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Research report

Data-driven atypical profiles of depressive symptoms: Identification and validation in a large cohort

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ABSTRACT

Background: Atypical response behavior on depression questionnaires may invalidate depression severity measurements. This study aimed to identify and investigate atypical profiles of depressive symptoms using a data-driven approach based on the item response theory (IRT).
Methods: A large cohort of participants completed the Inventory of Depressive Symptomatology self-report (IDS-SR) at baseline (n=2329) and two-year follow-up (n=1971). Person-fit statistics were used to quantify how strongly each patient's observed symptom profile deviated from the expected profile given the group-based IRT model. Identified atypical profiles were investigated in terms of reported symptoms, external correlates and temporal consistency.
Results: Compared to others, atypical responders (6.8%) showed different symptom profiles, with higher 'mood reactivity' and 'suicidal ideation' and lower levels of mild symptoms like 'sad mood'. Atypical responding was associated with more medication use (especially tricyclic antidepressants: OR=1.5), less somatization (OR=0.8), anxiety severity (OR=0.8) and anxiety diagnoses (OR=0.8–0.9), and was shown relatively stable (29.0%) over time.
Limitations: This is a methodological proof-of-principal based on the IDS-SR in outpatients. Implementation studies are needed.
Conclusion: Person-fit statistics can be used to identify patients who report atypical patterns of depressive symptoms. In research and clinical practice, the extra diagnostic information provided by person-fit statistics could help determine if respondents' depression severity scores are interpretable or should be augmented with additional information.

1. Introduction

Major Depressive Disorder (MDD) is a burdensome disorder with heterogeneous symptomatology (Lux and Kendler, 2010; Widiger and Clark, 2000; Widiger and Samuel, 2005) and course trajectories (Penninx et al., 2011; Wardenaar et al., 2014). This heterogeneity is a likely reason for the persistent lack of comprehensive etiological models for depression (Luyten et al., 2006). In order to improve this situation, researchers have attempted to identify more homogenous clinical entities (e.g. subtypes) that better capture the variability among depression patients in terms of phenomenology and etiology.

Depression subtypes are based on clinical consensus (e.g. melancholic or atypical depression; Stewart et al., 2007) or on empirically-derived common patterns of depressive symptoms. The latter have been investigated with latent class analyses (LCA), which has provided interesting insights into the heterogeneity among depressed patients (Baumeister and Parker, 2012; Sullivan et al., 1998). However, a consistent and well-replicated subtyping model to capture all their inter-individual differences has not yet been established (Van Loo et al., 2012). This could be due to the limitations of LCA (Lubke and Muthén, 2005), and sample/design inconsistencies across studies (Van Loo et al., 2012). However, a more basal issue is that the models are based on subjectively reported symptoms that are all assumed to reflect the construct of depression, which is not necessarily true.

Depressive symptoms can be reported for other reasons than the presence of MDD, such as comorbid somatic or psychiatric disorders, the presence of isolated symptoms, secondary gains by over- or underreporting of symptoms and the existence of specific

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subtypes of depression. This can result in *atypical* profiles of reported depressive symptoms, which means that patients with such patterns do not conform to definitions of depression. For instance, some depressive patients with somatic illness tend to more often endorse somatic-depressive symptoms, leading to patterns of reported symptoms that do not exclusively reflect depression severity (Leentjens et al., 2000). This is problematic for the assessment of depression severity because scores of persons with atypical profiles do not adequately reflect the assumed underlying construct of depression and cannot be classified or scaled accordingly on a depression severity dimension.

The above described heterogeneity of response behavior can be investigated with a data-driven approach based on *person-fit* statistics and item response theory (IRT; Embretson and Reise, 2000). Through person-fit statistics, researchers can investigate the extent to which a respondent's observed score pattern deviates from the expected pattern based on a group-based IRT model (Meijer, 2003). A particular pattern of depressive symptoms can be empirically classified as atypical when too many unexpected scores are observed (e.g. reporting severe symptoms but no mild symptoms). This approach allows for a data-driven identification of atypical response profiles, making no a priori assumptions about what these profiles look like. As a result, the technique is not limited to pre-specified depression classifications or subtypes and could yield new insights into variations in depressive symptom reporting.

To our knowledge, only three previous studies have used person-fit analyses in mental health-related research. First, Conijn (2013) identified atypical response patterns on health-related outcome measures among clinical outpatients. These patterns were associated with severe psychological distress and psychopathology, including somatoform disorders, psychotic disorders, and substance-related disorders. Second, Woods et al. (2008) found that atypical responding on personality questionnaires was associated with personality pathology. These two studies suggest that person-fit statistics can identify atypical response patterns that are reflective of relevant inter-individual differences and do not arise merely due to chance or non-systematic influences (e.g. test behavior). In a third study, Conrad et al. (2010) used person-fit analyses to screen for 'atypical suicide risk', using a questionnaire of internalizing symptoms that was administered to patients with substance-related problems. Those that reported suicidality, but no or few other internalizing symptoms were identified as atypical responders. These patients reported suicidality out of the blue, not in the context of severe internalizing symptomatology. By identifying the latter group, this study showed the extra diagnostic information that person-fit statistics could provide on top of traditional compound scores.

