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Brief report

Genuine clinical predictors of bipolar II disorder: An exploration of temporal and contextual characteristics

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ABSTRACT

Background: Symptoms of the initial prodrome of bipolar disorder (BD) are too nonspecific to reliably prospectively predict BD. An assessment of symptoms' temporal and contextual characteristics may help identify clinical indicators with enhanced predictive power.
Methods: Fifteen bipolar II disorder (BD-II) patients and 22 family members were interviewed about characteristics of symptoms that emerged before the first major affective episode (FMAE). The textual data of transcribed interviews were analyzed utilizing qualitative methodology. To identify genuine clinical predictors (GCPs), we outlined three alternative definitions and investigated the extent to which the reported symptoms in different symptom categories survived successively narrower inclusion criteria.
Results: Most of the reported symptom instances met the broadest GCP criteria as episodic or chronic. "Mood swings" and "irritability/aggressiveness" were the only symptom categories in which most of the reported symptom instances met our intermediate strict criteria as episodic/chronic, and exaggerated/inexplicable. The mood swings were mainly characterized as episodic and occurred for no apparent reason; conversely, irritability and aggressiveness were typically characterized as episodic and exaggerated responses to life events.
Limitations: This is a retrospective and hypothesis-generating study.
Conclusions: Recurrent mood swings and irritability/aggressiveness are characterized as inexplicable and exaggerated responses, respectively, and may be the most prominent genuine clinical predictors of the FMAE of BD-II. Future studies need to investigate the extent to which the presence of different characteristics of the same symptoms discriminate between individuals who later develop BD and those who do not.

1. Introduction

Knowledge of symptoms and signs of the initial prodrome of bipolar disorders (BD) may facilitate early identification and may enable early intervention (Skjelstad et al., 2010). Subthreshold affective symptoms, general psychiatric symptoms, and to a lesser degree psychotic symptoms are, in retrospect, frequently reported to have occurred before the onset of BD (Carlson et al., 2000; Conus et al., 2010; Correll et al., 2007; Egeland et al., 2000; Faedda et al., 2004; Fergus et al., 2003; Hirschfeld et al., 2003; Lish et al., 1994; Luckenbaugh et al., 2009; Ozgurdal et al., 2009; Rucklidge, 2008). It is questionable whether subthreshold affective symptoms, and especially general psychiatric symptoms, are useful early clinical indicators of a subsequent BD because of their high base rate in the general

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population (Angst et al., 2003; Brand et al., 2010; Carlson et al., 2009; Lewinsohn et al., 2003; Regeer et al., 2006; Tijssen et al., 2010).

Given the apparently low specificity and predictive value of these symptoms, it might prove helpful to explore the existence of certain clinical features, such as temporal patterns of symptoms and contextual influences on symptom onset, which better differentiate symptoms and predict a subsequent BD ("genuine clinical predictors", GCPs). Persistent symptoms (episodic or chronic) may be more likely to be related to the subsequent BD than temporary symptoms that occur only once (Tijssen et al., 2010). Given the episodicity of BD, recurrent symptoms may be potential early manifestations. Whether chronic symptoms should be regarded as GCPs is less self-evident. Chronic symptoms may be manifestations of other mental disorders that precede the BD, such as anxiety disorders, which may or may not be related to the subsequent BD. However, on the basis of findings suggesting that bipolar symptoms often have a more chronic presentation during childhood (e.g., rapid and severe mood cycling and chronic irritability) than from mid-adolescence onwards (Pavuluri et al., 2005), we tentatively regard chronic symptoms as GCPs. Similarly, considering their psychosocial context, symptoms that are exaggerated or inexplicable may predict an upcoming BD better than appropriate ("normal") responses to life events. Exaggerated responses might be manifestations of an underlying and possibly biological impairment or immaturity of a mood-regulating system that may be associated with the mood dysregulation characteristic of BD. Similarly, inexplicable responses, which by definition are not elicited by identifiable exogenous factors, might be early expressions of endogenous or biological vulnerability factors of BD that manifest during bipolar episodes. In contrast, normal responses to life events are contingent on and presumably more related to exogenous factors than to the subsequent BD. In sum, we hypothesize that prodromal symptoms characterized as episodic or chronic, and as exaggerated or inexplicable, may be the most genuine and specific predictors of an upcoming BD.

