Research paper

Depressive subtypes in an elderly cohort identified using latent class analysis

E.M. Veltman[a,*], F. Lamers[b], H.C. Comijs[b], M.W.M. de Waal[d], M.L. Stek[b], R.C. van der Mast[a,c], D. Rhebergen[b]

[a] Department of Psychiatry, Leiden University Medical Center, The Netherlands
[b] GGZ inGeest/Department of Psychiatry and the EMGO+ Institute for Health and Care Research, VU University Medical Center, Amsterdam, The Netherlands
[c] Department of Psychiatry, CAPRI-University of Antwerp, Belgium
[d] Department of Public Health and Primary Care, Leiden University Medical Center, The Netherlands

ARTICLE INFO

ABSTRACT

Background: Clinical findings indicate heterogeneity of depressive disorders, stressing the importance of subtyping depression for research and clinical care. Subtypes of the common late life depression are however seldom studied. Data-driven methods may help provide a more empirically-based classification of late-life depression.

Methods: Data were used from the Netherlands Study of Depression in Older People (NESDO) derived from 359 persons, aged 60 years or older, with a current diagnosis of major depressive disorder. Latent class analysis (LCA) was used to identify subtypes of depression, using ten CIDI-based depression items. Classes were then characterized using various sociodemographic and clinical characteristics.

Results: The most prevalent class, as identified by LCA, was a moderate-severe class (prevalence 46.5%), followed by a severe melancholic class (prevalence 38.4%), and a severe atypical class (prevalence 15.0%). The strongest distinguishing features between the three classes were appetite and weight and, to a lesser extent, psychomotor symptoms and loss of interest. Compared with the melancholic class, the severe atypical class had the highest prevalence of females, the lowest mean age, the highest BMI, and highest prevalence of both cardiovascular disease, and metabolic syndrome.

Limitations: The strongest distinguishing symptoms, appetite and weight, could be correlated. Further, only longitudinal studies could demonstrate whether the identified classes are stable on the long term.

Discussion: In older persons with depressive disorders, three distinct subtypes were identified, similar to subtypes found in younger adults. The strongest distinguishing features were appetite and weight; moreover, classes differed strongly on prevalence of metabolic syndrome and cardiovascular disease. These findings suggest differences in the involvement of metabolic pathways across classes, which should be considered when investigating the pathogenesis and (eventually) treatment of depression in older persons.

1. Background

Late-life depression is a very common disorder. In older persons living in different settings (e.g. from private households to institutions) prevalence rates of major depressive disorder (MDD) are estimated at 1–16% (Djernes, 2006). In addition, depressive disorders among older persons are frequently of a chronic nature, with a high burden for both patients (Gallo et al., 2007) and their caregivers (Scazufca et al., 2002) and with high societal costs (Hughes et al., 1997; Unützer et al., 2009). Insight into the pathogenesis and possible treatment options is therefore of paramount importance. However, research on the etiology and pathogenesis is impeded by the heterogeneity of depression and differences in biological underpinnings across subtypes, as demonstrated in younger adults (Marijnissen et al., 2011; Lamers et al., 2013; Liu et al., 2014; Vogelzangs et al., 2014; Mansur et al., 2015; Milaneschi et al., 2016).

Data-driven techniques are a fruitful way to investigate heterogeneity in depressive disorders (Lubke and Muthén, 2005). These techniques cluster patients based on their congregate of different depressive symptoms, without a pre-conceived hypothesis. Studies using latent class analysis (LCA) in depressed, younger adult populations (Kendler et al., 1996; Sullivan et al., 1998; Lamers et al., 2010; Li et al., 2014) identified an 'atypical' class, characterized by increased appetite and increased sleep, and a 'typical' (often named 'melancholic') class, characterized by loss of appetite and weight, and by the presence of psychomotor symptoms. Subsequently, these empirically-

Table 1
Estimated symptom profile probabilities of endorsing depressive symptoms from LCA (n = 359).

