International Psychogeriatrics (2016), 28:12, 1989–1999 © International Psychogeriatric Association 2016
doi:10.1017/S1041610216001216

Gender differences in clusters of NPS in Dutch nursing homes – a factor analysis

Janny Ho,[1] Roland B. Wetzels,[2,3] Hans Bor[2] and Sytse U. Zuidema[4]

[1]*Sensire, Care Organization, Varsseveld, the Netherlands*
[2]*Department of Primary and Community Care, Centre for Family Medicine, Geriatric Care and Public Health, Radboud University Medical Centre, Nijmegen P.O. Box 9101, 6500 HB Nijmegen, the Netherlands*
[3]*Pleyade, Elderly Care Organization, Arnhem, the Netherlands*
[4]*Professor of elderly care medicine and dementia, Department of General Practice, University of Groningen, University Medical Centre Groningen, Groningen, the Netherlands*

ABSTRACT

Background: Neuropsychiatric symptoms (NPS) have a high prevalence among patients with dementia, up to 80%. NPS can be grouped by type and stage of dementia. However, NPS have not previously been grouped by gender. Our objective was to investigate whether NPS cluster differently in men or women in the nursing home patients.

Methods: Factor analysis to assess the clustering of items in the Cohen-Mansfield Agitation Inventory (CMAI) and Neuropsychiatric Inventory-Nursing home version (NPI-NH) into components, for both scales and for gender. Differences in symptom clustering between male and female patients were assessed using a three-step procedure: (1) identifying a gender specific distinctive item, (2) describe the correlation between the distinctive item with any other item in this cluster, (3) testing whether the correlation between a distinctive item and any other item in the cluster (which is present in both sexes) is different for males and females using a general linear model.

Results: Our database consisted of 1,609 patients. There were five male and three female clusters for NPI-NH and eight male and seven female clusters for CMAI. There were three distinctive items in the NPI-NH and ten in the CMAI.

Conclusions: There are other clusters of NPS in males and females. Our analysis revealed more significant relations in female than male patients. This might have an implication on the clinical course.

Key words: NPS, dementia, gender

Introduction

The World Health Organization estimated the total number of patients with dementia worldwide in 2010 at 35.6 million, and it is projected to be 65.7 million in 2030 and 115.4 million in 2050 (Batsch and Mittelman, 2012; Wortmann, 2012). Dementia is a major cause of suffering and disability. It encompasses complex brain diseases that affect many aspects of life; causing problems with memory, thinking, and behavior which affects work, family, social relationships, and eventually the activities of daily living. Cognitive impairment is the clinical hallmark in dementia, regardless of the etiology. Nevertheless, the non-cognitive symptoms are more often associated with lowered functional abilities and poorer prognosis, an increased caregiver distress, and suffering for the patient because of the impact on the quality of life (Pearson *et al.*, 1989; Black and Almeida, 2004; Neri *et al.*, 2007).

Non-cognitive symptoms, also known as neuropsychiatric symptoms (NPS), are for example agitation/aggression, depression, psychosis, and apathy. NPS are common among patients with dementia who live in institutions and over the course of the disease the prevalence universally increasing over time to 97% (Peters *et al.*, 2006; Zuidema *et al.*, 2007c; Wetzels *et al.*, 2010; Selbaek *et al.*, 2014). In the community, NPS and the associated burden for the caregiver is a

Correspondence should be addressed to: R. Wetzels, Department of Primary and Community Care, Centre for Family Medicine, Geriatric Care and Public Health, Radboud University Medical Centre, Nijmegen Huispost 117 ELG, P.O. Box 9101, 6500 HB Nijmegen, the Netherlands. Phone: +024-3613338; Fax: +024-3619553. Email: roland.wetzels@radboudumc.nl. Received 8 Oct 2015; revision requested 29 Nov 2015; revised version received 23 Jun 2016; accepted 1 Jul 2016. First published online 30 August 2016.

https://doi.org/10.1017/S1041610216001216 Published online by Cambridge University Press

risk factor for premature institutionalization, and institutionalized patients give an increased burden to the professionals(Rodney, 2000) and higher costs of care (Moore *et al.*, 2001).

Although NPS are considered a quite heterogeneous term for different symptoms, some symptoms differ according to type (Lyketsos *et al.*, 2000; Rockwell *et al.*, 2000; Kim *et al.*, 2003; Wetzels *et al.*, 2010) and stage (Aalten *et al.*, 2005; Testad *et al.*, 2007; Zuidema *et al.*, 2007b; 2009) of dementia. In addition, gender influences the prevalence of symptoms in dementia according to several studies. For example, physically aggressive behavior (Lovheim *et al.*, 2009; Zuidema *et al.*, 2009; Kitamura *et al.*, 2012), repetitive physical movements (Buchanan *et al.*, 2004; Lovheim *et al.*, 2009), and apathy (Zuidema *et al.*, 2009) were more common in male patients; depression (Lovheim *et al.*, 2009; Zuidema *et al.*, 2009; Kitamura *et al.*, 2012), anxiety (Lovheim *et al.*, 2009; Zuidema *et al.*, 2009; Kitamura *et al.*, 2012), apathy (Kitamura *et al.*, 2012), sad expressions (Buchanan *et al.*, 2004; Lovheim *et al.*, 2009), and crying (Buchanan *et al.*, 2004; Lovheim *et al.*, 2009) were more frequent present in female patients.

