
UNIVERSITE DE LAUSANNE - FACULTE DE BIOLOGIE ET DE MEDECINE

Département de Psychiatrie - CHUV
Service Universitaire de Psychiatrie de l'Age Avancé

**Cognition et psychopathologie chez les nonagénaires et centenaires
vivant en établissement médico-social gériatrique en Suisse :
focalisation sur l'anosognosie**

THESE

préparée sous la direction du Professeur Armin von Gunten

et présentée à la Faculté de biologie et de médecine de
l'Université de Lausanne pour l'obtention du grade de

DOCTEUR EN MEDECINE

par

Jean-Frédéric MALL

BMTÉ 3752

Médecin diplômé de la Confédération Suisse
Originaire de Luxembourg

Lausanne

2014

Bibliothèque Universitaire
de Médecine / BIUM
CHUV-BH08 - Bugnon 46
CH-1011 Lausanne

R0078 9319

VVT
150
MAL

Imprimatur

Vu le rapport présenté par le jury d'examen, composé de

Directeur de thèse Monsieur le Professeur Armin von Gunten

Co-Directeur de thèse

Expert Monsieur le Professeur Jean-François Démonet

*Directrice de l'Ecole Madame le Professeur Stephanie Clarke
doctorale*

la Commission MD de l'Ecole doctorale autorise l'impression de la thèse de

Monsieur Jean-Frédéric Mall

intitulée

*Cognition et psychopathologie chez les nonagénaires et
centenaires vivant en établissement médico-social gériatrique
en Suisse: focalisation sur l'anosognosie*

Lausanne, le 20 mai 2014

*pour Le Doyen
de la Faculté de Biologie et de Médecine*



*Madame le Professeur Stephanie Clarke
Directrice de l'Ecole doctorale*

RESUME

Les nonagénaires et centenaires voient actuellement leur nombre augmenter considérablement, beaucoup d'entre eux vivant en maison de retraite. Pour cette population, on dispose de très peu de données au sujet de la symptomatologie psychiatrique et des capacités cognitives autres que mnésiques. Cette étude exploratoire se concentre sur l'anosognosie et ses liens avec les symptômes psychiatriques et cognitifs courants.

Cinquante-huit sujets âgés de 90 ans ou plus ont été recrutés dans des établissements médico-sociaux gériatriques et divisés en 5 groupes selon le Mini Mental State Examination (MMSE). Les évaluations incluent le test des 5 mots, le CLOX, les fluences lexicales et catégorielles, le questionnaire d'anosognosie-démence (AQ-D), l'inventaire neuropsychiatrique (NPI) et l'index de comorbidité de Charlson.

Les sujets étudiés présentent une atteinte cognitive modérée, le MMSE moyen (\pm DS) étant à 15.41 ± 7.04 . L'anosognosie augmente avec l'atteinte cognitive, étant associée avec tous les domaines cognitifs, mais aussi avec les symptômes psychopathologiques d'apathie et d'agitation. Les sujets ayant une atteinte cognitive légère semblent moins anosognosiques que ceux avec l'atteinte cognitive la plus faible ou ceux ne présentant aucune atteinte. Ni l'anosognosie ni les symptômes psychopathologiques ne sont liés aux comorbidités somatiques.

Chez les résidents très âgés étudiés vivant en maison de retraite, l'anosognosie est principalement légère. Elle est associée à des changements cognitifs, mais aussi psychopathologiques. Des investigations supplémentaires sont toutefois nécessaires pour déterminer s'il existe un lien causal entre l'anosognosie et les atteintes psychopathologiques.

ORIGINAL ARTICLE

Cognition and psychopathology in nonagenarians and centenarians living in geriatric nursing homes in Switzerland: a focus on anosognosia

Jean-Frédéric MALL,¹ Leila CHOUITER,¹ Jean-Philippe ANTONIETTI,² Karsten EBBING¹ and Armin von GUNTEN¹

¹Service of Old Age Psychiatry, Department of Psychiatry, Centre Hospitalier Universitaire Vaudois (CHUV), Prilly-Lausanne, and ²Institute of Psychology, University of Lausanne, Lausanne-Dorigny, Switzerland

Correspondence: Dr Jean-Frédéric Mall MD, Service of Old Age Psychiatry, Department of Psychiatry, Centre Hospitalier Universitaire Vaudois (CHUV), Site de Cery, CH-1008, Prilly-Lausanne, Switzerland. Email: jean-frederic.mall@chuv.ch

Received 7 April 2013; revision received 20 October 2013; accepted 12 December 2013.

Key words: anosognosia, apathy, cognition, depression, oldest old, psychopathology.