Class description Prevalence	Total sample 359 (100%)	Class 1, Severe atypical 54 (15.0%)	Class 2, Severe melancholic 138 (38.4%)	Class 3, Moderate severity 167 (46.5%)	Cramer V Statistic	P-value (df)
DSM-IV criterion symptoms						
Depressed mood	0.97	0.94	1.00	0.95	0.14	0.028(2)
Loss of interest	0.92	0.96	0.99	0.86	0.25	< 0.001(2)
Weight					0.59	< 0.001(8)
No weight change	0.57	0.54	0.27	0.84		
Weight loss	0.34	0.00	0.71	0.14		
Weight gain	0.06	0.37	0.01	0.00		
Both gain and loss	0.03	0.09	0.01	0.02		
Appetite					0.79	< 0.001(8)
No change in appetite	0.30	0.04	0.02	0.61		
Decreased appetite	0.53	0.00	0.92	0.38		
Increased appetite	0.12	0.80	0.00	0.00		
Both increase and decrease	0.05	0.17	0.06	0.01		
Sleep					0.16	0.004(8)
No change in sleep	0.10	0.09	0.04	0.14		
Less sleep	0.60	0.48	0.66	0.59		
More sleep	0.08	0.06	0.09	0.08		
Both less and more sleep	0.22	0.37	0.22	0.17		
Psychomotor					0.26	< 0.001(8)
No psychomotor change	0.28	0.28	0.11	0.41		
Psychomotor retardation	0.30	0.24	0.33	0.30		
Psychomotor agitation	0.15	0.17	0.17	0.16		
Both agitation and retardation	0.26	0.32	0.39	0.13		
Fatigue/energy loss	0.91	0.94	0.98	0.84	0.22	< 0.001(2)
Guilt/worthlessness	0.79	0.85	0.87	0.71	0.19	0.002(2)
Concentration/indecisiveness	0.96	1.00	0.98	0.94	0.12	0.063(2)
Suicidal ideation	0.69	0.70	0.79	0.59	0.20	0.001(2)

derived classes could be linked to distinct biological correlates (Lamers et al., 2010, 2013; Milaneschi et al., 2015) as well as different genetic profiles (Milaneschi et al., 2016).

To what extent similar subtypes can be identified in late-life major depression needs to be established. Some studies have implemented LCA in late-life depression (Hybels et al., 2009, 2013; Lee et al., 2012; Mezuk and Kendler, 2012), finding subtypes based mainly on severity. However, most of these studies also included non-depressed persons (Hybels et al., 2009, 2013; Mezuk and Kendler, 2012), or persons with at least one depressive symptom (Lee et al., 2012), without a formal diagnosis of major depression. Whereas inclusion of subthreshold depressive disorders may generate insight into the heterogeneity of depression, it impedes examination of the assumed heterogeneity of particularly major depressive disorder (MDD). Furthermore, in populations with depression of varying severity, data-driven techniques are at risk to detect classes that are mainly driven by different levels of severity. Furthermore, because most studies included persons from community samples, no insight was provided into clinical (outpatient) populations (Lee et al., 2012; Mezuk and Kendler, 2012; Hybels et al., 2013). Lastly, previously demonstrated in younger depressed adults, a differentiation between increased or decreased appetite, weight and/or sleep served as a core feature for differentiation between atypical and melancholic subtypes (Kendler et al., 1996; Sullivan et al., 1998; Lamers et al., 2010; Li et al., 2014). However, few studies among older, depressed persons distinguished between increased and decreased appetite, weight and sleep (Hybels et al., 2009, 2013; Lee et al., 2012), and the majority of data-driven studies in the older population identified subtypes primarily based on depression severity only (Hybels et al., 2009; Mezuk and Kendler, 2012).

Therefore, this study aimed to gain more insight into the assumed heterogeneity of MDD in older persons by performing LCA, based on depressive symptoms. If distinct classes are identified, these are examined to establish whether they differ with respect to demographic and clinical characteristics, as well as other risk factors and comorbidity patterns.

2. Methods

2.1. Sample

Data were derived from the baseline measurements of the Netherlands Study of Depression in Older persons (NESDO), a longitudinal multi-site naturalistic cohort study, examining the course and consequences of depression in older people. The NESDO cohort (n = 510) consists of persons aged 60–93 years, including 378 persons with a depressive disorder in the previous 6 months, and 132 non-depressed controls. Depressed older persons were recruited from both mental health care institutes and general practitioners in five regions in the Netherlands, in order to include persons with current late-life depression in various developmental and severity stages. Depression included a 6-month diagnosis of Major Depressive Disorder (MDD) (95%) and/or 6-month Dysthymic Disorder (26.5%), or minor depression (two to four depressive symptoms lasting at least two weeks, 5.0%) according to DSM-IV-R criteria. Age-of-onset of depression did not serve as an selection criterion. Non-depressed older persons were recruited from general practices and were included when no lifetime diagnosis of depression was present. Exclusion criteria are (suspected) dementia, and insufficient command of the Dutch language. The study design of NESDO is described in detail elsewhere (Comijs et al., 2011).

For the current study, we selected all persons with a 6-month DSM-IV diagnosis of major depression, as assessed with the Dutch version of the Composite International Diagnostic Interview (CIDI) lifetime version 2.1 (World Health Organization, 1998; Andrews and Peters, 1998). The CIDI was conducted by specially trained clinical research staff. Persons with a diagnosis of minor depression (n = 13) or dysthymia only (n = 6) were excluded. In addition, individuals with incomplete data on CIDI items for depressive disorder were excluded (n = 10), thus retaining a data set of 359 persons. Attrition was non-differential with respect to age and gender but, compared to included persons, individuals with missing data had more years of education (OR 1.55; 95% CI 1.06–2.17) and lower severity of depression, as measured by the Inventory of Depression Symptomatology (IDS) (OR 0.21; 95% CI 0.13–0.36).