Syndromes or clusters of NPS in patients with dementia are described in the literature using factor analysis and are performed in a community (Hope *et al.*, 1997; Aalten *et al.*, 2005; Aalten *et al.*, 2007), hospital setting (Frisoni *et al.*, 1999), or even a mixed population of community and nursing home patients (Hollingworth *et al.*, 2006). The European Alzheimer's Disease Consortium (Aalten *et al.*, 2007) has proposed grouping NPS into hyperactive (agitated) behavior, affective behavior, psychosis, and apathy. In addition, factor analysis studies also propose clusters within Cohen-Mansfield Agitation Inventory (CMAI) symptoms (Zuidema *et al.*, 2007a) (Cohen-Mansfield, 1989), i.e. physically aggressive, physically non-aggressive, and verbally agitation behavior.

Clusters of NPS in nursing home patients are not often described. Only a study in Sweden (Lovheim *et al.*, 2006) found 11 clusters in institutionalized patients using the Multi-Dimensional Dementia Assessment Scale (MD-DAS) and a Dutch study (Zuidema *et al.*, 2007a; b) of nursing homes patients found five clusters using the Neuropsychiatric Inventory-nursing home version (NPI-NH) and for the CMAI six/three clusters. In these studies, the authors did not do a separate analysis by gender even though gender influences the relative prevalence of individual symptoms. It could be assumed that gender specific difference in prevalence of individual symptoms may also affect how symptoms cluster. Different clustering in male and female patients may underpin different syndromes, which may have consequences for treatment.

It is clinically important to study behavioral syndromes in dementia instead of individual symptoms because of a possible common neurobiological pathogenesis or possible reaction to the same treatment, whether physical, psychological, or social (Lawlor and Bhriain, 2001; Kales *et al.*, 2014). There are indications that men and women differ for neurochemical, biochemical, and psychosocial aspects but the underlying mechanisms are not fully understood/elucidated. For example, differences were found in the corticotropin-releasing factor (CRF) signaling in the cortex, which would translate to an enhanced sensitivity to acute stress and decreased ability to adapt to chronic stress in females, CRF also has an impact on mood and anxiety (Valentino *et al.*, 2013), endogenous pain inhibitory systems might be less efficient in female patients, and past history may influence pain sensitivity (Racine *et al.*, 2012). These findings were found in the general population and we assume this also applies to the elderly population and dementia patients.

The hypothesis is that there are gender-related differences in clusters of NPS. The aim of this study is to investigate whether NPS clusters differently in male and female nursing home patients, which to our knowledge, this has not been studied before.

Methods

For this study, the databases of WAALBED I and WAALBED II were combined. WAALBED I and II were designed to study the prevalence and two-year course of NPS in nursing home residents in the Eastern, Northern, and Southern parts in the Netherlands with DSM-IV diagnosis of dementia, respectively. Both datasets included NPS, dementia stage, psychotropic drug use, age, and gender. Waalbed-II also included quality of life, ALD-function, cognition, and etiology. The studies were a cross-sectional and longitudinal cohort, data collection was performed by licensed vocational nurses. Exploratory factor analysis was used. More details of Waalbed I (Zuidema *et al.*, 2007a, b; 2009) and Waalbed-II (Wetzels *et al.*, 2010) are published elsewhere.

NPS were assessed using the NPI-NH. The NPI-NH was originally developed by Cummings *et al.* (Cummings *et al.*, 1994). The nursing home version has been adapted for use by professional caregivers in nursing home facilities and has proven to be valid and reliable for use by trained nursing staff (Wood *et al.*, 2000; Zuidema *et al.*, 2011). A Dutch translation is reliable and valid (Kat *et al.*, 2002). The NPI-NH includes 12 NPS: delusions,

https://doi.org/10.1017/S1041610216001216 Published online by Cambridge University Press

hallucinations, agitation, depression/dysphoria, anxiety, euphoria/elation, apathy/indifference, disinhibition, irritability/lability, aberrant motor behavior, sleep disturbances, and appetite/eating change. The frequency (F) and severity (S) of each symptom were rated on a five-point (0– 4) and four-point (0–3) Likert scale, respectively. A separate score was calculated for each symptom by multiplying the frequency and severity scores, resulting in values ranging from 0 to 12 for each symptom. Summing F x S scores reveals a total score that ranges from 0 to 144.

Agitation was measured with the 29-items CMAI Dutch version (CMAI-D). CMAI-D items were rated on a seven-point scale (1–7) ranging from "never" to "several times an hour." The CMAI has a well-established (test–retest and inter-rater) reliability (Zuidema *et al.*, 2011) and concurrent validity (Zuidema *et al.*, 2007a) in both community samples (Koss *et al.*, 1997) and in nursing homes patients.