INTRODUCTION

Very old age has moved in recent years from the status of an anecdotal phenomenon to a significant concern for society. Data on dementia in the oldest old have begun to be commonly available. For example, the prevalence of dementia for persons older than 90 years in Western Europe has been estimated at 48% for women and 33% for men.¹ In Switzerland, more than half of the nonagenarians live at home. After age 80, the proportion of persons living in nursing homes rises sharply. More than 70% of those institutionalized over 75 suffer from dementia.^{2,3} However, little is known about their psychological

Abstract

Background: The number of nonagenarians and centenarians is rising dramatically, and many of them live in nursing homes. Very little is known about psychiatric symptoms and cognitive abilities other than memory in this population. This exploratory study focuses on anosognosia and its relationship with common psychiatric and cognitive symptoms.

Methods: Fifty-eight subjects aged 90 years or older were recruited from geriatric nursing homes and divided into five groups according to Mini-Mental State Examination scores. Assessment included the five-word test, executive clock-drawing task, lexical and categorical fluencies, Anosognosia Questionnaire-Dementia, Neuropsychiatric Inventory, and Charlson Comorbidity Index.

Results: Subjects had moderate cognitive impairment, with mean \pm SD Mini-Mental State Examination being 15.41 ± 7.04 . Anosognosia increased with cognitive impairment and was associated with all cognitive domains, as well as with apathy and agitation. Subjects with mild global cognitive decline seemed less anosognosic than subjects with the least or no impairment. Neither anosognosia nor psychopathological features were related to physical conditions.

Conclusions: Anosognosia in oldest-old nursing home residents was mostly mild. It was associated with both cognitive and psychopathological changes, but whether anosognosia is causal to the observed psychopathological features requires further investigation.

state and the presence of psychopathological features because of a lack of specific studies.

Among the common symptoms observed in this specific population, seemingly in relation to the high prevalence of dementia, is unawareness of one's own deficits, a complex notion that could be described as an impaired ability to see oneself from a third-person perspective. Unawareness is preferentially viewed as a dimensional rather than categorical function, with various methods of assessment producing different outcomes.⁴ There is no perfect tool to assess unawareness as a whole. Anosognosia covers generally a narrower range than the concept of impaired

insight. Lack of insight could be considered intrinsic to mental illness, a psychological reaction to mental illness or shaped by environmental factors. Anosognosia was first linked to the recognition of neurological deficits, to neurological and neuropsychological impairment, and distances itself from denial, which implies psychological mechanisms.⁵

As anosognosia seems strikingly frequent and empirically problematic in clinical settings, we have chosen to focus specifically on anosognosia, a limited but extensively explored aspect of unawareness, and its links with other cognitive and psychopathological deficits. In younger subjects, anosognosia has been correlated to a threefold increase in the risk of dangerous behaviours or putting oneself at risk for neglect;⁶ it is also a predictor of apathy in Alzheimer's disease.⁷ Anosognosia is closely associated with cognitive decline and psychiatric and behavioural disorders. More specifically, higher anosognosia is associated with lower depression scores.⁸ Depressive symptoms, including dysthymia but less clearly major depressive disorder, may have a potentially confounding effect between anosognosia and dementia severity, as people with depression show less diminished insight.⁹ In nursing homes, the prevalence of depression seems to be slightly lower in the very old than in younger subjects: 8.9% for persons aged 85 and older versus 13.3% for those aged 65–74.¹⁰ Residing in a nursing home is indicative of more frequent and increased depressive symptoms in the oldest old.¹¹

In this study, we hypothesized that anosognosia is related to cognitive and/or psychiatric disorders in the oldest old. As is the case in younger subjects, the magnitude of anosognosia depends on the severity of the symptoms. We expect that higher positive scores correlate with higher cognitive impairment, whereas negative scores correlate with depressive symptoms.

METHODS

Sample

The study is a naturalistic preliminary and exploratory study, with a cross-sectional design. A total of 58 subjects were assessed between October 2007 and November 2009 in three geriatric nursing homes located in Lausanne, Switzerland, where the Lausanne University Hospital Old-Age Psychiatry Liaison Unit intervenes on a regular basis. These institutions are not specialized in hosting people with advanced cognitive or psychiatric disorders, and

unless evident and severe, behavioural problems do not affect selection criteria on admission. An information note was sent to all residents aged 90 years or older and to their families. We aimed to obtain informed consent, if possible, from the subjects themselves and, in all cases, from a relative, in accordance with the Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects (2008). The study was approved by the Cantonal Research Ethics Committee (Protocol 12/07) in Vaud. A voluntary daytime caregiver (nurse or assistant-nurse) was also asked to complete the required questionnaires after each subject interview, in the interviewer's presence. Inclusion was limited to French-speaking men or women 90 years or older. Exclusion criteria were applied to a few tests only (e.g. severe auditory or visual deficiency, behavioural disorders, poor knowledge of the French language), and missing values did not prompt exclusion. Assessment by a family member, nurse or assistant nurse was always collected.

