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Research report

Latent class analysis of manic and depressive symptoms in a population-based sample in São Paulo, Brazil

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ABSTRACT

Background: Current diagnostic criteria cannot capture the full range of bipolar spectrum. This study aims to clarify the natural co-segregation of manic–depressive symptoms occurring in the general population.
Methods: Using data from the Sao Paulo Catchment Area Study, latent class analysis (LCA) was applied to eleven manic and fourteen depressive symptoms assessed through CIDI 1.1 in 1464 subjects from a community-based study in Sao Paulo, Brazil. All manic symptoms were assessed, regardless of presence of euphoria or irritability, and demographics, services used, suicidality and CIDI/DSM-IIIR mood disorders used to external validate the classes.
Results: The four obtained classes were labeled Euthymics (EU; 49.1%), Mild Affectives (MA; 31.1%), Bipolars (BIP; 10.7%), and Depressives (DEP; 9%). BIP and DEP classes represented bipolar and depressive spectra, respectively. Compared to DEP class, BIP exhibited more atypical depressive characteristics (hypersomnia and increase in appetite and/or weight gain), risk of suicide, and use of services. Depressives had rates of atypical symptoms and suicidality comparable to oligosymptomatic MA class subjects.
Limitations: The use of lay interviewers and DSM-IIIR diagnostic criteria, which are more restrictive than the currently used DSM-IV TR.
Conclusions: Findings of high prevalence of bipolar spectrum and of atypical symptoms and suicidality as indicators of bipolarity are of great clinical importance, due to different treatment needs, and higher severity. Lifetime sub-affective and syndromic manic symptoms are clinically significant, arguing for the need of revising DSM bipolar spectrum categories.

1. Introduction

Recent epidemiological data have demonstrated that the lifetime prevalence of bipolar spectrum disorders is high, ranging from 3.5% to 10.9% (Angst et al., 2003; Goodwin and Jamison, 2007). Several subtypes of bipolar spectrum disorders have been proposed (Akiskal and Mallya, 1987; Akiskal and Pinto, 1999; Angst, 1998; Klerman, 1981), together with the interest on the prevalence of bipolar spectrum in the community, including not only the classic bipolar I subtype, but also bipolar II, cyclothymia and minor or subthreshold bipolar disorders not meeting current diagnostic criteria (Angst et al., 2003; Judd and Akiskal, 2003; Merikangas et al., 2007; Moreno and Andrade, 2005). Softer manifestations of bipolar spectrum are difficult to diagnose and are often not adequately treated (Stang et al., 2006), with consequences such as negative social and functional outcomes (Merikangas et al., 2007), and risk of suicide and substance abuse and/or dependence (Angst et al., 2003; Grant et al., 2005).

Bipolar disorder and the bipolar spectrum have been increasingly studied (Angst, 2007; Benazzi, 2007a; Ghaemi, 2008; Hantouche et al., 2006), but along decades depression and the entire depressive spectrum received more attention.

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Searching for subtypes of depression, the natural clusters emergent from the general population have been studied since the 80s, through latent class analyses (LCA) of depressive symptoms in community samples, such as the Epidemiologic Catchment Area study (Eaton et al., 1989), the Virginia twins study (Kendler et al., 1996; Sullivan et al., 2002) and the National Comorbidity Survey (NCS) (Sullivan and Kendler, 1998). The LCA was important in the validation of atypical depression, allowing eliciting categories from underlying latent structures, regardless of strict diagnostic criteria. This is important, among other factors, because of growing data pointing towards the insufficiency of DSM-IV major depressive disorder (MDE) criteria in not separating unipolar from bipolar depressive episodes (Cassano et al., 2004; Forty et al., 2009), which is important, as different treatment strategies should be adopted in each case, due to the risk of mania induction. Moreover, the presence of even minimal manic symptoms in a full-blown depressive episode apparently represents risk factors for the cycling to mania or hypomania (Frye et al., 2009).