Clinically relevant NPS were defined as a "Frequency x Severity" score >= 4 for each individual symptom in the NPI-NH (Wood *et al.*, 2000; Margallo-Lana *et al.*, 2001) and a score of "at least once a week" (frequency score > 2) in CMAI-items.

We used exploratory factor analysis (Principal Component Analysis) to assess the clustering of the items in the CMAI and the items in the NPI-NH into components, separately for both scales and gender. We analyzed whether the components differ between males and females. Different components in males and females indicate a different correlation between questionnaire items for male and female patients. The results were displayed in a pattern matrix.

Kaiser–Meyer–Olkin measure of sampling adequacy (whether the sample size is adequate) and Bartlett's test of sphericity (intercorrelation between the variables) were determined. In the factor analyses, all the items of CMAI (29 questions) and NPI-NH (12 F x S) were used for the analysis. We applied oblique rotation, which allows the components themselves to be correlated with one another. Components were retained using the Kaiser criteria (eigenvalues of component >1). Components consisting of just one variable were excluded. We characterized components based on loadings equal or greater than 0.4 in the pattern matrix (Stevens, 1992).

Differences in symptom clustering between male and female patients were assessed using a three-step procedure, displayed in a table for CMAI and NPI-NH separately:

1. We identified distinctive items per component, that is items clustering in males but not in females, or vice versa in components identifying similar traits.
2. We described the correlation coefficients between this distinctive item with the other items in this component for males and females separately.
3. We tested whether the correlation between a distinctive item and any another item in the component (which is present in both sexes) is different for males and females using an ANCOVA (analysis of covariance) with the distinctive item as dependent variable, any other item as independent variable, and an interaction term between gender and independent variable added to the model.

Example

For example, in female patients, a component consists of ITEMS X1, X2, X3, and X4, whereas in males a component consists of ITEMS X2, X3, and X4. The item X1 is identified as a distinctive item, indicating a different (cor)relation for male and female patients with the other items. The correlations between X1 and X2, X1and X3, and X1 and X4 are calculated separately for males and females. Difference in correlation of X1 and X2 between males and females is examined using a general linear model assessing the interaction between X1 and gender (step 3), depicted as X2=b0+b1xX1 + b2xGENDER + b3xX1xGENDER. A significant interaction (b3) indicates a different correlation between item X1 and X2 for male and female patients. Similar models are tested for X1and X3, and for X1 and X4.

All statistical analyses were conducted using SPSS statistics version 20.

Results

Baseline – Data on a total of 1,609 patients in nursing homes with dementia (WAALBED I N = 1322, WAALBED II N = 287) was available (see Table 1). The mean age was 83.1 years, almost 80% of the patients were female. In the database, the mean number of clinically relevant items of CMAI and NPI are 4.3 and 2.4, respectively. The number of patients with clinical relevant behavior was 80% in the NPI and 61% for the CMAI. The mean total score of CMAI and NPI was 46.9 and 20.8, respectively.

Factor analysis NPI-NH

FACTOR LOADING: The results of the factor analysis are shown in Table 2. In the male patients, five clusters were retained consisting of two to three items. The five clusters explained 63.1% of the variance in the data. The first cluster could be described as "frontal/agitation" which has high loadings on agitation, disinhibition, and

https://doi.org/10.1017/S1041610216001216 Published online by Cambridge University Press

Table 1. Description of nursing home patients ($N = 1609$)

Mean age mean (SD) years	83.1 (7.9)
Gender, female *N* (%)	1274 (79.2)
CMAI total score (mean (SD) range)	46.95 (16.2) 29–154 M = *47.03 (15.0)* F = *46.93 (16.5)*
Number of clinically relevant behaviors on the CMAI (f > 2) (mean (SD) range)	4.3 (3.7) 0–23
NPI-NH score (total mean (SD) range)	20.84 (17.9) 0–123 M = *21.82 (18.3)* F = *20.58 (17.8)*
Number of clinically relevant symptoms on the NPI-NH (F x S > 3) mean (SD) range	2.43 (2.1) 0–11

N Number, SD standard deviation

Table 2. Clusters NPS – NPI-NH factor loading (Pattern matrix)

	COMPONENT							
	1		2		3		4	5
	M	F	M	F	M	F	M	M
Agitation/aggression	0.867#	0.668#						
Disinhibition	0.507#	0.742#						
Irritability	0.820#	0.715#						
Euphoria		0.558#					0.713 €	
Delusions			−0.784					
Hallucinations			−0.911	0.406$				
Depression				0.629$				0.858$
Anxiety				0.695$				0.681$
Motor disturbance				0.561€			0.568€	
Night-time behavior				0.478€			0.690€	
Apathy					0.788	0.765		
Appetite/eating					0.639	0.573		
Total variance explained (%)	24.4	24.8	11.3	10.3	9.1	9.7	9.7	8.7

Symbols indicate a clustering of symptoms in both male and female patients and correlate with the clusters in Table 3 (correlation coefficients)/€ in F motor disturbance, night-time behavior is a cluster, in M same items with euphoria added.
$ in M depression, anxiety is a cluster, in F same items with hallucinations added.
# in M agitation, disinhibition, irritability is a cluster, in F same items with euphoria added.

irritability. The second cluster is "psychosis" with high loadings on delusions and hallucinations. The third cluster is "physical disturbance/hyperactivity" consisting euphoria, motor disturbance, and night-time behavior. Cluster four is "apathy" with high loadings on apathy and appetite/eating, and the last cluster is "affect/mood" with loadings on depression and anxiety.

