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Research paper

Validation of the Seven Up Seven Down Inventory in bipolar offspring: screening and prediction of mood disorders. Findings from the Dutch Bipolar Offspring Study

E. Mesman[a,*], E.A. Youngstrom[b], N.K. Juliana[a], W.A. Nolen[c], M.H.J. Hillegers[a]

[a] Brain Center Rudolf Magnus, department of Psychiatry, University Medical Center Utrecht, A00.241, PO Box 85500, Utrecht, The Netherlands
[b] Department of Psychology, University of North Carolina at Chapel Hill, Davie Hall, CB 3270, Chapel Hill, USA
[c] Department of Psychiatry, University Medical Center Groningen, University of Groningen, cc11, PO box 30001, 9700 RB Groningen, The Netherlands

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ABSTRACT

Objective: To validate the Seven Up Seven Down (7U7D), an abbreviated version of the General Behavior Inventory (GBI), as screener for mood disorders and test its ability to predict mood disorders over time in individuals at risk for bipolar disorder (BD).
Methods: Bipolar offspring (*n*=108) were followed from adolescence into adulthood and assessed at baseline, 1-, 5- and 12 years follow-up (T1-T4 respectively). Offspring were assessed using the Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime Version, Structured Clinical Interview for DSM-IV Axis I Disorders and the GBI.
Results: Performance of the GBI and 7U7D was functionally similar for the depression (7D) scale, but variable for the mania (7U) scale. As screener for mood disorders (T4), the 7D showed fair diagnostic efficiency (area under the curve (AUC) 0.68, $p < 0.01$, OR 1.53, 95% CI 1.15–2.03). The discriminative validity for BD and unipolar disorder was only close to significant (7D AUC 0.66, p=0.078; 7U AUC 0.67, p=0.067). In terms of prediction of mood disorder onset between T1 and T4, the 7D, but not the 7U, was associated with new onset (AUC 0.67, $p < 0.05$; HR 1.14, 95% CI 1.07–1.23). The 7U7D did not achieve significant prediction of BD.
Limitations: Relative small sample size and limited generalizability.
Conclusions: Based on the current study, the 7U7D shows limited potential as screening instrument for mood disorders in bipolar offspring. The clinical utility of the 7U7D needs further exploration for use in clinical and research settings.

1. Introduction

Early recognition of bipolar disorder (BD) remains challenging for clinicians. BD often presents with a (mild) depressive episode during early adolescence/adulthood followed by (hypo)mania years later (e.g. Duffy, 2010; Mesman et al., 2013). The diagnostic delay of BD after the first (hypo)manic episode is on average 5–10 years (Drancourt et al., 2013; Suppes et al., 2001). More importantly, a prolonged duration of unrecognized and thus untreated BD may have serious consequences, including suicide attempts and poorer long-term outcome (Drancourt et al., 2013). Therefore, sound methods for early detection of BD, and ultimately prediction, are of great value. Screening instruments could be a first important step in assisting clinicians to detect BD in the early phase. Presently, several diagnostic and screening instruments exist to examine past or present mania or depression in adults. However, only a few studies thus far have focused on the most critical stage for age of onset of BD, i.e. between 15 and 25 years or high risk populations such as bipolar offspring (for reviews see Miller et al., 2009; Waugh et al., 2014). Performance of screening instruments in young people differ often from adult populations, and also the type of population matters (e.g. clinical versus non-clinical), and hence with the purpose of early detection critical issues to study (Waugh et al., 2014).

The General Behavior Inventory (GBI) is a validated self-report instrument used to screen for BD in the general population that aims to detect both depressive and hypomanic/manic dimensions of BD (Depue et al., 1989, 1981). The GBI was designed to capture both threshold and subthreshold affective conditions and their fluctuation over time. In the past decades, the GBI has shown its potential as screening instrument for BD in several adult and adolescent populations in the community and clinic (e.g. Danielson et al., 2003; Depue

* Corresponding author.
E-mail address: e.mesman@umcutrecht.nl (E. Mesman).

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et al., 1989, 1981; Findling et al., 2002; Klein et al., 1986, 1985). In a previous study from our group, we have shown in the Dutch Bipolar Offspring Study that the GBI is also of value in high-risk populations and has the potential to screen for mood disorders in bipolar offspring. Moreover, we found that the GBI has potential to detect future BD and other mood disorders; higher scores on the depression scale were significantly associated with the development of mood disorders across 5 years of follow-up (Reichart et al., 2005). Although these findings are meaningful in terms of screening potential and possibly prediction, the GBI's considerable length, with an approximate completion time of 20–40 min, reduces its clinical applicability (Youngstrom et al., 2013).

Youngstrom et al. (2013) recently introduced an abbreviated version of the full-length GBI: the Seven Up Seven Down GBI (7U7D) and validated the inventory for adolescents and adults in the age range 11–86 years. The 7U7D is a 14-item instrument carved from the full-length GBI. Initial findings suggest that the brief 7U7D has good psychometric properties, showing high internal consistency, criterion- and a fair discriminative validity for diagnostic groups (a.o. BD, unipolar depression and ADHD) among clinical and non-clinical samples. Taken together, the 7U7D appears to be a promising screening instrument for BD in adolescents and adulthood. In this study, we aim to test the utility of the 7U7D in a prospectively followed bipolar offspring study. To date, the 7U7D has not been validated in a high risk population for BD nor studied in a longitudinal context. The study has three aims: I) validation of the 7U7D as compared to the full length GBI in a high risk population for mood disorders and BD; II) test the utility of the 7U7D to screen for offspring with lifetime mood disorders and more importantly BD in bipolar offspring; and III) test the capacity of the 7U7D to predict transition to mood disorders and BD during follow-up.

