Prevalence, symptoms and risk profiles of apathy at old age

Koolhoven, I.

Chapter 2

Latent Class Analysis of the Apathy Scale does not identify subtypes of apathy in general population-based older persons

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Abstract

Objectives: To identify clinically relevant subtypes of apathy in older persons using Latent Class Analysis (LCA) and investigate the distribution of different characteristics across these subtypes.

Measurements: Cross-sectional data of 122 older persons (mean age 84 years, 60% female) participating in the general population-based PROactive Management Of Depression in the Elderly (PROMODE) study, with apathy according to a score of 14 or higher on the Apathy Scale, were included for LCA. All 14 items of the Apathy Scale were used as indicator variables. Several characteristics were examined including sociodemographics; depressive and anxiety symptoms; global cognitive function; quality of life indicators; hazardous alcohol intake (drinking ≥ 14 consumptions per week); and perceived chronic pain.

Results: Three distinct LCA classes were found classifying 17%, 7% and 76% of the participants, respectively. Individuals in the first class had a higher level of education and were less likely to live alone. Those in the second class had higher apathy and depression scores, lived more frequently alone and used more alcohol. Individuals in the third class showed a lower level of education and worse cognitive function. In multivariable multinomial analyses, only a lower educational level and higher scores on the Apathy Scale were significant predictors for class membership.

Conclusion: Differences between LCA-derived classes were minimal, suggesting that in a general population-based cohort the Apathy Scale measures a homogeneous construct.

Introduction

Apathy is an important behavioral syndrome of several late-life neuropsychiatric disorders, such as depression and dementia.[1-4] The main clinical feature of apathy is diminished motivation, as is apparent from a lack of goal-directed behaviour, and cognition and/or emotions that lead to functional impairments.[5-7] The presence of apathy is associated with worse daily functioning, higher mortality, less likelihood to benefit from rehabilitation services, and poorer perception of quality of life.[8-14]

In community-based older populations the prevalence of apathy was found to range from 6-51%.[3;15-21] Risk factors for apathy include increasing age,[15-17;19;20] having no partner and/or living alone,[3] male gender,[16] lower level of education, [9;16] cognitive impairment,[3;16;22] depressive symptoms,[3;16;21] and cardiovascular disease (CVD) including stroke and/or risk factors for CVD.[8;17;21;23]

Separate classes of apathy may indicate different apathy subtypes that are related to specific characteristics and, therefore, require distinct treatment approaches.[24] However, no studies have empirically examined possible subtypes of apathy in relation to specific characteristics. Most studies on characteristics of apathy used the total apathy scores for the analysis of associations, thereby ignoring possible heterogeneity within the apathy syndrome. The use of total scale scores makes it impossible to detect possible associations between a particular determinant and presumed subtypes,[25] which could also apply to the Apathy Scale. Furthermore, instruments not primarily developed for the assessment of apathy (e.g. the Neuropsychiatric Inventory and the 3-item version of the Geriatric Depression Scale-15) have often been used.[16;20;21;23]

Free from any *a priori* assumption, data-driven techniques such as LCA that cluster persons based on a given outcome, may result in an empirically based classification and enable to identify distinct subtypes of apathy. Therefore, this study aimed to identify clinically relevant subtypes of apathy using LCA in 122 older persons participating in the community-based PROactive Management Of Depression in the Elderly (PROMODE) study. All participants had to have apathy according to a minimum score of 14 on the Apathy Scale. This study also investigated whether specific characteristics were present across the LCA-identified classes of apathy.

Methods

Study design

Data were obtained from the baseline assessment of the PROMODE study. This randomized controlled trial investigated the (cost-) effectiveness of a combined screening and treatment program for older persons aged ≥75 years with untreated depressive symptoms in 73 general practices in the Leiden region (the Netherlands).[26]

From April 2007 to July 2008, all registered persons aged ≥ 75 years in these 73 general practices were invited for screening at home for depressive symptoms. Exclusion criteria were: current treatment for depression, a clinical diagnosis of dementia or a Mini-Mental State Examination (MMSE) score < 19 points, loss of partner or child in the preceding 3 month, terminal illness with a life expectancy of ≤ 3 months, and not speaking Dutch. Informed consent was obtained from all participants.