In the female patients, only three clusters were retained consisting of two to five items. The clusters explained 44.7% of the variance of the data. The first cluster is "frontal/agitation" with high loadings on agitation, disinhibition, irritability, and euphoria. This cluster is comparable to the male cluster, except the item euphoria. The second cluster is a combination of psychosis, affect, and physical disturbance/hyperactivity when comparing with the male clusters on the NPI. The third and last cluster is "apathy" with high loadings on apathy and appetite/eating, which is the same as the male cluster of apathy.

In the female patients, the item delusions is not included in all the clusters due to the loading less than 0.4.

INTERACTION TERM (Table 3): Three distinctive items were identified. In the male population, a different relation can be seen between euphoria and motor disturbance (symbol €) compared to the female sample.

In the female sample, there is a different relation between euphoria and agitation and disinhibition, but not in males, displayed as a *p*-value with the symbol #. Furthermore, there is a different relation between euphoria and hallucinations and depression in the female population but not in the male population (symbol $).

Factor analysis CMAI

FACTOR LOADING: The results of the factor analysis of the CMAI variables are shown in Table 4. In the male patients, eight clusters were

https://doi.org/10.1017/S1041610216001216 Published online by Cambridge University Press

Table 3. Correlation coefficients distinctive items with other group items

		M	F	*p*-VALUE INTERACTION TERM
Distinctive item: Euphoria #	Agitation	0.051	0.168	**0.016**
	Disinhibition	0.204	0.258	**0.050**
	Irritability	0.118	0.171	0.175
Distinctive item: Hallucinations $	Depression	0.007	0.160	**0.038**
	Anxiety	0.110	0.140	0.868
Distinctive item: Euphoria €	Motor disturbance	0.234	0.054	**0.025**
	Night-time behavior	0.224	0.057	0.062

M Male, F Female, Symbols correlate with the clusters in Table 2 (factor loading).

retained consisting of two to five items. These clusters explained 57.6% of the variance of the data. The first cluster represented "physically non-aggressive behavior" and has high loadings on paces, trying to get into a different place, general restlessness, inappropriate dress or disrobing, and handling things inappropriately. The second cluster is "physically aggressive behavior" with high loadings on hitting, kicking, grabbing onto people, pushing. The third cluster is "verbally (non-)aggressive behavior" consisting of cursing or verbal aggression, complaining, and negativism. The fourth cluster is "sexual behavior" with the variables making verbal sexual advances and making physical sexual advances. The fifth cluster represents "vocal agitation" with strange noises and screaming. The sixth cluster is "hiding/hoarding objects" and consists hiding things and hoarding things. The seventh cluster represents "physically aggressive behavior" with high loading on biting and scratching. The last cluster is "inappropriate handling of objects" and has high loadings on tearing things or destroying property, eating/drinking inappropriate substances, and hurt self or others.

In the female patients, seven clusters were retained consisting of two to seven items. These clusters explained 53.9% of the variance of the data. The first cluster represents "physically non-aggressive behavior" and has high loadings on paces, trying to get into a different place, and general restlessness. The second cluster is "physically aggressive behavior" with high loadings on hitting, kicking, grabbing onto people, pushing, throwing things, biting, and scratching. The third cluster represents "verbally (non-)aggressive behavior" consisting of cursing or verbal aggression, complaining, negativism, and performing repetitious mannerisms. These three clusters are comparable with the male patients. The fourth cluster represents "sexual behavior" with the variables making verbal sexual advances and making physical sexual advances, identical to the male patients. The fifth cluster is "vocal agitation" with strange noises and screaming, also identical to the male patients. The sixth cluster is a combination of "hiding/hoarding objects" and "inappropriate handling of objects" and has high loadings on inappropriate dress or disrobing, handling things inappropriately, tearing things or destroying property, hiding things and hoarding things, partly comparable with the male patients. The last cluster is "verbally repetitive behavior" with high loadings on constant unwarranted request of attention or help and repetitive sentences or questions. This is a cluster not seen in the male patients.

INTERACTION TERM (Table 5): A total of ten distinctive items were identified. In the male population, there is a different relation between inappropriate dress or disrobing and paces and general restlessness (symbol *) compared to the female population.

In the female patients, a different relation is present between throwing things and hitting, kicking, grabbing, and pushing (symbol $), between performing repetitious mannerisms and biting and scratching (symbol %), between biting and hitting, kicking and pushing (symbol @), between scratching and hitting, kicking, grabbing, and pushing (symbol +), between performing repetitious mannerisms and complaining (symbol ^), between inappropriate dress or disrobing and hiding things (symbol !), compared to the male patients.