2. Methods

2.1. Population and procedure

Participants originated from the Dutch Bipolar Offspring Study, a prospective study following bipolar offspring from adolescence into adulthood. Details of the study design have been described elsewhere (Wals et al., 2001). Briefly, a total of 140 bipolar offspring (mean age 16.1 years, range 12–21) from 86 families with one parent with BD I or II were recruited between 1997 and 1999 and followed for 12 years. A family was only included if all offspring within the age range 12–21 agreed to participate. Exclusion criteria were a severe physical illness or handicap or an IQ below 70. Participants were recruited through the Dutch Association for Manic Depressives and Relatives (62 families; 102 children) and outpatient clinics in nine psychiatric hospitals (24 families; 38 children). All parents with BD were outpatients at time of recruitment. Offspring were assessed at baseline, and after one, five and 12 years of follow-up (T1, T2, T3 and T4 respectively) (Hillegers et al., 2005; Mesman et al., 2013; Reichart et al., 2004; Wals et al., 2001). One hundred and thirty-two offspring were reassessed at T2, 129 at T3 and 108 at T4, resulting in a retention rate of 77%. There were no statistically significant demographic or clinical differences between the 108 offspring who completed all 12 years of follow-up and the 32 offspring who dropped out (see Mesman et al. (2013) for details). The Medical Ethics Committee of the University Medical Center Utrecht approved the study. Written informed consent was obtained for both the offspring and their parents.

2.2. Instruments

2.2.1. Psychopathology

All psychiatric interviews were administered by intensively trained interviewers with graduate degrees in psychology or by a child and adolescent psychiatrist. All interviews were evaluated by psychiatrists certified in child and adolescent psychiatry as well as adult psychiatry to reach consensus on final diagnoses. At T1 and T2, DSM-IV diagnoses were obtained by a face-to-face interview with both the child and the parent using the Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1996). After offspring reached the age of 18, the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID) (First et al., 1996)replaced the K-SADS-PL. Each psychiatric assessment evaluated current and past symptoms during the interim period. Lifetime DSM-IV diagnoses at T4 were based on the psychiatric interviews that took place during all four assessments. Also the age at onset was documented for all diagnoses. At T4, 72% of the bipolar offspring developed any DSM-IV axis-I disorder, 54% a lifetime mood disorder including 13% bipolar spectrum disorders. For a full description on the lifetime psychopathology, comorbid disorders and demographic characteristics on the 12-years follow-up of the Dutch Bipolar Offspring Study, please see Mesman et al.(2013). Lifetime psychopathology rates are in concordance with findings of other prospective bipolar offspring studies (Axelson et al., 2015; Duffy et al., 2011).

2.2.2. The General Behavior Inventory

At each assessment, participating offspring completed the 73-item GBI self-report. The GBI entails 73 items and comprises a depression-(46 items) and hypomania-/biphasic scale (21 and 7 items respectively, one also scored on the depression scale) (Depue et al., 1989, 1981). Each of the 73 items asks the subject to which extent he/she has experienced the symptom or feeling to which the item alludes. The response set is based on a four-point Likert scale; 0 (hardly ever), 1 (sometimes), 2 (often) and 3 (very often). The GBI has good psychometric properties including internal reliability exceeding .90, test-retest reliabilites of .70 predictive validity and good convergent and discriminant validity.

2.2.3. The Seven Up Seven Down Inventory

The 7U7D was extracted from the original full length GBI according to the work of Youngstrom *et al.* (Youngstrom et al., 2013). The 7U7D follows the same response set as the full length GBI. The seven down (7D) scale and the seven up (7U) reflect the depression and hypomania- and biphasic scale respectively. In the first study on the 7U7D, both the 7D and 7U scale showed adequate psychometric properties with internal reliability exceeding .80 and decent construct and discriminant validity (Youngstrom et al., 2013).

2.3. Data analysis

To address the first two aims of the study, i.e., validation of the 7U7D as compared to the full length GBI and the utility of the 7U7D as screener, cross-sectional data analyses were performed. As we were primarily interested in the use of the GBI/7U7D in relation to BD, we chose to focus on the latest assessment of the Dutch Bipolar Offspring Study (T4) to capture the highest, but still relatively low in absolute numbers, prevalence of BD (n=13). Based upon the psychopathology outcome at T4, participants were assigned into diagnostic outcome categories. Bipolar offspring diagnosed with a mood disorder during the study were assigned to the any mood disorder category, hereafter referred to as *AnyMD*. The *AnyMD* category included major depressive disorder, bipolar spectrum disorders (type I, II, schizoaffective disorder-bipolar type and cyclothymia) and depression not otherwise specified. Offspring without a mood disorder diagnosis during the study, but possibly other diagnoses, were assigned to the *NoMD* category. For more detailed analyses we divided the *AnyMD* category into two more precise categories: bipolar disorder (*BD*) and unipolar mood disorder (*UD*). The *BD* category included all bipolar spectrum disorders as noted above, the *UD* category included all offspring with a diagnosis of major depressive disorder or depression NOS. Finally, offspring without a bipolar spectrum disorder were also assigned to the *NoBD* category. The following a-priori comparisons were planned: a)