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Research report

Symptom-based subtypes of depression and their psychosocial correlates: A person-centered approach focusing on the influence of sex

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ABSTRACT

Background: Reducing the complexity of major depressive disorder by symptom-based subtypes constitutes the basis of more specific treatments. To date, few studies have empirically derived symptom subtypes separated by sex, although the impact of sex has been widely accepted in depression research.
Methods: The community-based sample included 373 males and 443 females from the Zurich Program for Sustainable Development of Mental Health Services (ZInEP) manifesting depressive symptoms in the past 12 months. Latent Class Analysis (LCA) was performed separately by sex to extract sex-related depression subtypes. The subtypes were characterized by psychosocial characteristics.
Results: Three similar subtypes were found in both sexes: a severe typical subtype (males: 22.8%; females: 35.7%), a severe atypical subtype (males: 17.4%; females: 22.6%), and a moderate subtype (males: 25.2%; females: 41.8%). In males, two additional subgroups were identified: a severe irritable/angry-rejection sensitive (IARS) subtype (30%) comprising the largest group, and a small psychomotor retarded subtype (4%). Males belonging to the severe typical subtype exhibited the lowest masculine gender role orientation, while females of the typical subtype showed more anxiety disorders. The severe atypical subtype was associated with eating disorders in both sexes and with alcohol/drug abuse/dependence in females. In contrast, alcohol/drug abuse/dependence was associated with the severe IARS subtype in males.
Limitations: The study had a cross-sectional design, allowing for no causal inferences.
Conclusions: This study contributes to a better understanding of sex-related depression subtypes, which can be well distinguished on the basis of symptom profiles. This provides the base for future research investigating the etiopathogenesis and effective treatment of the heterogeneous depression disorder.

1. Introduction

Growing dissatisfaction with the heterogeneity of major depressive disorder (MDD) has led researchers to search for specific depression subtypes of MDD that would facilitate the development of subtype-specific treatments (Baumeister and Parker, 2012). Robins and Guze (1970) emphasized the advantage of examining homogeneous subtypes in their classic paper as follows (McKay et al., 2004):

> "Homogeneous diagnostic grouping provides the soundest base for studies of etiology, pathogenesis, and treatment. The roles of heredity, family interactions, intelligence, education, and sociological factors are most simply, directly, and reliably studied when the group studied is as homogeneous as possible" (p. 984).

The current version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) allows for description of the symptom-based MDD subtypes melancholic, psychotic and atypical depression by specifiers (APA, 2013). Comorbidity is a further source of heterogeneity (Carragher et al., 2009). Hence, differentiation of heterogeneous depressive symptomatology and overlap with comorbid disorders/syndromes represent a major challenge for diagnostic classification.

Indicative person-centered methodological techniques such as latent class analysis (LCA) offer a promising statistical approach by extracting homogeneous subgroups of individuals based on their symptom profiles. The resultant depressive subtypes of the

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previous LCA subtyping studies vary between three (Carragher et al., 2009; Eaton et al., 1989; Lamers et al., 2012a, 2010), six (Sullivan et al., 1998), and seven (Kendler et al., 1996; Sullivan et al., 2002) latent classes. Not all of these LCA studies assessed the complete set of criteria for atypical depression. In addition, not all studies considered the variable sex, despite many research findings demonstrating the impact of sex on depression (Möller Leimkühler et al., 2004). For example, only two LCA studies in depression research to date have differentiated separate analyses by sex (Alexandrino-Silva et al., 2013; Crum et al., 2005). This lack of differentiation stands in contrast to the frequently voiced importance of analyses comparing population subgroups (e.g., Eaton et al., 1989).

Irrespective of the LCA findings, the repeatedly found higher rates of MDD in females (Kessler, 2003; Kessler et al., 1993; Weissman and Klerman, 1977) have been explained by the existence of the three subtypes atypical, anxious, and somatic depression, which are more prevalent in women and hence could form sex-preferred subtypes of MDD (Angst et al., 2002b; Clayton et al., 1991; Halbreich and Kahn, 2007; Silverstein, 1999, 2002). Overall, the focus has remained mostly on the situation of females, particularly outside the US (Möller Leimkühler et al., 2004).

Nevertheless, researchers and clinicians have speculated about a masculine subtype of MDD being defined by a distinct set of depressive symptoms (Cochran and Rabinowitz, 2000; Magovcevic and Addis, 2008; Rutz et al., 1995). One of the few measurements that aims at assessing a male depressive syndrome is the Gotland Scale of Male Depression, which defines male depression by symptoms such as irritability, restlessness, loss of self-control, alcohol or substance abuse and overwork. The existing definition and operationalization of the male depressive syndrome particularly needs to be validated in unbiased community samples and specified with respect to differential diagnoses (Möller Leimkühler et al., 2007).