Discussion

This study examined the differences in gender in clustering of NPS in the nursing home patients with dementia using factor analysis. We found differences in the clusters of NPS between gender. There is no homogenous clustering in both male and female patients. Some clusters appear in both male as female patients, some are only seen in male and not in female and vice versa, and last, there are clusters which have partly the same variables.

https://doi.org/10.1017/S1041610216001216 Published online by Cambridge University Press

https://doi.org/10.1017/S1041610216001216 Published online by Cambridge University Press

Table 4. Cluster NPS – CMAI factor loading (Pattern matrix)

	COMPONENT														
	1		2		3		4		5		6		7	8	
	M	F	M	F	M	F	M	F	M	F	M	F	M	M	F
Paces	0.792*#	0.811*#													
Trying to get to a different place	0.679*#	0.753*#													
Inappropriate dress or disrobing	0.547*											−0.427!			
Handling things inappropriately	0.427#											−0.637?			
General restlessness	0.783*#	0.610*#													
Hitting			0.823$@+	0.819$@+											
Kicking			0.758$@+	0.823$@+											
Grabbing onto people			0.447$@+	0.412$@+											
Pushing			0.691$@+	0.691$@+											
Throwing things				0.536 $											
Biting				0.691 % @									0.752%		
Scratching				0.602 % +									0.696%		
Cursing or verbal aggression					0.473^	0.438^									
Complaining					0.818^	0.702^									
Negativism					0.844^	0.696^									
Constant unawarranted request for attention or help															−0.817
Repetitive sentences or questions															−0.867

https://doi.org/10.1017/S1041610216001216 Published online by Cambridge University Press

Table 4. Continued

	COMPONENT														
	1		2		3		4		5		6		7	8	
	M	F	M	F	M	F	M	F	M	F	M	F	M	M	F
Making verbal sexual advances							0.901	0.801							
Making physical sexual advances							0.920	0.826							
Strange noises									0.752	0.783					
Screaming									0.648	0.648					
Performing repetitious mannerisms						−0.413^							0.573%		
Hiding things											0.872&!?	−0.750&!?			
Hoarding things											0.848&!?	−0.757&!?			
Tearing things or destroying property												−0.580 &		0.638	
Eating/drinking inappropriate substances														0.793	
Hurt self or others														0.495	
Total variance explained	14.9	10.0	10.4	18.6	7.3	3.5	6.3	4.7	4.2	5.1	4.7	4,5	5.4	4.4	7.3

M male, F female, Symbols indicate a clustering of symptoms in both male and female patients and correlate with the clusters in Table 5 (correlation coefficients with *p*-value).
* in F paces, trying to get to a different place, general restlessness is a cluster, in M same items with inappropriate dress or disrobing added.
# in F paces, trying to get to a different place, general restlessness is a cluster, in M same items with handling things inappropriately added.
$ in M hitting, kicking, grabbing onto people, pushing is a cluster, in F same items with throwing things added.
@ in M hitting, kicking, grabbing onto people, pushing is a cluster, in F same items with biting added.
+ in M hitting, kicking, grabbing onto people, pushing is a cluster, in F same items with scratching added.
% in F biting, scratching is a cluster, in M same items with performing repetitious mannerisms added.
^ in M cursing, complaining, negativism is a cluster, in F same items with performing repetitious mannerisms added.
& in M hiding things, hoarding things is a cluster, in F same items with tearing things or destroying property added.
! in M hiding things, hoarding things is a cluster, in F same items with inappropriate dress or disrobing added.
? in M hiding things, hoarding things is a cluster, in F same items with handling things inappropriately added.

Table 5. Correlation coefficients distinctive items with other group items

		M	F	*p*-VALUE INTERACTION TERM
Distinctive item: inappropriate dress or disrobing*	paces	0.458	0.329	**0.001**
	trying to get to a different place	0.242	0.258	0.628
	general restlessness	0.408	0.240	**0.000**
Distinctive item: Handling things inappropriately #	paces	0.352	0.252	0.139
	trying to get to a different place	0.251	0.187	0.279
	general restlessness	0.344	0.267	0.116
Distinctive item: throwing things$	hitting	0.166	0.369	**0.000**
	kicking	0.241	0.428	**0.000**
	Grabbing onto people	0.143	0.257	**0.014**
	pushing	0.192	0.361	**0.002**
Distinctive item: biting @	hitting	0.338	0.509	**0.000**
	kicking	0.311	0.446	**0.000**
	Grabbing onto people	0.268	0.275	0.129
	pushing	−0.014	0.289	**0.000**
Distinctive item: scratching+	hitting	0.130	0.414	**0.000**
	kicking	0.093	0.382	**0.000**
	Grabbing onto people	0.146	0.240	**0.009**
	pushing	−0.031	0.309	**0.000**
Distinctive item: performing repetitious mannerisms%	biting	0.219	0.117	**0.037**
	scratching	0.181	0.152	0.237
Distinctive item: performing repetitious mannerisms^	cursing	0.168	0.123	0.665
	complaining	0.114	−0.027	**0.029**
	negativism	0.102	0.029	0.251
Distinctive item: tearing things or destroying property &	hiding things	0.051	0.172	0.098
	hoarding things	0.145	0.223	0.316
Distinctive item: inappropriate dress or disrobing!	hiding things	0.285	0.260	**0.035**
	hoarding things	0.165	0.258	0.654
Distinctive item: Handling things inappropriately?	hiding things	0.215	0.322	0.364
	hoarding things	0.274	0.366	0.446

M male, F female, Symbols correlate with the cluster in Table 4 (factor loading).