Because of the tests used, the small sample size, the lack of normative data for subjects over 90 for most of the tests and unclear criteria for dementia in the oldest old, we deliberately chose not to have a diagnostic approach. We preferred a dimensional description of cognitive and psychiatric signs and symptoms without determining any cut-offs or a specific diagnosis of dementia. The study subjects were divided into five groups according to Mini-Mental State Examination (MMSE) scores,¹² which provided a global cognitive functioning assessment. However, it was not the intention to classify subjects with any degree of dementia based on the widespread cut-offs used for younger persons, which are not applicable in this population. The MMSE groups were arranged based on scores as follows: Group 1, very severe global cognitive alteration (MMSE range: 0–6); Group 2, severe global cognitive alteration (range: 7–12); Group 3, moderate cognitive alteration (range: 13–18); Group 4, mild global cognitive alteration (range: 19–24), and Group 5, no or very mild alteration (range: 25–30).

Measures

We assessed the subjects using neuropsychological tests chosen according to how easily and quickly they could be administered and their suitability to the specific population in terms of auditory or visual

impairment. They had to be validated or at least be widely used with the oldest old. Interviewers were trained for these tests.

Cognitive variables included the MMSE as well as the five-word test (FWT) to obtain a more precise memory evaluation.¹³ The latter measures encoding, consolidation and recall, and has the benefit of assessing sensitivity to cueing. The FWT is scored on a 20-point weighted scale that assigns more points to free recall than to cued recall.¹⁴ We also assessed some aspects of executive function using easy-to-administer tools. The executive clock-drawing task (CLOX) is a modified clock-drawing test strongly associated with the MMSE and the Executive Interview. It consists of two parts: the CLOX 1, a directed clock-drawing task linked to executive function that is focused on procedural control, and the CLOX 2, a copy task involving visuospatial abilities.¹⁵ A 2-min categorical fluency (animals) and 2-min lexical verbal fluency (letter R) task was also administered.¹⁶ The two types of fluencies may have different vulnerabilities to the effects of normal and pathological ageing. Thus, lexical fluency is not affected by age. Categorical fluency may be more sensitive to dementia.¹⁷

Psychiatric variables were assessed using the Neuropsychiatric Inventory Questionnaire administered during an interview.¹⁸ It covers 12 neuropsychiatric symptom domains: delusions, hallucinations, agitation/aggression, depression/dysphoria, anxiety, euphoria/elation, apathy/indifference, disinhibition, irritability/lability, aberrant motor, night-time disturbances and appetite/eating disturbances. The Neuropsychiatric Inventory Questionnaire aims to bring to light major psychopathological issues. The severity of neuropsychiatric symptoms is assessed on a 3-point scale and distress experienced by the caregiver on a 5-point scale, yielding a total severity score of 0–36.

We used the term 'anosognosia' as defined by Starkstein *et al.*⁸ By this definition, anosognosia consists of two domains: the unawareness of cognitive deficits and the unawareness of behavioural problems. Anosognosia was assessed using the Anosognosia Questionnaire-Dementia (AQ-D),¹⁹ which was administered as an interview. The AQ-D is a validated and reliable scale for people with Alzheimer's disease. It is divided into two sections. The first section (22 questions) assesses intellectual functioning, which corresponds to basic activities of daily living and

instrumental activities of daily living. The second section (eight questions) assesses changes in interests and personality. Each answer is rated on a 4-point scale (0–3), according to the perceived frequency of the specific symptom. The same questionnaire was administered to the subject (Form A) and to the caretaker (Form B, written in the third person). The total score for each questionnaire ranges from 0 to 90. The final outcome, a discrepancy score, consists of subtracting the subject's from the caretaker's score (B – A) and reflects the degree of anosognosia. Positive scores indicate a higher degree of anosognosia, and negative scores indicate that the subjects consider themselves to be more severely affected than the caregiver does. The least anosognosic subjects are not those with the lowest scores, but those closest to the 0 value. Using data from medical records, we determined the Charlson Comorbidity Index,²⁰ an age-adjusted survival prognosis tool covering 19 comorbidities. Dementia was considered as the main potential clinical outcome and no point was given to this condition.

Statistical analysis

Data were processed with the SPSS Statistics ver. 20 software (IBM, Armonk, NY, USA) and R software (2009) (R Development Core Team, Vienna, Austria). A descriptive analysis was performed by calculating mean, median, standard deviations, range for continuous variables and frequencies for categorical variables. The significance of correlations for the AQ-D discrepancy scores with other variables was investigated using the Spearman's correlation coefficient (*r*). For categorical variables, χ^2 was used, and continuous variables were compared using the Kruskal–Wallis test. For multiple comparisons based on the Kruskal–Wallis test, critical values were adjusted with Bonferroni procedure to limit type I errors. Familywise error rate was set at 0.05.

RESULTS

Subjects' characteristics

The subjects' characteristics are presented in Table 1. These oldest old are mainly women, with an overall low education and moderate comorbidities.

Psychopathological features and cognitive assessment

The distribution of the MMSE values is not homogeneous, especially in the lowest range (0–5) (Fig. 1).