More recently the method rendered it possible to study latent factors underlying subtypes of mania in clinical settings, identifying three groups, named "typical mania" (59% of patients), "psychotic mania" (27%), and "dual mania" (13%) with a high proportion of substance abuse (Haro et al., 2006). LCA was also applied to DSM-IV diagnoses of mental disorders in epidemiological samples in the National Comorbidity Survey Replication (NCS-R), yielding 7 clinically meaningful classes, one of which was defined as "highly comorbid bipolar disorder", and represented 0.7% of the sample, but BP was also found in 3 other classes (Kessler et al., 2005). However, there is a lack in the literature of studies considering the full range of depressive and manic symptoms, as proposed by Angst (2009). Skip-out points of structured and semi-structured interviews do not allow the investigation of manic symptoms when an individual denies having had euphoria or irritability in most of population-based studies, being difficult to replicate findings from the Zurich Study (Angst et al., 2003), like, for instance, showing that overactivity is a key symptom in bipolar II subjects.

We have recently reported the lifetime prevalence, use of health services, and associated suicide behaviors of bipolar spectrum in the city of São Paulo, Brazil (Moreno and Andrade, 2005). The weighted lifetime prevalence of the bipolar spectrum groups in this sample was 8.3%, being 1.7% according to strict DSM-IIIR criteria and the remaining 6.6% representing softer "CIDI" manic syndrome criteria, derived from the DSM-IIIR algorithm. Given this high prevalence of bipolar spectrum we have found, we aimed to identify here how the whole CIDI affective symptoms, from depressive to manic, cosegregate in the general population to elicit "natural" boundaries of full bipolar spectrum, through LCA, as it was already studied in the depressive spectrum (Kendler et al., 1996; Sullivan and Kendler, 1998; Sullivan et al., 2002). No study so far applied LCA simultaneously on manic and depressive symptoms in clinical and general population samples.

The purposes of this study are: to use LCA to determine the prevalence and symptom profile of the classes identified, and characterize them in terms of demographical correlates, utilization of health services and suicide behaviors. Also we will examine how obtained classes correlate with the above-mentioned bipolar spectrum groups from the previous report (Moreno and Andrade, 2005).

2. Methods

Data were from the São Paulo Catchment Area Study, a household survey conducted in two boroughs in the city of São Paulo, Brazil (Andrade et al., 2002). Eligible respondents included non-institutionalized adults aged 18 years old or older, with an oversampling of persons aged 18–24 years. One thousand nine hundred six people were selected to participate, of which 442 individuals refused, resulting in a final sample of 1464 subjects, with an individual response rate of 76.8%. Face-to-face interviews were conducted in 1995, using the Brazilian version of the Composite International Diagnostic Interview (CIDI), version 1.1 (Miranda et al., 1990; Wittchen, 1994). Prior to starting the CIDI interview, and hence without the influence of the questions on psychopathological symptoms, all subjects answered a questionnaire about general health status, and use of health care services in the 30 days prior to the interview, including both private and public health systems.

Twenty-nine subjects were excluded from the present analysis, due to incomplete data and latent class analysis was performed in manic–depressive symptoms from 1435 subjects. LCA was applied to 17 depressive and 11 manic lifetime symptoms of the CIDI 1.1 version, in which manic symptoms are considered present when the duration is $\geq$2 days, and depressive symptoms when they last at least 2 weeks. Every manic or depressive symptom was asked during interview, even if the respondent had denied symptoms assessed in stem questions. Symptoms were assessed for a lifetime episode, usually the most severe. As our aim was to determine the co-segregation of manic–depressive symptoms, independently of the cause attributed by interviewer or subject, symptoms were considered present even if rated as due to medical condition or substance use. The exception was the symptom grandiosity, rated positive when subjects described special gifts or powers (i.e., delusional grandiosity) and still rated as positive when considered "plausible" by the lay interviewer.

The 27 CIDI depressive symptoms (of a total 31) were grouped together in 17 variables (Table 1). Four depressive symptoms used for the characterization of dysthymia were excluded, but "depressed for at least 2 years" retained, and this variable was named "chronicity". Symptoms about appetite/weight, psychomotor agitation or retardation, and 4 types of insomnia were disaggregated to create distinct variables. These were separated to determine if and how different sleep disturbances cosegregate within the manic–depressive spectrum. Finally, to characterize suicide behavior, we used 3 variables: ideas of death, suicide ideas, and suicide attempts. Of 12 CIDI manic items, one refers to an example of delusional grandiosity, remaining 11 as distinct variables for LCA (Table 1).

LCA is a statistical method to investigate a correlation among a group of categorical or dichotomous variables (as is the case of CIDI symptoms), and was frequently considered the categorical variant of factor analysis (Neuman et al., 2001). LCA assumes that each observation is a member of