Research paper

Using a hybrid subtyping model to capture patterns and dimensionality of depressive and anxiety symptomatology in the general population

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ARTICLE INFO

Keywords:
Depression
Anxiety
Heterogeneity
Subtypes
Latent class analysis
Mixed measurement item response theory

ABSTRACT

Background: Researchers have tried to identify more homogeneous subtypes of major depressive disorder (MDD) with latent class analyses (LCA). However, this approach does no justice to the dimensional nature of psychopathology. In addition, anxiety and functioning-levels have seldom been integrated in subtyping efforts. Therefore, this study used a hybrid discrete-dimensional approach to identify subgroups with shared patterns of depressive and anxiety symptomatology, while accounting for functioning-levels.

Methods: The Comprehensive International Diagnostic Interview (CIDI) 1.1 was used to assess previous-year depressive and anxiety symptoms in the Netherlands Mental Health Survey and Incidence Study-1 (NEMESIS-1; n=5583). The data were analyzed with factor analyses, LCA and hybrid mixed-measurement item response theory (MM-IRT) with and without functioning covariates. Finally, the classes' predictors (measured one year earlier) and outcomes (measured two years later) were investigated.

Results: A 3-class MM-IRT model with functioning covariates best described the data and consisted of a 'healthy class' (74.2%) and two symptomatic classes ('sleep/energy' [13.4%]; 'mood/anhedonia' [12.4%]). Factors including older age, urbanicity, higher severity and presence of 1-year MDD predicted membership of either symptomatic class vs. the healthy class. Both symptomatic classes showed poorer 2-year outcomes (i.e. disorders, poor functioning) than the healthy class. The odds of MDD after two years were especially increased in the mood/anhedonia class.

Limitations: Symptoms were assessed for the past year whereas current functioning was assessed.

Conclusions: Heterogeneity of depression and anxiety symptomatology are optimally captured by a hybrid discrete-dimensional subtyping model. Importantly, accounting for functioning-levels helps to capture clinically relevant interpersonal differences.

1. Introduction

The specific mechanisms underlying depression are still poorly understood, which may partly be due to the heterogeneity of the used categorical depression construct (e.g. Widiger and Clark, 2000). To overcome this problem, researchers have used data-driven statistical models such as Latent Class Analysis (LCA) to identify more homogeneous depression subgroups (Eaton et al., 1989; Kendler et al., 1996; Sullivan and Kendler, 1998; Sullivan et al., 1998, 2002; Parker et al., 1999; Carragher et al., 2009; Hybels et al., 2009; Lamers et al., 2010, 2012; Li et al., 2014; Ulbricht et al., 2015). Promisingly, there is some evidence that the resulting subgroups differentiate persons with distinct treatment responses (Ulbricht et al., 2015), biomarkers and course-trajectories (Lamers et al., 2013, 2016). However, although these studies provide valuable insights into the heterogeneity of depression, the interpretability of LCA results is hampered by the underlying key-assumption that all heterogeneity among persons is explained by class-membership and that no additional variation exists within classes. This means that the discrete LCA models are rather crude approximations of reality, where psychopathology is known to be a continuous phenomenon (Kendell, 1989; Kendell and Jablensky, 2003).

To account for the dimensional nature of psychopathology when identifying data-driven depression subgroups, researchers can use a hybrid mixture approach, such as mixed measurement item response theory (MM-IRT; Rost, 1990, 1991; Mislevy andVerhelst, 1990) models that integrate LCA with an IRT measurement model. MM-IRT is closely related to factor mixture models (FMM, Lubke and...
Muthén, 2005; Muthén & Asparouhov, 2006; Lubke and Miller, 2015), which integrate LCA with a factor model (Lubke et al., 2007; Kuo et al., 2008; Picardi et al., 2012; Sunderland et al., 2013; Pattyn et al., 2015; ten Have et al., 2016). In MM-IRT, a measurement model is taken as a point of departure and heterogeneity in response behavior is explained by estimating latent classes for which different IRT-model parameters may hold (e.g. Cohen and Bolt, 2005; Maij-de Meij et al., 2010). Here, LCA and IRT complement each other. On the one hand, one can investigate latent population heterogeneity while accounting for response-behavior variations. On the other hand, one can investigate the dimensionality of symptoms, while accounting for latent population heterogeneity (Clark et al., 2013). Helpfully, covariates can be included in the MM-IRT models to further improve class-differentiation (MM-IRT-C; Tay et al., 2011). MM-IRT has previously been used to investigate response-behavior heterogeneity on personality questionnaires (e.g. Maij-de Meij et al., 2005, 2008; Egberink et al., 2010), patterns of tobacco-use/dependence symptoms (Muthén and Asparouhov, 2006) and the use of special response scales (e.g. Austin et al., 2006).

Apart from not accounting for dimensionality, some other limitations can also be seen in previous subtyping studies. First, many only analyzed depression symptoms, whereas these co-occur more often than not with anxiety symptoms (e.g. Mineka et al., 1998). Indeed, a recent study found that anxiety symptoms may play an important role in the differentiation between depression subgroups (ten Have et al., 2016). Second, previous studies have paid little attention to the role of persons’ level of functioning as source of heterogeneity, despite the fact that it is important to determine whether present symptomatology is actually pathological or reflects sub-clinical problems (e.g. Kramer et al., 2004).