In a previous publication, we reported findings of clinically significant symptoms (and behaviors) before the first major affective episode (FMAE) of bipolar II disorder (BD-II) (Skjelstad et al., 2011). The phenomena were organized into six primary categories (mood swings, depression-type symptoms, mania-type symptoms, anxiety, irritability/aggressiveness, and sleep disturbances) and one residual category (other). In this article, we explore the extent to which the prodromal symptoms included in these categories might be regarded as GCPs.

2. Methods

This project was an exploratory retrospective study that utilized qualitative methodology. The final sample was composed of 15 BD-II (APA, 2000; WHO, 1992) outpatients (11 females and 4 males). The mean age at the FMAE was 15.9 years (3.6; 12.0–23.1). Twenty-two family member informants participated. Each patient had at least one parent participating (see Skjelstad et al., 2011 for more details on the demographic and clinical characteristics of the sample).

Recent clinical BD diagnoses were reassessed and axis I comorbidities were examined via Mini International Neuropsychiatric Interview (Sheehan et al., 1998) or the Schedule for Affective Disorders and Schizophrenia for School-Age Children (Kaufman et al., 1997). Demographic and clinical characteristics were obtained utilizing a modified version of the Stanley Network Entry Questionnaire (Suppes et al., 2001).

A series of in-depth interviews covering the patients' life course from birth to the FMAE was carried out. Typically, the patients were first interviewed alone and then again with family members. The exploration continued in repeated question-and-answer cycles until no new information of significance was obtained.

The interviews were loosely structured to elicit descriptions of clinically significant changes (e.g., symptomatic and behavioral), the context in which the changes took place, how the changes were understood by the participants, and how the symptoms evolved from emergence to the onset of the FMAE. A phenomenon was regarded as present if it was described by either the patient or a family member. When a symptom was recalled by both the patient and family members, they typically reconstructed a narrative and reached a common understanding about the symptom's temporal and contextual characteristics.

Data were analyzed case-by-case and then compared across cases. Audio and video recordings of the interviews were transcribed verbatim. Segments of text were thematically coded and labeled according to the phenomenon being described by the participants (e.g., "intense anger"). The segments of text included descriptions of temporal and contextual aspects of the phenomenon. Codes were then categorized according to common features, such as "irritability and aggressiveness."

In an attempt to disentangle symptoms that were likely to be GCPs, we approached the reported symptoms as follows. First, we coded each symptom according to its temporal presentation in the interim between symptom onset and the onset of the FMAE. Symptoms labeled "*temporary*" were only present for a limited time period and did not reappear before the onset of the FMAE. However, if the same symptom occurred for a limited time period at two contextually independent occasions (e.g., sadness after the parents' divorce at age 4 and again after the grandfather's death at age 10), we regarded it as temporary and only counted it once. Symptoms labeled "*episodic*" were recurrent before the onset of the FMAE. Symptoms labeled "*chronic*" were almost constantly present (e.g., multiple daily mood swings/temper tantrums) or were repeatedly elicited by special situations or circumstances (e.g., the presence of a phobic object). If the temporal characteristic of a symptom changed during the pre-FMAE phase (e.g., chronic mood swings that became episodic), we coded the later characteristic.

Second, symptoms were coded according to whether life events at the time of the symptom onset were recollected by the participants as having precipitated or elicited the symptom. If so, the symptom intensity was coded as appropriate or exaggerated in relation to the life event. Three contextual codes were used. A symptom viewed as an understandable reaction of appropriate intensity in relation to a specific life event (e.g., sadness following parents' divorce) was labeled as a "*normal response*". A symptom assessed as having disproportionally strong intensity in relation to the eliciting life event (e.g., violence toward others when not getting one's way) was labeled as an "*exaggerated response*". A symptom that appeared to be unrelated to the context or to a specific life event, such as the