Apathy and agitation in institutionalized older adults: an empirically derived classification

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ABSTRACT

Background: Apathy and agitation are often recognized as the most problematic behavioural and psychological symptoms in care settings. In this study, we analyze the relationship between apathy and agitation symptoms other and their relationship with demographic, cognitive, and neuropsychiatric variables and psychotropic medication use.

Methods: A retrospective study was conducted at a gerontological care centre in Láncara, Spain. Participants were 196 residents of the gerontological care centre, including 143 with a diagnosis of dementia. Apathy and agitation were assessed with

the Apathy Scale for Institutionalized Patients with Dementia, Nursing Home version, and the Spanish version of the Cohen-Mansfield Agitation Inventory, respectively. Two-stage hierarchical cluster analysis (hierarchical cluster analysis in a first exploratory stage and K-means clustering to obtain the final solution in the second stage) was conducted to assign residents to different groups based on apathy and agitation scores.

Results: In cluster 1, a certain level of apathy, the highest levels of agitation, and the most frequent intake of atypical antipsychotics and clomethiazole were observed. The highest levels of apathy and the most frequent intake of memantine were seen in cluster 2. The lowest levels of agitation and apathy and the highest levels of cognitive performance were found in cluster 3.

Conclusions: In this study, subjects with dementia were in a state of high agitation and eventual apathy, had low cognitive status, and were very old. Patients with this profile require well-designed non-pharmacological interventions.

INTRODUCTION

Behavioural and psychological symptoms of dementia (BPSD) represent a heterogeneous group of non-cognitive disturbances that are frequently experienced by patients with degenerative dementia at some stage of the disease.[1–3] BPSD are commonly associated with significant levels of distress and poorer quality of life in people with dementia (PWD) and their caregivers, as well as an increased use of health resources, earlier institutionalization, and greater cost of care. The prevalence of BPSD may reach 98% in hospital units and 61.9% in nursing homes,[4, 5] and it has been reported to be higher in care environments in which there is sensory overstimulation, care staff have overprotective attitudes, or patients experience excess movement or

restrictions.[1]

Apathy is a complex syndrome characterized by a persistent lack of motivation not attributable to altered levels of consciousness that may affect self-generated behaviours, cognitive performance, and emotional-affective processing.[14, 15] It has been shown to be the most common syndrome in degenerative dementia and is strongly associated with higher cognitive impairments.[15–18] Apathy is related to executive impairment and the capacity of the frontal cortex to select, initiate, maintain, and shift actions.[19, 20] Less attention is paid to apathy than other BPSD, possibly because in an institutional con-text it is less intrusive, despite being directly linked with high levels of disability in PWD.

Agitation in PWD takes the form of inappropriate verbal, vocal, or motor activities resulting from unmet needs or states of confusion.[21] Usually, aggressive and non-aggressive physical-verbal dimensions such as the following are detected in agitated behaviours: (i) physically non-aggressive behaviours (e.g. escape attempts, inappropriate eating, hiding things, wandering, restlessness); (ii) physically aggressive behaviours (e.g. biting, kicking, physical sexual advances, inten-tional falling, throwing things); (iii) verbally non-aggressive behaviours (e.g. irrelevant vocalizations, complaining, repetitive questioning); and (iv) verbally aggressive behaviours (e.g. screaming, making noise, verbal sexual behaviours). The impact of agitated behaviours depends on the frequency and degree of disruptiveness.[22] The risk of agitation increases with the progression of dementia severity through different stages of the disease.[23, 24]

In a sample of 491 memory clinic patients with mild to moderate suspected Alzheimer's disease, Vilalta-Franch *et al*. conducted a cluster analysis using three Neuropsychiatric Inventory (NPI) factors: (i) a psychosis factor, including aberrant motor behaviours; (ii) a depressive factor (depression, anxiety, agitation, and apathy);

and (iii) a hypomanic factor (euphoria and disinhibition).[3]

The analysis revealed a three-group categorization of study patients: (i) a group with high scores for the three factors; (ii) a group with high scores in the depressive factor; and (iii) a group with low scores for the three factors. There were no cluster differences in cognitive func-tion, but patients classified in the first and second clusters had greater functional decline and higher levels of BPSD.

Considering the relevance of apathy and agitated behaviours in institutionalized older adults, we decided to perform a cluster analysis of scores from apathy and agitation scales specifically designed for these contexts to explore demographic, neuropsychological, neuropsychiatric, and pharmacological differences in the resulting groups. We hypothesize three clusters: (i) high scores in agitation; (ii) high scores in apathy; and (iii) low scores in agitation, apa-thy, and BPSD in general. We also hypothesized that the third group would be the youngest, with the highest cognitive function scores and the lowest intake of mood-altering drugs.