From the original 2759 study population 366 persons were excluded for the following reasons: a life expectancy of ≤ 3 months (n=22), current treatment for depression (n=141), loss of partner ≤ 3 months ago (n=21), a diagnosis of dementia (n=114), and various other reasons (n=68). Of the 2393 invited persons, 1054 were non-respondents (response rate 56%) and 101 persons were excluded before/during the baseline interview because of current treatment for depression, severe cognitive impairment (MMSE baseline score < 19 points), and for other reasons. Another 120 persons were excluded because of inadequate or missing data, resulting in 1118 persons with complete data on the Apathy Scale scores. Apathy, according to a score of 14 or higher on the Apathy Scale,[27] was found in 122 persons, who were included in the present sub-study.

When comparing non-respondents (n=1174) to included participants (n=1118) of the PROMODE study, we found no differences with respect to sex (p=0.84) and age group (p=0.54).

Apart from the exclusion criteria 'current treatment for depression' GP's were asked to give their clinical judgement about the presence of depressive symptoms. GP's judgement on the presence of (possible) depression was higher in non-respondents compared to respondents (respectively 24% and 18%, p<0.005). Unfortunately, among non-respondents no information about apathy was available.

This study was approved by the Medical Ethical Committee of the Leiden University Medical Centre.

Measures

Assessment of apathy

Apathy was assessed using the 14-item Apathy Scale,[27] which is an abbreviation of the Apathy Evaluation Scale.[28] The Apathy Scale consists of 14 items with scores ranging from 0-3 points per item (maximum score of 42), with higher scores indicating more severe apathy.[27] For the LCA, all 14 items of the Apathy Scale were used as indicator variables and dichotomised as follows: absence of an item (score of 0 or 1) and presence of an item (score 2 or 3).

Assessment of possible characteristics for apathy

To characterize the LCA-identified classes of apathy, several characteristics were used including sociodemographics; depressive and anxiety symptoms; global cognitive function; quality of life indicators; hazardous alcohol intake (drinking ≥ 14 consumptions

per week); and perceived chronic pain (assessed with one item of the Short-Form 36 Health Survey). The 15-item Geriatric Depression Scale (GDS-15) was administered as a screening instrument for depressive symptoms.[29;30] The score of the GDS-15 ranges from 0 to 15 points with higher scores indicating more depressive symptoms.[31;32] Presence of anxiety was measured using the 7-item anxiety subscale of the Hospital Anxiety and Depression Scale (HADS-A) with scores ranging from 0 to 21 points and higher scores indicating more symptoms of anxiety.[33;34] Global cognitive functioning was assessed with the MMSE using total scores. The MMSE is a screening instrument with a good inter-rater and test-retest reliability.[35-37]

Overall quality of life was assessed using Cantril's Ladder, which is a visual analogue scale with scores ranging from 1 to 10 and higher scores indicating better experienced quality of life.[38] Subjective health quality was measured with the EuroQol (EQ)-5D thermometer,[39] scored from 0 to 100 with a higher score indicating better quality of life.[40] Perceived loneliness was assessed with the De Jong-Gierveld Loneliness questionnaire consisting of 6 items; scores ≥ 2 indicated the presence of perceived loneliness and a maximum score of 6 indicates more severe loneliness.[41;42]

Statistical analyses

Data are presented as numbers with percentages, means with standard deviations (SD), and median with interquartile ranges (IQR), where appropriate.

To investigate the presence of subtypes of apathy, LCA was used. LCA (often described as the 'categorical equivalent' of factor analysis) assumes that an unobserved, latent categorical variable explains the association between a set of observed symptoms. Mixture models, like LCA, are extensively described in an earlier report.[43] The LCAs were conducted using M-plus version 5.[44] To determine which model best fitted the data, we examined the Bayesian Information Criterion (BIC), sample size adjusted BIC (ssaBIC), entropy, the Lo-Mendell-Ruben (LMR) likelihood ratio test, the proportion of respondents in each class, and the interpretability and clinical relevance of the latent classes. Lower BIC and ssaBIC values indicate better model fit. The LMR provides a p-value, which indicates whether the k-1 class model is rejected in favour of the k class model. Entropy, as a measure of the quality of classification, is presented for models with more than one class and ranges from 0 to 1 with values closer to 1 indicating greater classification accuracy. Finally, the proportions of individuals in each class are presented. To identify clinically relevant classes, we aimed to recognize classes with > 5% of the sample. Currently, there is no consensus as to which criterion identifies the best fitting number of classes.