Table 1 Demographic characteristics of the sample

MMSE score		0-6	6-12	12-18	18-24	24-30	0-30
<i>n</i>		6	10	23	13	6	58
Age (years)	Mean ± SD	94.17 ± 2.14	93.30 ± 2.63	93.96 ± 3.65	93.00 ± 2.97	93.33 ± 2.94	93.59 ± 3.07
	Range	91-97	90-98	90-103	90-98	90-98	90-103
Gender	Men	1	0	0	3	1	5
	Women	5	10	23	10	5	53
Educational level	No diploma	0	1	2	0	0	3
	Practical training	1	7	18	11	3	40
	Basic school-leaving qualification	1	1	2	2	1	7
	Secondary school	0	1	0	0	2	3
	High school	0	0	1	0	0	1
Charlson Comorbidity Index (age adjusted)	Not available	4	0	0	0	0	4
	Mean ± SD	5.83 ± 0.98	7.70 ± 1.06	7.13 ± 1.49	8.15 ± 2.34	7.17 ± 1.83	7.33 ± 1.73
	Range	5-7	6-9	5-10	5-12	5-10	5-12

Note that Swiss high schools are a type of secondary school that prepares students for university matriculation. MMSE, Mini-Mental State Examination.

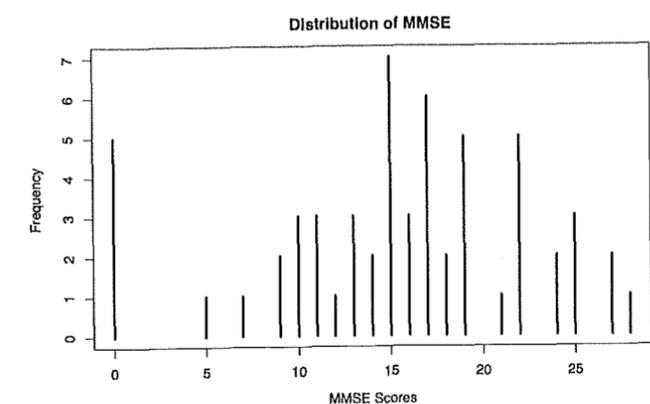


Figure 1 Frequency of distribution of MMSE scores in the sample. MMSE, Mini-Mental State Examination.

Based on the FWT, most of the subjects had a clinically obvious memory impairment. The scores on the other cognitive tests, including executive tests, were particularly low but with a wide variability across the sample. Some subjects have maintained very good cognitive abilities, while others are overtly demented. Two-minute verbal fluencies, both lexical and categorical, showed poor word production, which was more pronounced for the lexical than categorical fluency.

Psychopathological symptoms were usually minimal, with a mean ± SD Neuropsychiatric Inventory (NPI) total severity score of 6.24 ± 4.60 (range: 0-22; median: 5). The predominant symptoms were, in descending order, depression, anxiety and apathy.

The subjects' cognitive and psychopathological characteristics are shown in Table 2 and the severity of each neuropsychiatric symptom in Figure 2.

The descriptions of patients often do not coincide with those of their caretakers ($\chi^2_{(4)} = 29.462, P < 0.001$).

Anosognosia and its relation to cognitive and psychopathological variables

Anosognosia was significantly negatively correlated with the MMSE ($r = -0.723, P < 0.01$), FWT, CLOX 1, CLOX 2, and verbal fluency, both lexical and categorical ($P < 0.01$ for all correlations). Anosognosia was correlated positively with the NPI agitation subscale, NPI apathy subscale and NPI total severity scores ($P < 0.01$ for all correlations), as well as with the NPI aberrant behaviour subscale ($P < 0.05$). Quantitative results are shown in Table 3.

The perception subjects have of their difficulties does not always reflect their caretakers' perceptions. Overall, the discrepancies increase as cognitive impairment worsens, as shown in Figure 3.

Association between comorbidities and psychopathological features

There was no correlation between the Charlson Comorbidity Index and the NPI total severity score ($r = -0.085, P = 0.526$) or any of the NPI subscales.

DISCUSSION

The main findings of this study are the frequent occurrence of affective symptoms and mild anosognosia in the elderly dwelling in geriatric nursing homes. The magnitude of anosognosia was associated with symptoms of apathy and agitation. Depression,

Table 2 Cognitive and psychopathological characteristics ($n = 58$)