METHODS

Procedure

We applied an assessment protocol, including behavioural, cognitive, and social evaluation, on 196 institutionalized old subjects, including 143 with a diagnosis of dementia, in a gerontological care centre in Láncara, Spain. Residents with dementia had a score below the Mini-Mental State Examination (MMSE) cut-off,[23] as well as clinically significant cog-nitive and functional impairments in activities of daily living unrelated to other physical or psychiatric impairments. Cognitive impairments had been pre-sent for at least 6 months in each PWD. The 53 residents without a diagnosis of cognitive impairment or dementia had a score higher than MMSE cut-off. The centre's geriatrician and psychogerontologist administered the tests.

Information was collected between January 2016 and March 2018.

Social and cognitive status, cognitive screening, psychopharmacological records, and global assessment of BPSD were routinely collected during the biannual assessment of residents. Specific information on apathy and agitation was collected for this Apathy and agitation are often recognized as the most problematic BPSD in care environments.[6–9] These symptoms have been linked to self-destructive behaviours among older residents and increased incidence of accidents and falls, complicating patient integration and hampering non-pharmacological therapeutic interventions. Furthermore, apathy and study. All the instruments were administered to each participant over a period of 10–15 days. The CMAI-verbally non-aggressive, and CMAI-verbally aggressive were used for the statistical analyses.

In a first exploratory stage, hierarchical cluster ana-lyses were performed, while in the second stage, we performed K-means clustering to obtain a final solution. We chose Euclidean distances as a measure of similarity and Ward's agglomerative clustering method.[32, 33]

After checking the coefficients (within-cluster sum of squares) in the agglomeration schedule and examining the dendrograms,[34] we obtained an optimal result of three conglomerates. We validated this outcome by executing a second hierarchical analysis (method of within-group average linkage). The highest percentage of correspondence between Ward's method and within-group linkage in terms of subjects' group assign-ments was obtained with a three-group solution, which showed high convergent validity for the three clusters. In the second stage of our clustering process, we con-ducted an iterative K-means procedure (SPSS com-mand; SPSS; IBM Corp., Armonk, NY, USA) using the means of the three-cluster solution as seeds. This pro-cedure was followed to improve the assignment of par-ticipants to clusters and obtain a final solution. Iterative

procedures such as K-means are more powerful and reliable than hierarchical procedures but need prior specification of the number of clusters and initial cen-tres. Inter-group comparisons were carried out using ANOVA or the Kruskal–Wallis test for continuous variables and standard χ^2 for categorical variables, as well as effect size (η^2 and Cramer *V*) and post-hoc comparisons of the clusters. Analyses were conducted using IBM SPSS Statistics for Windows version 24.

RESULTS

Overall study sample data are shown in Table 1. The three clusters were assigned to the apathy or agita-tion subgroups based on Z-scores (Table 2). Cluster 1 included 26 subjects and showed the highest levels of agitation and some degree of apathetic behaviours. Cluster 2 included 52 participants that showed the highest levels of apathy and low levels of agitated behaviours. Cluster 3 included 65 participants with the lowest levels of apathy and agitated behaviours.

(insert Tables 1 and 2 around here)

Table 3 shows demographic, neuropsychological, neuropsychiatric, and pharmacological variables and the significant inter-cluster differences that were found. Clusters 1 and 2 revealed a higher pro-portion of participants with Clinical Dementia Rating 3, whereas in cluster 3, a higher number of participants with Clinical Dementia Rating 0.5, 1, and 2 were detected. Accordingly, higher MMSE and Severe Mini-Mental State Examination scores were seen for participants in cluster 3. Subjects in cluster 1 obtained significantly higher scores on the Neuropsychiatric Inventory than those in clusters 2 and 3. A higher percentage of patients in cluster 2 were prescribed memantine, whereas atypical antipsychotics and clomethiazole was higher for subjects in cluster 1. No significant differences were found in demographic variables (age, gender, level of education) or the use of selective serotonin reuptake inhibitors, classic

antipsychotics, benzodiazepines, or antidepressants.

(insert Table 3 around here)

DISCUSSION

The cluster analysis with the study participants reveals three groups of institutionalized PWD. The first group had the highest levels of agitation, a certain level of apathy, and the highest level of BPSD. This group seems comparable to one with high scores on the three BPSD factors in the study by Vilalta-Franch et al.3 However, that study included participants with Alzheimer's disease living in the community, whereas the present study included institutionalized PWD, highlighting the relevance of agitation in institutionalized settings.3 In institutions, the management of agitation may be essential to ensure quality of life, limit the stability of cognitive and affective deterioration progression, and improve the organization of care and staff perception of care activities. As expected, this group had the highest intake of atypical antipsychotics and clomethiazole, drugs that are routinely used in clinical practice to control disruptive behaviours, agitation, and insomnia in institutionalized patients.