After identification of the classes, persons were assigned to their most likely class based on model probabilities. For dichotomous variables, Chi-square statistics or Fisher's exact test (where appropriate), and for continuous variables Kruskal-Wallis non-parametric test, were used to test differences in the distribution of characteristics between classes.

Additional pairwise comparisons were performed to test for differences between pairs of classes. A p-value < 0.05 was considered statistically significant. To further test the association between the characteristics and the classes, we conducted multivariate multinomial logistic regression analyses by entering variables that showed a significance level of p<0.1 in the Chi-square or Kruskal-Wallis tests, next to age and gender that were forced into the model. Odds ratios (ORs) and their 95% confidence intervals (95% CI) were computed. A p-value < 0.05 was considered statistically significant. All comparisons were conducted using SPSS version 21.0 for Windows (SPSS INC., 2012).

Results

Demographic and clinical characteristics

Table 1 presents the sociodemographic and clinical characteristics of the 122 older persons with an Apathy Scale score ≥ 14 points.

Table 1. Characteristics of the study population (n=122)

Sociodemographic characteristics		
Age in years, mean (SD)	82	(5)
Female gender, n (%)	74	(61)
Low level of education, n (%)[a]	58	(48)
Living alone, n (%)	80	(66)
Clinical characteristics		
Alcohol use > 14 drinks/week, n (%)	12	(10)
Presence of chronic pain, n (%)	67	(55)
Quality of life		
Cantril's Ladder score, median (IQR)	7	(6-8)
EuroQol-5D thermometer score, median (IQR)	65	(50-76)
De Jong-Gierveld Loneliness score, median (IQR)	2	(1-3)
De Jong-Gierveld Loneliness score ≥ 2, n (%)	65	(53)
Neuropsychiatric characteristics		
Apathy Scale score, median (IQR)	16	(14-18)
Geriatric Depression Scale score, median (IQR)	2.5	(1-4)
Hospital Anxiety Scale-Anxiety score, median (IQR)[b]	2	(0.8-4)
Mini-Mental Status Examination score, median (IQR)[c]	27	(24-29)

Notes: Data are presented as numbers (percentages), means (standard deviations) or medians (interquartile ranges), where appropriate.

[a] Maximum of 6 years of schooling;

[b] Anxiety subscale of the Hospital Anxiety Depression Scale;

[c] Persons with a Mini-Mental Status Examination score < 19 were excluded.

This study population had a mean age of 82 (SD=5, range 75-96) years, 74 (61%) of them were female, the median score on the GDS-15 was 2.5 (IQR 1-4) and the median score on the MMSE was 27 (IQR 24-29).

Latent class analyses

The parameters of fit and the proportion of individuals in each class of the LCA are presented in Table 2. Whereas the BIC was lowest for the two-class model, the ssaBIC continued to decrease across higher class models. In addition, the LMR test did not reach significance, thereby indicating that the one-class model best fits the data. Finally, the bootstrapped likelihood ratio test (BLRT) no longer reached significance from the 4-class model onwards, suggesting that the 3-class model best fits the data. Since simulation studies have demonstrated the superiority of (BLRT) over other parameters of fit,[43] we decided that the 3-class model provided the best data fit. Figure 1 shows the probability endorsement per item of the Apathy Scale for each class. The first class was particularly characterised by endorsement of mood symptoms. The second class showed high endorsement on most items of the Apathy Scale, except for items concerning external stimulation. The third class showed high endorsement on learning new things and future planning.

Table 2. Parameters of fit of Latent Class Analysis

No. of classes	Maximum likelihood	BIC	ssaBIC	BLRT	ENT	Lo-Mendell-Rubin		Proportion of individuals in class					
						2LL	p-value						
2	-930.5	2000.4	1908.7	<0.001	0.82	58.3	0.17	0.18	0.82				
3*	-909.8	2031.1	1891.9	0.02	0.89	41.4	0.3	0.17	0.07	0.76			
4	-893.7	2070.7	1884.2	0.1	0.83	32.4	0.22	0.14	0.27	0.5	0.09		
5	-879.8	2115.1	1881.1	0.4	0.87	28.5	0.22	0.2	0.14	0.07	0.25	0.34	
6	-864.7	2156.9	1875.5	0.3	0.88	29.4	0.38	0.09	0.21	0.11	0.26	0.18	0.15