Empirical evidence has demonstrated that not only sex but also gender, more specifically gender role orientation, has an impact on depression (Helgeson, 2005). Gender role orientation is a personality trait that an individual forms as member of a social system in which certain attributes and attitudes are stereotyped as masculine or feminine (Williams and Best, 1982). Two meta-reviews showed that masculine gender role orientation is a protective factor against depression, whereas feminine gender role orientation is unrelated to depression (Helgeson, 2005). To our knowledge, no study has examined whether gender role orientation differs between empirically derived depressive symptom subtypes.

The first aim of this study was to derive depressive subtypes separately for males and females by performing LCAs to a community sample. The second aim was to characterize the resultant subtypes by psychosocial correlates, such as demographic features, gender role orientation, male depressive syndrome, and comorbid disorders. Our main expectations were to find (1) a typical and atypical subtype for both sexes, (2) a male-related subtype with a delimitable symptom profile, (3) higher scores for masculinity in non-severe depression subtypes, and (4) differing comorbidity profiles between depressed males and females. Beyond these expectations we had an exploratory strategy. We assessed a wide range of depressive symptoms, including atypical depression, to potentially capture further sex-related depressive subtypes.

2. Methods

2.1. Sample and procedures

The data were derived from the epidemiology survey of the Zurich Program for Sustainable Development of Mental Health Services (ZInEP; German: ***Z**ürcher **I**mpulsprogramm zur **n**achhaltigen **E**ntwicklung der **P**sychiatrie*). The survey was conducted to generate comprehensive data about mental health in the general population of adults in the canton of Zurich (total population about 1.4 million). Methodologically, and regarding age and sex, the survey was designed as a cross-sectional sequel to the longitudinal Zurich Study (Angst et al., 2005). It consisted of three components: (a) a brief telephone screening, (b) a structured face-to-face-interview supplemented by self-report questionnaires, and (c) a longitudinal survey. The survey was carried out between August 2010 and September 2012. For more details see Ajdacic-Gross et al. (in press).

A computer assisted telephone interview (CATI) was administered for the initial telephone screening. The CATI was conducted by a market and field research institute, with support from experienced associates of the Zurich University Hospital of Psychiatry. The records of the screening sample were taken from the communal public authority register of the canton of Zurich. The sample was confined to subjects with Swiss nationality aged between 20 and 41 y at the beginning of the study. In analogy to the age profile of the Zurich Study, the participants were randomly selected from 12 sex-birth-year subgroups. Initially, $n=9829$ screenings (males: 4920; females: 4909) representative of the canton of Zurich were carried out. In cases where the target person could be reached by telephone, the response rate was 73.9% (males: 70.6%; females: 77.6%). The overall response rate was 53.6%.

In the next step, we randomly selected subjects from the screening sample for a comprehensive semi-structured face-to-face-interview. To increase the probability of the occurrence of mental disorders, we applied a stratifying sampling procedure with 60% high-scorers (defined as above the 75th percentile of the global severity index (GSI) of the Symptom Checklist-27 (SCL-27) (Hardt et al., 2004)) and 40% low-scorers (defined by scores below the 75th percentile). The face-to-face interviews were administered either in the subjects' homes or at the research division of the Zurich University Hospital of Psychiatry. The interviews were conducted by 21 clinical psychologists who had been intensively trained in use of the instrument. Six of them accomplished 61% of all 1500 interviews. The research team and the interviewers met periodically for supervision, but also for the exchange of experiences in order to improve the survey instruments and interview procedures. In addition, quality assurance measures were performed periodically, based on various outcome parameters (interview duration, response patterns, return of checklists, positive answers regarding continuing participation, symptom load, and symptom patterns). In one single case, an interviewer had to be dismissed due to insufficient quality.

Of the 9829 subjects who had completed the screening, 66.3% were initially interested in a face-to-face interview. When asked for an appointment, 64.9% (males: 69.4%, females: 60.0%) actually showed up. The final sample included 1500 subjects. Similarly to the Zurich-Study, this sample was composed of six female ($n=125$, 22 y; $n=125$, 24 y; $n=125$, 29 y; $n=125$, 31 y; $n=125$, 36 y; $n=125$, 42 y) and six male subgroups ($n=125$, 21 y; $n=125$, 23 y; $n=125$, 28 y; $n=125$, 30 y; $n=125$, 35 y; $n=125$, 41 y). To consider supplemental issues, all participants completed additional self-report questionnaires. Overall, $n=1179$ complete questionnaires were returned, i.e., the refusal rate was 21.4% (males: 28.4%; females: 14.4%).

The study was approved by the Ethics Committee of the Canton of Zurich (KEK). After being extensively informed about study procedure and aims both verbally and in writing, the participants gave their written consent.

2.2. Measurements

2.2.1. Assessment of depressive symptoms and comorbid disorders

The computer-assisted Mini-SPIKE, a shortened form of the SPIKE (Structured Psychopathological Interview and Rating of the