This study aimed to use person-fit analyses to investigate symptom reporting on the Inventory of Depressive Symptomatology Self Report (IDS-SR) in a large cohort study. First, person-fit statistics were used to identify persons with atypical response patterns, given the underlying IRT model of depression severity. Second, item-responses in the atypical responders were investigated. Third, associations of atypical response patterns with external factors were investigated. Finally, the consistency of atypical response behavior over time was investigated.

2. Methods

2.1. Participants and procedures

Data came from the Netherlands Study of Depression and Anxiety (NESDA), a large scale longitudinal cohort study among 2981 adult participants (aged 18–65; 1002 men, 1979 women). Participants were recruited in the general population (19%), primary care (54%), and secondary care (27%). Exclusion criteria were not being fluent in Dutch and/or having a primary diagnosis of bipolar disorder, obsessive compulsive disorder, psychotic disorder, or severe addiction disorder. A follow-up assessment was conducted after two years with a response rate of 87.1% ($n=2596$). Details about the rationale, objectives, and methods of the study can be found in Penninx et al. (2008).

All participants had a face-to-face assessment session with a trained research assistant, consisting of a standardized psychiatric and demographic interview, biomedical measurements, a blood-draw and a battery of self-report questionnaires. The protocol of the NESDA study was approved by the Ethical Committees of all participating universities. All participants signed informed consent.

Data for the current study came from the baseline assessment and the two-year follow up. Only participants with a lifetime anxiety or depression diagnosis ($n=2329$; 78.1%) were included. Of these, 1971 (84.6%) provided follow up data. From these samples, patients with >5 missing values on the IDS-SR were excluded, leading to a baseline sample of 2292 patients and a follow-up sample of 1942 patients.

2.2. Measures

2.2.1. Depressive symptoms

The IDS-SR (Rush et al., 1996) is a self-report questionnaire consisting of 30 items rated on a 4-point (0–3) Likert scale. A participant could either endorse 'appetite increase' or 'appetite decrease' and either 'weight increase' or 'weight decrease'. Therefore, these items were combined respectively into compound 'appetite change' and 'weight change' items. The IDS-SR assesses all DSM-IV criterion symptoms for MDD and the most commonly associated symptoms (e.g. anxiety, irritability).

2.2.2. External variables

As no previous studies investigated person-fit in depression, there were no a priori hypotheses about factors that might be associated with atypical depressive symptom reporting. Therefore, a data-mining strategy was used to investigate which out of a wide range of explanatory variables predicted atypical symptom reporting. The used external variables included socio-demographic, clinical, and biological factors. Socio-demographic factors (gender, age, healthcare setting, years of education and north-European ancestry) were assessed at baseline. The Composite International Diagnostic Interview (CIDI, WHO version 2.1) was conducted at baseline to assess the presence of lifetime and current (past six months) DSM-IV diagnoses of MDD, dysthymia, social phobia, generalized anxiety disorder, panic disorder and agoraphobia, alcohol use disorder (alcohol abuse/alcohol dependence). Dichotomous DSM-IV MDD subtype specifiers (atypical and melancholic) were derived from the IDS-SR and calculated regardless of CIDI diagnosis. Anxiety severity was measured with the 21-item Beck Anxiety Inventory (BAI; Beck et al., 1988). Both the continuous total BAI score and a categorical BAI severity indicator ($\geq$10:mild, $\geq$19:moderate, $\geq$30:severe; Beck et al.,1988) were investigated. Manic symptoms were assessed using the 15-item Mood Disorder Questionnaire (MDQ; Hirschfeld et al., 2000). Both the continuous total scale score and dichotomous indicator of positive screening (MDQ$\geq$7) for (hypo)manic episode were used. Of the Four Dimensional Symptom Questionnaire (4DSQ; Terluin et al., 2006), the *distress* (16 items, range 0–32) and *somatization* (16 items, range 0–31) scales were used as continuous indicators. In addition, a dichotomous somatization indicator (somatization$\geq$11) was used. Big-Five personality traits were assessed using the Neuroticism-Extraversion-Openness Five-Factor-Inventory (NEO-FFI; Costa and McCrae, 1992). Past month use of soft and hard drugs was assessed with a self-report questionnaire. Alcohol