Notes: BIC, Bayesian information criterion; ssaBIC, sample size adjusted Bayesian information criterion; BLRT, bootstrapped likelihood ratio test; ENT, entropy; 2LL= 2 log likelihood value
*Best-fitting model

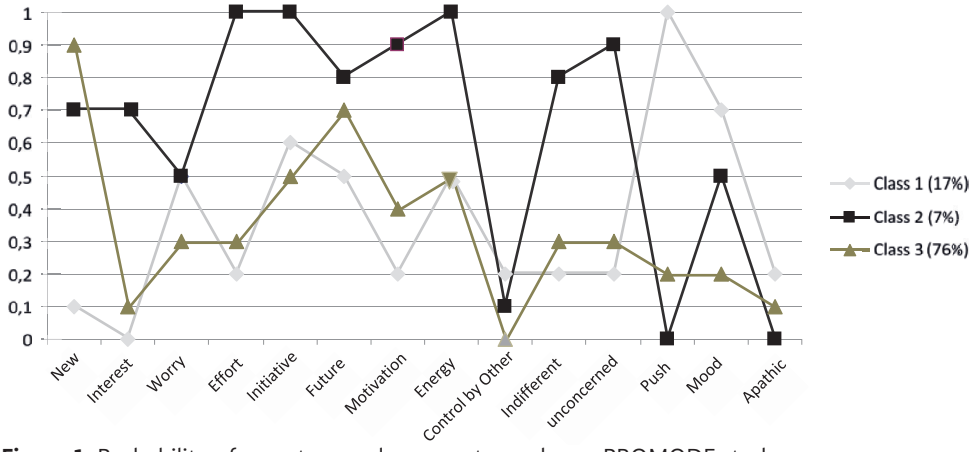

Figure 1. Probability of symptom endorsement per class – PROMODE study

Comparison between identified classes

Results of comparison of the characteristics across the three identified classes using univariate analyses are presented in Table 3**.** Highest scores on the Apathy Scale and the GDS were found in Class 2. Further, most persons in this Class showed high alcohol intake and lived alone, compared to the other two Classes. Lowest level of education, lowest scores on the MMSE (i.e. worst cognitive impairment), and highest scores on the Cantril's Ladder (i.e. best quality of life) were found in Class 3. No differences between the classes were found for age, gender, perceived chronic pain, the EQ-5D, the De Jong-Gierveld Loneliness questionnaire, and the HADS-A.

Finally, multivariate multinomial regression analyses, comparing class 2 and 3 with class 1 (reference), adjusted for age, gender and other putative confounders, showed that, for persons allocated to class 3, lower education (OR 0.2; 95% CI 0.03-0.8; Wald 5.3; *p* 0.02) and, for persons allocated to class 2, higher scores on the Apathy Scale (OR 0.3; 95% CI 0.1-0.8; Wald 5.4; *p* 0.02) was significantly associated with class membership, as compared with class 1. All other characteristics did not reach significance in multivariate multinomial regression analyses.

Discussion

This study, examined the presence of subtypes of apathy in general population-based older persons with apathy as assessed with the Apathy Scale using LCA and identified three classes. These three classes mainly differed in level of education, degree of hazardous alcohol intake, and severity of apathy, depression, and cognitive dysfunction. However, in multivariate multinomial regression analyses, only a lower level of education

Table 3. Distribution of characteristics across the identified latent classes (n-122)