In some of these clusters of NPS, there are different correlations between the items for male and female patients. In our interaction term analysis, there are more different relations in the female patients, compared to the males. Some correlations are based on coincidence.

We are aware that the found distinctive items can be tested in different combinations of independent variable, making it even possible that a distinctive item is tested as an independent variable. In our analysis, we did not explore all the combinations.

The clusters found in this study are partly consistent with those found in other studies in nursing home patients; Waalbed-I found four to five clusters in the NPI, our clusters frontal, psychosis, apathy, and mood are similar. These are comparable due to the fact that our database is largely composed by the Waalbed 1-database. The CMAI was also studied and found six clusters, where we found seven to eight clusters. This could be explained by the exclusion of low frequency questionnaire items (nine items). Physically aggressive, verbally agitated behavior, and hiding/hoarding are mostly comparable, and physically non-aggressive behavior and vocal agitation were identical clusters. In comparison with the study from Sweden, more clusters are described, using a different questionnaire than us, the MDDAS with 39 items (25 behavioral, 14 psychological). The Swedish study found six behavioral clusters (aggressive, restless, wandering, escape, verbally disruptive, regressive) and five psychological clusters (depressive, paranoid, hallucinatory, hyperactive, passiveness).

In the community-dwelling patients, the clusters were comparable with those in our study (Aalten *et al.*, 2003), the clusters in the combined community and nursing home patients were less comparable (Hollingworth *et al.*, 2006).

Our study extends previous analysis due to the dimension of gender; it shows extra clusters or splits clusters of previous studies.

https://doi.org/10.1017/S1041610216001216 Published online by Cambridge University Press

Our findings combined with the results of other studies implicate a clinical relevance of the dimension gender in dementia, especially with respect to differences in clusters of NPS. The differences due to gender could be explained in many ways, like anatomic, biochemical, neurochemical, and psychosocial. Several studies have tried to explain the gender differences in behavior but most were inconclusive. Certain trends can be observed. For example, male patients are less likely to have problems in mood and anxiety due to neurochemical mechanisms, and tend to have a different pain tolerance than females (Racine *et al.*, 2012). Female patients are more aware of their physical changes due to puberty, pregnancy and menopause, and express problems more often due to the social role (mother, caregiver) (Kamath, 2011).

There is no clear explanation for the found differences. We expect other studies to corroborate our findings.

The uniqueness of this study is that it shows the importance of the dimension of gender in NPS. Significant differences can be seen in several clusters. Our data consists of a large nursing home population, to our knowledge, the only and largest on which a factor analysis has been performed differentiated by gender. We used the NPI-NH and CMAI, which are well-validated instruments and universally accepted.

Our study also had some limitations. First, the database had no etiology of dementia in a large proportion of patients, due to the methodology of Waalbed 1. Second, we have a low percentage of male patients in the study.

Considering the clinical relevance, we did not exclude low prevalence items in view of the large patient population (for example, 10% in our database are 160 patients, and 5% are 80). These are relatively large numbers.

Conclusion

Our study found differences in clusters of NPS between gender using factor analyses. These clusters are partly comparable with previous studies and affirm the clinical differences seen in practice. Male and female patients differ from each other in terms of symptoms expressed.

The results of our study should be interpreted with care, since this is the first factor analysis between gender in clusters of NPS. There is a great need for exploration in other large nursing home populations. If our results are confirmed by others, it might improve our understanding of the behavior in patients with dementia and help clarify the role of neurochemical, biological, and psychosocial aspects. This might lead to a more rational pharmacologic and non-pharmacologic choice of treatment. Although the prevalence of NPS differ from country to country, the different behavioral dimensions that underly the different NPS is probably more robust across different countries and cultures. Therefore, we think, that although only Dutch data are used in this study, the results are generalizable to other countries.

Further research is needed to clarify the biological, social, and chemical role in NPS in patients with dementia: How are cause and effect really related to each other?

Our findings implicate that gender does make a difference in the clusters of NPS in dementia. This might require a different approach in treatment that takes into account the influence of neurochemical, biochemical, and psychosocial aspects. This also means that the sex-specific clustering of these NPS may reflect different underlying (behavioral) syndromes with different anatomical and neurochemical background, which should also be treated differently.

Conflict of interest

None.

Description of authors' roles

All authors participated in study concept and design, RBW and SUZ participated in acquisition of subjects and/or data, all authors participated in analysis and interpretation of data, and preparation of paper.

Acknowledgments

None.

References

Aalten, P. *et al.* (2003). Behavioral problems in dementia: a factor analysis of the neuropsychiatric inventory. *Dementia and Geriatric Cognitive Disorders*, 15, 99–105.

