that did not explicitly investigate bipolar prodrome were included when thematically relevant. The selected studies are methodologically diverse and the validity of some findings is questionable. Findings must be interpreted cautiously.

Conclusions: The initial prodrome of BD is characterized by dysregulation of mood and energy. Because of the apparently low specificity of prodromal symptoms and signs of BD, it is currently neither possible nor advisable to predict the development of BD based solely on early phenomenology. More well-designed in-depth studies, including qualitative ones, are needed to characterize the initial bipolar prodrome.

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1. Introduction

Bipolar disorder (BD) is a chronic and potentially debilitating illness. Approximately 60% of patients with BD experience onset before the end of their teens (Hirschfeld et al., 2003; Lish et al., 1994; Morken et al., 2009; Oedegaard et al., 2009; Perlis et al., 2004; Post et al., 2008), usually between age 15 and 19 (Goodwin and Jamison, 2007; Merikangas et al., 2007). Hence, people who develop BD are often afflicted during their most vulnerable and formative years. Adding to the burden is the lag of up to 10 years between illness onset and receiving a correct diagnosis (Hirschfeld et al., 2003; Suppes et al., 2001).

Untreated BD results in more episodes, severer episodes, and rapid cycling, which in turn may make effective treatment more difficult and perhaps result in neurological alterations ("kindling" effects) that may impair the prognosis (Post, 1992; Post et al., 1996). Thus, it may prove beneficial to investigate the possibility of detecting BD prior to full illness onset. Early interventions may prevent the development of the full disorder, or at least improve the outcome.

The aim of the present paper is to review the current status of knowledge on symptoms, signs and temporal aspects of the initial prodrome of BD. The initial prodrome may be defined as the time interval from the onset of the first noticeable symptoms and signs that deviate from a relatively stable or normal state of being, to the onset of a fully developed and

diagnosable disorder. The distal and proximal prodromes denominate the early and late stages of the initial prodrome, respectively. However, currently there is no consensus on how to define a bipolar prodrome. Various options are discussed in this paper. In contrast to recent reviews (Conus et al., 2008; Correll et al., 2007b), this review focuses exclusively on studies that address symptoms and signs of the initial prodrome of subjects diagnosed with BD. The following research questions are addressed. 1) Are there symptoms and signs that characterize the distal prodrome of BD? 2) Is there a developmental progression of symptoms and signs throughout the prodrome? 3) How specific to BD are the prodromal symptoms and signs? 4) Are there any differences in prodromal expressions between subtypes of BD? 5) Are there any differences in prodromal expressions associated with age at full BD onset? 6) Are there any differences in prodromal expressions associated with presence or absence of a family history of BD? 7) How common is it to experience a prolonged prodromal phase? 8) What is the typical duration of the prodrome?

2. Methods

2.1. Study acquisition

The databases PsycINFO (from 1806 to January 2009), PubMed (from 1950 to January 2009), EMBASE (from 1980 to January 2009), and British Nursing Index (from 1985 to

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