In the second group, we observed the highest levels of apathy. Although we did not include self-reported affective measures, the low cognitive status of most participants seemed to indicate that apathetic behaviour is a specific syndrome in this group, especially as more generalized behavioural and psychological alterations were observed in the first group, which had higher scores on the agitation sub-scales and general BPSD measurements. Apathy remains understudied, and it is not usually a priority for the management of BPSD despite its impact. Brodaty and Arasaratnam indicated that therapeutic activities, such as stimulation, creative activities, cooking, Montessori methods, and behavioural interventions, particularly when provided individually, offer the best available evidence for the non-pharmacological management of apathy in

PWD.[12]

Considering the variety of interventions that can effectively reduce apathy, Theleritis *et al*. recommend individualized treatments adapted from evidence-based programmes.[35] In this second group in the present study, we observed the highest frequency of memantine intake because of its indication for advanced stages of dementia, in which multi-domain cognitive deficits are associated with the increased prevalence of apathetic behaviours.

In the third group, we observed the lowest levels of agitation, apathy, and overall BPSD; the highest levels of cognitive performance; and the lowest intake of psychopharmacological drugs. Our hypothesis that this group would be made up of younger subjects was incorrect: the mean age of participants was 86 years. In residential centres with residents who are very old, have low cognitive performance, and are in a state of high agitation and eventual apa-thy, great effort and imagination are needed to design non-pharmacological therapies using environ-mental interventions based on individualized psycho-sensory stimulation techniques. Humanization strat-egy care, which has provided good results in other groups of fragile and dependent patients, is key for this population.

This study had some limitations, mainly a small sample size and the inclusion of a single gerontological care centre. Studies with a larger sample and subjects from different centres should be designed to validate the findings of this work in the context of increasingly complex care practices. In the present study, the type of unit in which the participants reside was not made explicit. In the gerontological centre under study, the residents are separated into different units that can be described as general units and a psychogeriatric unit. The residents of both types of units participated in this study. The most cognitively impaired are the most likely to reside in the psychogeriatric unit.

However, the locations are not polarized; there are variations in where residents spend their time—for example, residents may sleep in one unit and spend the day in another. Those residents with higher BPSDs usually reside in the psychogeriatric unit. In this unit, the care is similar to that provided in other units but reinforced with more personnel because of the exponential increase in functional dependence. Future studies should incorporate not only residents' cognitive status and psychoactive drug consumption profile, but also the type of units in which they reside within the gerontological centre and the type of care they receive according to this unit.

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Table 1. Demographic, neuropsychological and neuropsychiatric characteristics and psychopharmacological prescriptions for subjects with dementia (n = 143)

CDR (0.5/1/2/3)	4/24/40/75
SMMSE	17.48 ± 9.72
MMSE	10.76 ± 8.71
NPI total score	17.48 ± 9.72
APADEM	
DT	18.87 ± 10.85
EB	9.41 ± 6.33
CI	11.01 ± 5.41
CMAI	
PA	12.93 ± 5.76
PN	14.18 ± 7.52
VA	4.31 ± 2.73
VN	9.49 ± 6.34
SSRIs (Y/N)	31/112
Memantine (Y/N)	15/128
Atypical antipsychotics (Y/N)	52/91
Typical antipsychotics (Y/N)	18/125
Benzodiazepines (Y/N)	57/86
Antidepressants (Y/N)	56/87
Clomethiazole (Y/N)	1 5/128

Data are presented as frequencies or means ± SD. CDR, Clinical Dementia Rating; SMMSE, Severe Mini-Mental State Examination; MMSE, Mini-Mental State Examination; NPI, Neuropsychiatric Inventory; APADEM, Apathy Scale for Institutionalized Patients with Dementia; DT, deficit of thinking and self-generated behaviours; EB, emotional blunting; CI, cognitive inertia; CMAI, Cohen-Mansfield Agitation Inventory; PA, physically aggressive

behaviours; PN, physically non-aggressive behaviours; VA, verbally aggressive behav-iours; VN, verbally non-aggressive behaviours; SSRIs, selective serotonin reuptake inhibitors behaviours; Y, yes; N, no.

Table 2. Characteristics and comparisons of the three empirical groups.