	MMSE (0-30)			MMSE (18-24)			MMSE (24-30)			
	Mean ± SD	Median	Range	Mean ± SD	Median	Range	Mean ± SD	Median	Range	
MMSE	15.41 ± 7.04	16	0-28	21.08 ± 1.89	22	19-24	26.17 ± 1.33	26	25-28	
Five-word test	7.90 ± 5.98	7	0-20	13.08 ± 3.55	13	8-20	15.83 ± 2.56	16	12-19	
CLOX 1	3.57 ± 3.91	2	0-14	6.23 ± 4.25	5	0-14	8.67 ± 3.98	9.5	4-13	
CLOX 2	6.22 ± 5.40	5.5	0-15	10.85 ± 3.89	13	4-15	12.50 ± 1.52	12.5	10-14	
Lexical fluency (letter R)	4.91 ± 4.85	4	0-21	5.85 ± 3.69	6	1-11	12.83 ± 4.96	11.5	8-21	
Categorical fluency (animals)	8.40 ± 6.96	7	0-33	12.00 ± 4.92	13	4-21	20.33 ± 9.11	20.5	9-33	
Anosognosia (difference)	23.40 ± 26.87	21.5	-19-75	3.23 ± 15.97	3	-19-42	-1.00 ± 10.24	-3	-9-19	
NPI	Delusions	0.34 ± 0.74	0	0-3	0.08 ± 0.28	0	0-1	0.00 ± 0.00	0	0-0
	Hallucinations	0.28 ± 0.72	0	0-3	0.00 ± 0.00	0	0-0	0.00 ± 0.00	0	0-0
	Agitation	0.64 ± 0.87	0	0-3	0.38 ± 0.77	0	0-2	0.50 ± 0.84	0	0-2
	Depression	1.12 ± 0.99	1	0-3	0.85 ± 0.90	1	0-2	1.33 ± 0.82	1.5	0-2
	Anxiety	0.91 ± 1.01	1	0-3	0.77 ± 0.73	1	0-2	0.50 ± 0.84	0	0-2
	Euphoria	0.21 ± 0.52	0	0-2	0.15 ± 0.55	0	0-2	0.00 ± 0.00	0	0-0
	Apathy	0.90 ± 1.14	0	0-3	0.38 ± 0.77	0	0-2	0.33 ± 0.52	0	0-1
	Disinhibition	0.14 ± 0.51	0	0-3	0.00 ± 0.00	0	0-0	0.00 ± 0.00	0	0-0
	Irritability	0.74 ± 0.97	0	0-3	0.46 ± 0.78	0	0-2	0.50 ± 0.84	0	0-2
	Aberrant behaviour	0.33 ± 0.80	0	0-3	0.00 ± 0.00	0	0-0	0.00 ± 0.00	0	0-0
	Sleep disorder	0.40 ± 0.72	0	0-2	0.08 ± 0.28	0	0-1	0.67 ± 1.03	0	0-2
	Appetite changes	0.34 ± 0.87	0	0-3	0.15 ± 0.55	0	0-2	0.00 ± 0.00	0	0-0
	Total severity score	6.24 ± 4.60	5	0-22	3.31 ± 2.50	3	0-10	3.67 ± 2.42	3.5	1-8

CLOX, executive clock-drawing test; MMSE, Mini-Mental State Examination; NPI, Neuropsychiatric Inventory.

anxiety and apathy were the three most common neuropsychiatric symptoms in our sample. Unlike in younger subjects, depression is not associated with increased mortality hazards in this population.²¹ Similarly, in our study, there were no correlations between physical comorbidities and neuropsychiatric symptoms, including depressive symptoms.

As in other studies,²² our results show that anosognosia has a negative correlation with the total MMSE score, which has also been found with younger subjects, as well as with executive functioning assessed with the CLOX test and with categorical and lexical fluencies. There is no correlation between anosognosia and age itself in our very elderly sample. In the present nursing home sample, the weight of somatic comorbidities is moderate, but there is no association with anosognosia or cognitive functioning. Moreover, there has been little research on this topic.²³ In our sample of oldest-old subjects, the anosognosia discrepancy score was positively correlated with apathy but not with depression, thus confirming findings of previous studies on younger subjects.⁴ Apathy was associated with poor awareness of cognitive and behavioural impairment, and was also associated with older age. Additionally, in the case of Alzheimer's dementia, apathy may be a

marker of more malignant forms of Alzheimer's disease and a predictor of depression in Alzheimer's disease.²⁴

This study showed that the least cognitively impaired subjects tended to exaggerate their difficulties as compared to the descriptions made by their caregivers, which is also a form of anosognosia. Subjects with greater cognitive impairment generally minimized their difficulties relative to their caretakers' descriptions, whereas subjects with only mild cognitive impairment seemed to do the opposite. However, this trend did not reach the threshold of statistical significance; the least anosognosic were those with mild to moderate global cognitive impairment according to MMSE scores. Depressive symptoms may be a mediating factor between cognitive impairment and self-awareness, with subjects having depressive symptoms being less likely to demonstrate diminished insight.⁹ Indeed, depression has been shown to be negatively correlated with anosognosia, as higher anosognosia has been associated with lower depression scores.⁸ In addition, feelings of depression have been shown to predict a greater awareness of cognitive impairment in Alzheimer's dementia.²⁵ Furthermore, sub-syndromal depression and anxiety have been associated with a higher level of awareness.²⁶