Wanders et al. (2016) addressed all the above-described issues by using MM-IRT on data from a large cohort (n=73,403) to identify subgroups based on depressive and anxiety symptoms, while accounting for the role of functioning levels. The results showed that a 5-class MM-IRT-C model with functioning scales incorporated as covariates, optimally differentiated between subgroups with different symptom profiles (‘healthy’, ‘somatic’, ‘worried’, ‘subclinical’ and ‘clinical’ subgroups) and patterns of associations with external factors (e.g. sociodemographics, lifestyle). These results clearly showed the promise of MM-IRT-C to identify hybrid discrete-dimensional patient subgroups.

The current study used a similar MM-IRT-C approach to identify cross-diagnostic subtypes of depressive and anxiety symptomatology, incorporating functioning levels as covariates. However, this study also extended on the previous work by making use of a representative population sample (n=5583; the Netherlands Mental Health Survey and Incidence Study-1, NEMESIS-1). In addition, the 3-wave longitudinal design of NEMESIS-I (baseline, 1-year follow-up and 3-year follow-up) allowed for a thorough investigation of the longitudinal correlates of the estimated classes. MM-IRT-C models were estimated on the data collected at 1-year follow-up. Next, the prediction of subgroup membership by baseline variables, as well as the subgroups’ prediction of 3-year follow-up outcomes was investigated.

2. Methods

2.1. Participants

Participants came from NEMESIS-1, a longitudinal cohort study in a randomly selected adult population sample (aged 18–65 years) from the Netherlands. The study consisted of a baseline measurement (T0; n=7076; 69.7% response; in the year 1996) a measurement after 1 year (T1; n=6518; 79% response; in the year 1997) and a measurement after 3 years (T2; n=4796; 85% response; in the year 1999). The detailed design, rationale and goals of NEMESIS-1 have been described previously (Bijl et al., 1998). The research protocol was approved by the ethics committee of the Netherlands Institute of Mental Health and Addiction, Utrecht, the Netherlands. All participants provided oral informed consent in line with the prevailing Dutch law at the time the fieldwork took place.

In each measurement-wave, participants were interviewed with the Composite International Diagnostic Interview (CIDI; version 1.1) generating DSM-III-R diagnoses. The depression questions (Section E) and anxiety symptom questions (Section D: Panic Disorder, Generalized Anxiety Disorder [GAD], Agoraphobia, Social Phobia and Specific phobia) were used in the current study. The T1 data (collected 1 year after the baseline measurement) were used to estimate an optimal subtyping model because the time frame of these CIDI symptom assessments was limited to the 1-year period between T0 and T1 (see Supplementary Figure 1). This ensured that the assessed symptoms (co)occurred roughly within the same 1-year time-interval. A previous multivariate analysis showed that sample attrition between T0 and T1 was associated with younger age, lower education, urbanity, not cohabiting with a steady partner, unemployment, being born outside the Netherlands, agoraphobia, social phobia and eating disorders. The presence of any DSM-III-R disorder was only weakly related to attrition, controlled for demographics (OR=1.20; de Graaf et al., 2000a). Of the 5618 respondents at T1, 5583 (99.4%) provided all the data that was needed for the current analyses (measures of depressive and anxiety symptomatology and functioning). The current analyses were conducted using data from the different measurement waves. The MM-IRT and MM-IRT-C analyses were run in the T1 sample, identifying a range of subgroups. Next, factors assessed at T0 were used to predict subgroup-membership at T1. Finally, the subgroups at T1 were associated with outcomes measured at T2 to evaluate the prognostic value of the identified subgroups. This was done using all subjects that were included in the MM-IRT analyses and had T2 assessments for the relevant outcomes (see below). When adjusted for sociodemographic factors, attrition between T1 and T2 was associated with the presence of MDD, dysthymia and alcohol dependence (de Graaf et al., 2000b).

2.2. Measurements

2.2.1. Symptom-assessments and functioning at T1

The presence of depressive symptoms was assessed with the depression section of the CIDI 1.1. All depressive symptoms were evaluated irrespective of whether the key-symptoms were endorsed (there were no symptom skips in the depression section). In addition, the responses to CIDI screening questions for a range of common anxiety disorders (Panic Disorder, GAD, Agoraphobia, Social Phobia and Specific phobia) were used in the current study. Here, only the screening questions could be used because the anxiety sections of the CIDI skipped all detailed questions if the screening questions were not endorsed. Taken together, the analyzed symptom-dataset contained 28 depressive symptoms and 5 anxiety symptoms.

The Medical Outcome Study Short Form-36 (SF-36; Stewart et al., 1988) was used to assess several domains of functioning.

2.3. Predictors at T0

Sociodemographic variables (age, gender, employment status, urbanicity and educational attainment) were assessed at baseline. The Mastery scale (Pearlin and Schooler, 1978) was used to assess the extent to which individuals feel in control and/or feel responsibility for the events occurring in their lives. The Rosenberg Self Esteem scale (Rosenberg, 1965) was used to assess self-esteem. The General Health Questionnaire-12 (GHQ-12; Goldberg and Williams, 1988) was used to assess severity and the SF-36 was used to assess levels of functioning. The CIDI was used to determine 1-year CIDI-based DSM-III-R diagnoses, using disorder hierarchies and exclusion rules.
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