Variables	Cluster 1 (n = 26)	Cluster 2 (n = 52)	Cluster 3 (n = 65)	Test†	Effect size‡	Distinct groups§
APADE						
M						
DT						
Z-value	0.32 ± 0.55	0.98 ± 0.52	−0.91 ± 0.47	F = 210.04**	0.750	3 < 1 < 2
Score	22.31 ± 5.99	29.50 ± 5.65	8.98 ± 5.08			
EB						
Z-value	0.31 ± 0.63	0.95 ± 0.58	−0.89 ± 0.47	H = 100.03**	0.711	3 < 1 < 2
Score	11.38 ± 3.98	15.44 ± 3.68	3.80 ± 2.95			
CI						
Z-value	0.34 ± 0.65	0.90 ± 0.42	−0.85 ± 0.69	H = 94.08**	0.650	3 < 1 < 2
Score	12.85 ± 3.51	15.87 ± 2.26	6.38 ± 3.73			
CMAI						
PA						
Z-value	1.33 ± 1.77	−0.26 ± 0.21	−0.32 ± 0.28	H = 58.72**	0.395	3, 2 < 1
Score	20.58 ± 10.22	11.40 ± 1.19	11.09 ± 1.64			
PN						
Z-value	1.26 ± 1.25	−0.04 ± 0.89	−0.47 ± 0.33	H = 53.99**	0.391	3 < 2 < 1
Score	23.62 ± 9.44	13.90 ± 6.68	10.62 ± 2.45			
VA						
Z-value	1.55 ± 1.28	−0.43 ± 0.24	−0.28 ± 0.57	H = 60.50**	0.544	2, 3 < 1
Score	8.54 ± 3.48	3.13 ± 0.66	3.55 ± 1.56			
VN						

Z-value	1.59 ± 0.79	−0.34 ± 0.64	−0.36 ± 0.63	F = 91.81**	0.567	3, 2 < 1
Score	19.58 ± 5.02	7.31 ± 4.03	7.20 ± 3.97			

Data are presented as means ± SD. ** P < 0.01. † F degrees of freedom $2_{,}140$ or H (2, n = 143). ‡ ŋ2 . § Post-hoc comparisons, Tukey's honestly significant differ-ence test (after F) and Mann–Whitney U-test (after H). APADEM, Apathy Scale for Institutionalized Patients with Dementia; DT, deficit of thinking and self-generated behaviours; EB, emotional blunting; CI, cognitive inertia; CMAI, Cohen-Mansfield Agitation Inventory; PA, physically aggressive behaviours; PN, physically non-aggressive behaviours; VA, verbally aggressive behaviours; VN, verbally non-aggressive behaviours.

Table 3 Demographic, neuropsychological, and neuropsychiatric characteristics and psychopharmacological prescriptions of the three clusters for variables not included in the cluster analyses

	Cluster 1 (n = 26)	Cluster 2 (n = 52)	Cluster 3 (n = 65)	Test†	Effect size‡	Distinct groups§
CDR (0.5/1/2/3)	0/0/4/22	0/3/6/43	4/21/30/10	$\chi2 = 67.65$**	0.486	1 = +3 2 = +3 3 = +0.5, 1, 2
SMMSE	13.35 ± 9.95	10.56 ± 7.78	24.66 ± 4.94	H = 72.22**	0.469	2, 1 < 3
MMSE	6.69 ± 6.26	4.12 ± 5.48	17.69 ± 6.13	F = 83.35**	0.544	2, 1 < 3
NPI total score	37.42 ± 11.47	14.52 ± 9.00	11.88 ± 8.18	H = 54.46**	0.523	3, 2 > 1
Memantine (Y/N)	0/26	10/42	5/60	$\chi2 = 7.82$*	0.234	2 = +Y
Atypical antipsychotics (Y/N)	14/12	21/31	17/48	$\chi2 = 6.73$*	0.217	1 = +Y 3 = +N
Clomethiazole (Y/N)	7/19	7/45	1/64	$\chi2 = 13.51$**	0.307	1 = +Y 3 = +N

Data are presented as frequencies or means ± SD. * P < 0.05. ** P < 0.01. † ANOVA F2,140, Kruskal–Wallis non-parametric H (2, n = 143), and $\chi2$ (2, n = 143). ‡ η_p^2 with F and H; V with $\chi2$. § Tukey's honestly significant difference test (after F-test), Mann–Whitney U-test (H). CDR, Clinical Dementia Rating; SMMSE, Severe Mini-Mental State Examination; MMSE, Mini-Mental State Examination; NPI, Neuropsychiatric Inventory; Y, yes; N, no.