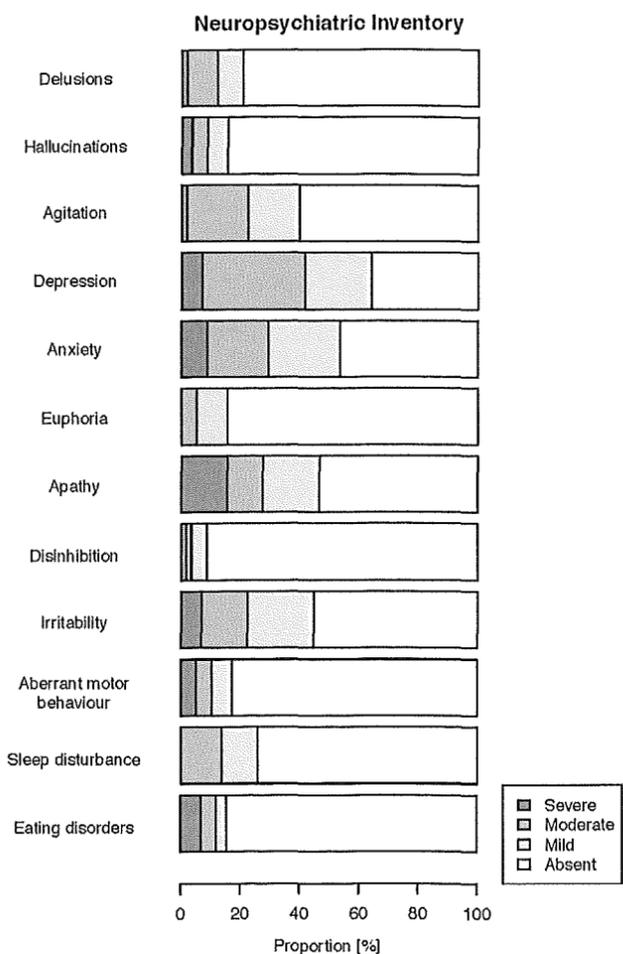


Figure 2 Severity of neuropsychiatric symptoms based on the Neuropsychiatric Inventory.

We assume that there might be some intrinsic depressiveness in this group of oldest old. Remarkably, depression prevalence may increase substantially with age in non-demented patients, as the prevalence of depression in nonagenarians is twice as high as in octogenarians.²⁷

Biologic ageing of the brain may induce an elevated vulnerability for increased incidence of diseased states, including corticolimbic disruption and low mood associated with depression.²⁸ Additionally, institutional status may reflect increased depressive symptoms for centenarians without cognitive impairment or with mild cognitive impairment.¹¹ Some authors have found that there is an unequal frequency of overestimation by patients of essentially instrumental deficits as opposed to functional deficits in the case of major or minor depression.²⁴ Others have reported an overesti-

Table 3 Correlations between anosognosia score, patient characteristics, neuropsychiatric and neuropsychological testing

Variable	r
Age	0.144
MMSE	-0.723**
Five-word test	-0.703**
CLOX 1	-0.539**
CLOX 2	-0.555**
Lexical fluency (letter R)	-0.455**
Categorical fluency (animals)	-0.470**
NPI delusions	0.022
NPI hallucinations	0.110
NPI agitation	0.375**
NPI depression	0.071
NPI anxiety	0.141
NPI euphoria	0.066
NPI apathy	0.481**
NPI disinhibition	0.246
NPI irritability	0.178
NPI aberrant behaviour	0.320*
NPI sleep	0.081
NPI appetite	0.121
NPI total severity score	0.488**
Charlson Age Adjusted	-0.137

*P < 0.05, **P < 0.01. CLOX, executive clock-drawing test; MMSE, Mini-Mental State Examination; NPI, Neuropsychiatric Inventory; r, Spearman correlation coefficient.

mation of cognitive deficits in mild cognitive impairment in contrast to Alzheimer's disease patients,²⁹ but the conclusions are controversial and not shared by others who have found an association with unawareness, even in cases of slight cognitive impairment. This apparent contradiction could be explained by the multidimensionality of awareness and the various assessment methods used.³⁰

The tests we have used have several limitations. A specific depression scale should be used in further studies to better characterize affective symptoms. The depression subscale of the NPI is probably too little discriminating and has shown no correlation with anosognosia in previous studies or in ours.²² The relationship between insight, depression and dementia is manifold, as depression in dementia patients is likely to arise from intertwined biological and psychological processes.⁵ The low amplitude of symptoms measured with the NPI subscales suggests the need for the development of a specific instrument to assess psychopathological features and offer a possible explanation of the negative discrepancy of anosognosia scores for the least cognitively impaired subjects. Another limitation of the present study is that the AQ-D, though widely used, only measures some targets of