Aalten, P. *et al.* (2007). Neuropsychiatric syndromes in dementia. Results from the European Alzheimer disease consortium: part I. *Dementia and Geriatric Cognitive Disorders*, 24, 457–463.

Aalten, P., de Vugt, M. E., Jaspers, N., Jolles, J. and Verhey, F. R. (2005). The course of neuropsychiatric symptoms in dementia. Part II: relationships among behavioural sub-syndromes and the influence of clinical

https://doi.org/10.1017/S1041610216001216 Published online by Cambridge University Press

variables. *International Journal of Geriatric Psychiatry*, 20, 531–536.

Batsch, N. L. and Mittelman, M. S. (2012). World Alzheimer Report 2012 Overcoming the stigma of dementia. *Alzheimer's Disease international*. https://www.alz.co.uk/research/WorldAlzheimerReport2012.pdf; last accessed 4 August 2016.

Black, W. and Almeida, O. P. (2004). A systematic review of the association between the behavioral and psychological symptoms of dementia and burden of care. *International Psychogeriatrics*, 16, 295–315.

Buchanan, R. J., Wang, S., Ju, H. and Graber, D. (2004). Analyses of gender differences in profiles of nursing home residents with Alzheimer's disease. *Gender Medicine*, 1, 48–59.

Cohen-Mansfield, J., Marx, M. S. and Rosenthal, A. S. (1989). A description of agitation in a nursing home. *Journal of Gerontology*, 44, M77–84.

Cummings, J. L., Mega, M., Gray, K., Rosenberg-Thompson, S., Carusi, D. A. and Gornbein, J. (1994). The neuropsychiatric inventory: comprehensive assessment of psychopathology in dementia. *Neurology*, 44, 2308–2314.

Frisoni, G. B. *et al.* (1999). Behavioral syndromes in Alzheimer's disease: description and correlates. *Dementia and Geriatric Cognitive Disorders*, 10, 130–138.

Hollingworth, P. *et al.* (2006). Four components describe behavioral symptoms in 1,120 individuals with late-onset alzheimer's disease. *Journal of the American Geriatrics Society*, 54, 1348–1354.

Hope, T., Keene, J., Fairburn, C., McShane, R. and Jacoby, R. (1997). Behaviour changes in dementia. 2: are there behavioural syndromes? *International Journal of Geriatric Psychiatry*, 12, 1074–1078.

Kales, H. C., Gitlin, L. N., Lyketsos, C. G., Detroit Expert Panel on, A. and Management of Neuropsychiatric Symptoms of, D. (2014). Management of neuropsychiatric symptoms of dementia in clinical settings: recommendations from a multidisciplinary expert panel. *Journal of the American Geriatrics Society*, 62, 762–769.

Kamath, A. F. (2011). Gender and ethnic disparities in pain management. *Clinical Orthopaedics and Related Research*, 469, 1962.

Kat, M. G., de Jonghe, J. F., Aalten, P., Kalisvaart, C. J., Droes, R. M. and Verhey, F. R. (2002). [Neuropsychiatric symptoms of dementia: psychometric aspects of the Dutch Neuropsychiatric Inventory (NPI)]. *Tijdschrift Gerontologie en Geriatrie*, 33, 150–155.

Kim, J. M., Lyons, D., Shin, I. S. and Yoon, J. S. (2003). Differences in the behavioral and psychological symptoms between Alzheimer's disease and vascular dementia: are the different pharmacologic treatment strategies justifiable? *Human Psychopharmacology*, 18, 215–220.

Kitamura, T., Kitamura, M., Hino, S., Tanaka, N. and Kurata, K. (2012). Gender differences in clinical manifestations and outcomes among hospitalized patients with behavioral and psychological symptoms of dementia. *The Journal of Clinical Psychiatry*, 73, 1548–1554.

Koss, E. *et al.* (1997). Assessing patterns of agitation in Alzheimer's disease patients with the cohen-mansfield agitation inventory. The Alzheimer's disease cooperative study. *Alzheimer Disease and Associated Disorders*, 11, S45–50.

Lawlor, B. and Bhriain, S. N. (2001). Psychosis and behavioural symptoms of dementia: defining the role of neuroleptic interventions. *International Journal of Geriatric Psychiatry*, 16, S2–6.

Lovheim, H., Sandman, P. O., Kallin, K., Karlsson, S. and Gustafson, Y. (2006). Relationship between antipsychotic drug use and behavioral and psychological symptoms of dementia in old people with cognitive impairment living in geriatric care. *International Psychogeriatrics*, 18, 713–726.

Lovheim, H., Sandman, P. O., Karlsson, S. and Gustafson, Y. (2009). Sex differences in the prevalence of behavioral and psychological symptoms of dementia. *International Psychogeriatrics*, 21, 469–475.

Lyketsos, C. G., Steinberg, M., Tschanz, J. T., Norton, M. C., Steffens, D. C. and Breitner, J. C. (2000). Mental and behavioral disturbances in dementia: findings from the Cache county study on memory in aging. *The American Journal of Psychiatry*, 157, 708–714.