	Class 1 (n=21, 17%)		Class2 (n=8, 7%)		Class 3 (n=93, 76%)		K-W[a]/χ^2 p-value
Sociodemographic characteristics							
Age in years, mean (SD)	81	(5)	80	(4)	83	(5)	0.2
Female gender, n (%)	9	(43)	5	(63)	60	(65)	0.2
Low level of Education, n (%)[b]	3	(14)	3	(38)	52	(56)	0.002
Living alone, n (%)	11	(52)	8	(100)	61	(66)	0.054
Clinical characteristics							
Alcohol use > 14 drinks/week, n (%)	3	(14)	3	(38)	6	(7)	0.02
Chronic pain, n (%)	10	(48)	5	(63)	52	(56)	0.8
Quality of life							
Cantril's Ladder score, median (IQR)	7	(5-7)	7	(5-7)	7	(6-8)	0.05
EuroQol-5D thermometer score, median (IQR)	63	(50-75)	69	(35-78)	65	(50-80)	0.8
De Jong-Gierveld Loneliness score, median (IQR)	1	(0.5-3)	3	(1-5.8)	2	(1-3)	0.3
De Jong-Gierveld Loneliness score ≥ 2, n (%)	10	(48)	5	(63)	50	(54)	0.8
Neuropsychiatric characteristics							
Apathy Scale score, median (IQR)	16	(14.5-18)	22	(20-26)	15	(14-17)	<0.005
Geriatric Depression Scale score, median (IQR)	3	(1.5-4.5)	6	(3-8.5)	2	(1-4)	0.03
Hospital Anxiety Scale-Anxiety score, median (IQR)[c]	2	(1-4.5)	3	(0-3.8)	2	(0-4)	0.7
Mini-Mental Status Examination scale score, median IQR)[d]	29	(28-30)	27	(25-29)	26	(25-29)	0.009

Notes: Data are presented as numbers (percentages), means (standard deviations) or medians (interquartile ranges), where appropriate.

[a] Non-parametric Kruskal-Wallis test, when count <5, Fisher's exact test was used

[b] Maximum of 6 years of schooling.

[c] Anxiety subscale of the Hospital Anxiety Depression Scale.

[d] Persons with a Mini-Mental Status Examination score < 19 were excluded.

and severity of apathy were independent predictors for class membership, indicating that LCA, based on the Apathy Scale, merely identified classes based on different levels of apathy severity and level of education, rather than on distinct subtypes of apathy.

Studies using data-driven models (such as LCA) to determine possible subtypes of apathy are lacking. The Apathy Scale itself was examined in one study investigating persons with Parkinson's disease, using factor analysis; distinct clusters of items (factors) were found, revealing a 'cognitive-behaviour' and a 'general' factor.[45] However, the aim of factor analyses is to reveal fewer underlying non-observable variables in a greater amount of observable variables, in this case all items of the Apathy Scale. Hence, this approach is 'instrument' centred, whereas LCA is a 'person-centred approach', aiming to identify groups of persons based on distinct symptom profiles, enabling further examination of associated risk factors.

Earlier studies among community-dwelling older persons and in depressed older persons, reported that a lower level of education was independently associated with apathy, except in the oldest old (mean age ≥ 80 years).[3;21] A higher education level may protect against apathy in late life, just as it had been shown to protect against dementia,[46] perhaps because of a greater cognitive reserve[9] or for example due to healthier lifestyle or diet, presumed to be more present among persons with higher levels of education.[47] The findings of the present study should be interpreted within the context of the following limitations and strengths. First, exclusion criteria for the original PROMODE study included current treatment for depression, and a MMSE-score < 19 or a clinical diagnosis of dementia; this could have led to selection bias excluding older persons with more severe depression and serious cognitive impairment, resulting in insufficient heterogeneity to detect distinct subtypes. Similarly, older persons with more severe apathy might not have participated in our study because of lack of motivation, resulting in inclusion of persons with only mild to moderate apathy and therefore less heterogeneity. This limits the generalizability of our results to the general population. The relatively low mean score on the Apathy Scale tends to support this idea, and therefore, findings may not be generalized to populations with higher apathy severity. Third, we had no information on neurological disorders (such as Parkinson's disease and stroke), on cardiovascular history and risk profile, objective health status and psychotropic medication use, all of which are possible predictors for class membership of apathy. Finally, since Class 2 consisted of only eight persons, the power to detect significant associations may have been too low. However, to our knowledge, this is the first study to examine apathy by LCA among general population-based older persons with apathy. Another strength of this study is the use of well-known validated measures to assess clinical characteristics, including apathy and depressive symptoms. In addition, we could use all items of the Apathy Scale for further analysis.

Conclusion

This study demonstrates that although three LCA classes of apathy emerged, these merely reflect different levels of education next to different levels of apathy severity. Therefore, in a general population-based cohort, the Apathy Scale seems to measure a relatively homogeneous construct, without indicating specific subtypes of possibly different etiology. Further research on possible subtypes of apathy is required in clinical populations, to further elucidate the position of apathy in different neuropsychiatric diseases.

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