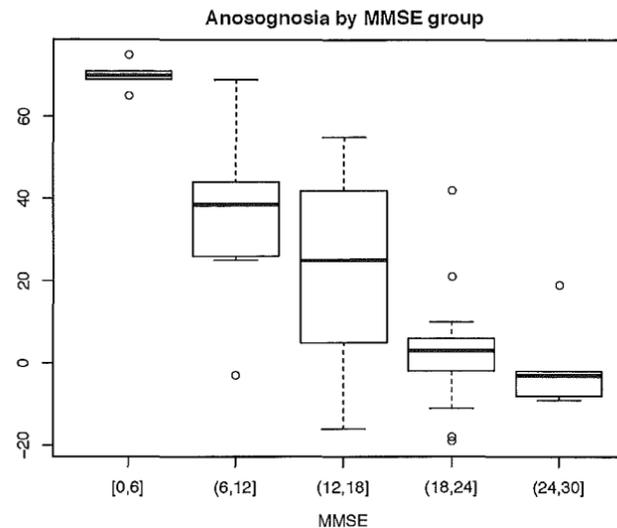


Figure 3 Anosognosia by MMSE group. Each box represents the interquartile range (IQR). The top and bottom of the box are the 25th and 75th percentiles of anosognosia score. The dark horizontal line inside the box represents the median. Upper and lower whiskers represent 1.5 times and -1.5 times IQR. If the range is positive, the whiskers extend to the most extreme data points, which are no more than range times the interquartile range from the box. A value of zero causes the whiskers to extend to the data extremes. Remaining outliers are plotted with an open circle. MMSE, Mini-Mental State Examination.

unawareness, specifically those associated with basic and instrumental activities of daily living and changes in mood and behaviour.²⁴ Many other aspects of self-awareness regarding, such as moral judgement or prospective memory, are not assessed by this scale. Cognitive deficiency has been shown to induce a heterogeneous impairment of self-consciousness.³¹ Thus, anosognosia as measured in this study may only reflect some fragmentary aspects of this reality. Because of the method of administration, results depend on the reliability of the caregivers' answers. In discrepancy methods, it may be difficult to distinguish between overestimations made by subjects and underestimations made by others. Carer evaluation depends on the type and quality of the relationship and time spent with the subject.⁵ By interviewing a professional daily caregiver, we assume that the interviewee bias was more limited than it would have been for a relative.

Testing nonagenarians and centenarians requires adjustment because of frequent sensorimotor disturbances, lower speed, and the lack of validated tools for this age category. Testing procedures need to be adapted, and appropriate tests have to be used. Thus,

sensory impairment did not affect the results as we selected tests that were easy to administer and adjusted font size and speech volume when needed.

Conclusion

Anosognosia in the oldest old was mostly mild and strongly associated with global and specific cognitive functions and psychopathological alteration as in younger subjects. There was, however, a different trend for the least cognitively impaired, who tended to exaggerate their difficulties.

An extension to a community-dwelling sample would help clarify the role of age itself in anosognosia in the least cognitively impaired subjects, identify any causal relationship between anosognosia and the psychopathological features observed, and specify the possible role of mediating factors to explain if this emphasis on one's perceived difficulties is a particular feature of the institutionalized very elderly or a defining characteristic of the cognitively unimpaired oldest old.

REFERENCES

- World Health Organization. *Dementia: A Public Health Priority*. Geneva, Switzerland: WHO Press, World Health Organization, 2012.
- Wanner P, Sauvain-Dugerdil C, Guilley E, Hussy C. *Âges et générations, la vie après 50 ans en Suisse*. Neuchâtel: Office Fédéral de la Statistique 2005 (in French).
- Ramaroson H, Helmer C, Barberger-Gateau P, Letenneur L, Dartigues JF. Prevalence of dementia and Alzheimer's disease among subjects aged 75 years or over: updated results of the PAQUID cohort. *Rev Neurol (Paris)* 2003; **159**: 405-411. (in French with English abstract).
- Derouesne C, Thibault S, Lagha-Pierucci S, Baudouin-Madec V, Ancrì D, Lacomblez L. Decreased awareness of cognitive deficits in patients with mild dementia of the Alzheimer type. *Int J Geriatr Psychiatry* 1999; **14**: 1019-1030.
- Marková IS. *Insight in Psychiatry*. Cambridge, UK: Cambridge University Press, 2005.
- Starkstein SE, Jorge R, Mizrahi R, Adrian J, Robinson RG. Insight and danger in Alzheimer's disease. *Eur J Neurol* 2007; **14**: 455-460.
- Starkstein SE, Brockman S, Bruce D, Petracca G. Anosognosia is a significant predictor of apathy in Alzheimer's disease. *J Neuropsychiatry Clin Neurosci* 2010; **22**: 378-383.
- Starkstein SE, Sabe L, Chemerinski E, Jason L, Leiguarda R. Two domains of anosognosia in Alzheimer's disease. *J Neurol Neurosurg Psychiatry* 1996; **61**: 485-490.
- Smith CA, Henderson VW, McCleary CA, Murdock GA, Buckwalter JG. Anosognosia and Alzheimer's disease: the role of depressive symptoms in mediating impaired insight. *J Clin Exp Neuropsychol* 2000; **22**: 437-444.
- Brown MN, Lapane KL, Luisi AF. The management of depression in older nursing home residents. *J Am Geriatr Soc* 2002; **50**: 69-76.