Margallo-Lana, M. *et al.* (2001). Prevalence and pharmacological management of behavioural and psychological symptoms amongst dementia sufferers living in care environments. *International Journal of Geriatric Psychiatry*, 16, 39–44.

Moore, M. J., Zhu, C. W. and Clipp, E. C. (2001). Informal costs of dementia care: estimates from the national longitudinal caregiver study. *The Journals of Gerontology, Series B, Psychological Sciences and Social Sciences*, 56, S219–228.

Neri, M., Bonati, P. A., Pinelli, M., Borella, P., Tolve, I. and Nigro, N. (2007). Biological, psychological and clinical markers of caregiver's stress in impaired elderly with dementia and age-related disease. *Archives of Gerontology and Geriatrics*, 44, 289–294.

Pearson, J. L., Teri, L., Reifler, B. V. and Raskind, M. A. (1989). Functional status and cognitive impairment in Alzheimer's patients with and without depression. *Journal of the American Geriatrics Society*, 37, 1117–1121.

Peters, K. R. *et al.* (2006). Characterizing neuropsychiatric symptoms in subjects referred to dementia clinics. *Neurology*, 66, 523–528.

Racine, M., Tousignant-Laflamme, Y., Kloda, L. A., Dion, D., Dupuis, G. and Choiniere, M. (2012). A systematic literature review of 10 years of research on sex/gender and pain perception - part 2: do biopsychosocial factors alter pain sensitivity differently in women and men? *Pain*, 153, 619–635.

Rockwell, E., Choure, J., Galasko, D., Olichney, J. and Jeste, D. V. (2000). Psychopathology at initial diagnosis in dementia with Lewy bodies versus Alzheimer disease: comparison of matched groups with autopsy-confirmed diagnoses. *International Journal of Geriatric Psychiatry*, 15, 819–823.

Rodney, V. (2000). Nurse stress associated with aggression in people with dementia: its relationship to hardiness, cognitive appraisal and coping. *Journal of Advanced Nursing*, 31, 172–180.

Selbaek, G., Engedal, K., Benth, J. S. and Bergh, S. (2014). The course of neuropsychiatric symptoms in

https://doi.org/10.1017/S1041610216001216 Published online by Cambridge University Press

nursing-home patients with dementia over a 53-month follow-up period. *International Psychogeriatrics*, 26, 81–91.

Stevens, J. (1992). *Applied Multivariate Statistics for the Social Sciences*. London: L. Erlbaum Associates.

Testad, I., Aasland, A. M. and Aarsland, D. (2007). Prevalence and correlates of disruptive behavior in patients in Norwegian nursing homes. *International Journal of Geriatric Psychiatry*, 22, 916–921.

Valentino, R. J., Bangasser, D. and Van Bockstaele, E. J. (2013). Sex-biased stress signaling: the corticotropin-releasing factor receptor as a model. *Molecular Pharmacology*, 83, 737–745.

Wetzels, R. B., Zuidema, S. U., de Jonghe, J. F., Verhey, F. R. and Koopmans, R. T. (2010). Course of neuropsychiatric symptoms in residents with dementia in nursing homes over 2-year period. *The American Journal of Geriatric Psychiatry*, 18, 1054–1065.

Wood, S. *et al.* (2000). The use of the neuropsychiatric inventory in nursing home residents. Characterization and measurement. *The American Journal of Geriatric Psychiatry*, 8, 75–83.

Wortmann, M. (2012). Dementia: a global health priority - highlights from an ADI and World Health Organization report. *Alzheimer' s Research & Therapy*, 4, 40.

Zuidema, S. U. *et al.* (2011). Assessing neuropsychiatric symptoms in nursing home patients with dementia: reliability and reliable change index of the neuropsychiatric inventory and the cohen-mansfield agitation inventory. *International Journal of Geriatric Psychiatry*, 26, 127–134.

Zuidema, S. U., de Jonghe, J. F., Verhey, F. R. and Koopmans, R. T. (2007a). Agitation in Dutch institutionalized patients with dementia: factor analysis of the Dutch version of the cohen-mansfield agitation inventory. *Dementia and Geriatric Cognitive Disorders*, 23, 35–41.

Zuidema, S. U., de Jonghe, J. F., Verhey, F. R. and Koopmans, R. T. (2007b). Neuropsychiatric symptoms in nursing home patients: factor structure invariance of the Dutch nursing home version of the neuropsychiatric inventory in different stages of dementia. *Dementia and Geriatric Cognitive Disorders*, 24, 169–176.

Zuidema, S. U., de Jonghe, J. F., Verhey, F. R. and Koopmans, R. T. (2009). Predictors of neuropsychiatric symptoms in nursing home patients: influence of gender and dementia severity. *International Journal of Geriatric Psychiatry*, 24, 1079–1086.

Zuidema, S. U., Derksen, E., Verhey, F. R. and Koopmans, R. T. (2007c). Prevalence of neuropsychiatric symptoms in a large sample of Dutch nursing home patients with dementia. *International Journal of Geriatric Psychiatry*, 22, 632–638.

https://doi.org/10.1017/S1041610216001216 Published online by Cambridge University Press