- 11 Margrett J, Martin P, Woodard JL *et al.* Depression among centenarians and the oldest old: contributions of cognition and personality. *Gerontology* 2010; **56**: 93–99.
- 12 Folstein MF, Folstein SE, McHugh PR. 'Mini-mental state'. A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975; **12**: 189–198.
- 13 Dubois B, Touchon J, Portet F, Ousset PJ, Vellas B, Michel B. 'The 5 words': a simple and sensitive test for the diagnosis of Alzheimer's disease. *Presse Med* 2002; **31**: 1696–1699. (in French with English abstract).
- 14 Cowppli-Bony P, Fabrigoule C, Letenneur L *et al.* Validity of the five-word screening test for Alzheimer's disease in a population based study. *Rev Neurol (Paris)* 2005; **161**: 1205–1212. (in French with English abstract).
- 15 Royall DR, Cordes JA, Polk M. CLOX: an executive clock drawing task. *J Neurol Neurosurg Psychiatry* 1998; **64**: 588–594.
- 16 Cardebat D, Doyon B, Puel M, Goulet P, Joannette Y. Formal and semantic lexical evocation in normal subjects. Performance and dynamics of production as a function of sex, age and educational level. *Acta Neurol Belg* 1990; **90**: 207–217. (in French with English abstract).
- 17 Crossley M, D'Arcy C, Rawson NS. Letter and category fluency in community-dwelling Canadian seniors: a comparison of normal participants to those with dementia of the Alzheimer or vascular type. *J Clin Exp Neuropsychol* 1997; **19**: 52–62.
- 18 Kaufer DI, Cummings JL, Ketchel P *et al.* Validation of the NPI-Q, a brief clinical form of the Neuropsychiatric Inventory. *J Neuropsychiatry Clin Neurosci* 2000; **12**: 233–239.
- 19 Migliorelli R, Teson A, Sabe L *et al.* Anosognosia in Alzheimer's disease: a study of associated factors. *J Neuropsychiatry Clin Neurosci* 1995; **7**: 338–344.
- 20 Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; **40**: 373–383.
- 21 Rapp MA, Gerstorff D, Helmchen H, Smith J. Depression predicts mortality in the young old, but not in the oldest old: results from the Berlin Aging Study. *Am J Geriatr Psychiatry* 2008; **16**: 844–852.
- 22 Kashiwa Y, Kitabayashi Y, Narumoto J, Nakamura K, Ueda H, Fukui K. Anosognosia in Alzheimer's disease: association with patient characteristics, psychiatric symptoms and cognitive deficits. *Psychiatry Clin Neurosci* 2005; **59**: 697–704.
- 23 Millan-Calenti JC, Maseda A, Rochette S, Vazquez GA, Sanchez A, Lorenzo T. Mental and psychological conditions, medical comorbidity and functional limitation: differential associations in older adults with cognitive impairment, depressive symptoms and co-existence of both. *Int J Geriatr Psychiatry* 2011; **26**: 1071–1079.
- 24 Starkstein SE, Jorge R, Mizrahi R, Robinson RG. A prospective longitudinal study of apathy in Alzheimer's disease. *J Neurol Neurosurg Psychiatry* 2006; **77**: 8–11.
- 25 Salmon E, Perani D, Collette F *et al.* A comparison of unawareness in frontotemporal dementia and Alzheimer's disease. *J Neurol Neurosurg Psychiatry* 2008; **79**: 176–179.
- 26 Aalten P, van Valen E, de Vugt ME, Lousberg R, Jolles J, Verhey FR. Awareness and behavioral problems in dementia patients: a prospective study. *Int Psychogeriatr* 2006; **18**: 3–17.
- 27 Bergdahl E, Gustavsson JM, Kallin K *et al.* Depression among the oldest old: the Umea 85+ study. *Int Psychogeriatr* 2005; **17**: 557–575.
- 28 McKinney BC, Sibille E. The age-by-disease interaction hypothesis of late-life depression. *Am J Geriatr Psychiatry* 2013; **21**: 418–432. doi:10.1097/JGP.0b013e31826ce80d.
- 29 Kalbe E, Salmon E, Perani D *et al.* Anosognosia in very mild Alzheimer's disease but not in mild cognitive impairment. *Dement Geriatr Cogn Disord* 2005; **19**: 349–356.
- 30 Clare L, Whitaker CJ, Nelis SM *et al.* Multidimensional assessment of awareness in early-stage dementia: a cluster analytic approach. *Dement Geriatr Cogn Disord* 2011; **31**: 317–327.
- 31 Gil R, Arroyo-Anllo EM, Ingrand P *et al.* Self-consciousness and Alzheimer's disease. *Acta Neurol Scand* 2001; **104**: 296–300.