JAMDA 17 (2016) 1037–1043

JAMDA

journal homepage: www.jamda.com

Original Study

Risk Factors of Caregiver Burden Evolution, for Patients With Subjective Cognitive Decline or Neurocognitive Disorders: A Longitudinal Analysis

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Keywords:
Caregiver burden
longitudinal study
Alzheimer disease or related disorder
risk factors
cognitive impairment
behavioral disorders
dependency

A B S T R A C T

Background/Objectives: The identification of factors used to predict caregiver burden may help preventive care. This study aimed to assess the relationship between evolution of patients with subjective cognitive decline (SCD) or progressive neurocognitive disorder (NCD) and evolution of caregiver burden.
Design: Observational, longitudinal study.
Setting: The study was conducted in the Clinical and Research Memory Center of the University Hospital of Lyon (France), between the November 1, 2011 and the June 30, 2014, with a maximum follow-up of 30 months.
Participants: The study population included outpatients with SCD or NCD at all stages, and their informal caregiver.
Measurements: The caregiver burden was assessed during 2 visits of the patients and their caregiver, with the short version of the Zarit Burden Inventory (ZBI). Functional, cognitive performance, and behavioral and psychological symptoms were measured twice, concomitantly with the ZBI, using the Instrumental Activities of Daily Living (IADL) scale, the Mini-Mental State Examination (MMSE), and the Neuropsychiatric Inventory (NPI), respectively. Etiology and stage of the cognitive impairment were collected.
Results: The population study included 222 patients (mean age at inclusion: 80 years old, 62.9% females), with an average follow-up 12.6 ± 6 months. Proportion of patients with major NCD at the second visit (62.2%) increased compared with inclusion (50.0%). MMSE and IADL decreased between the 2 visits ($P < .001$), whereas ZBI increased (mean ZBI: 3.2 ± 2 at baseline, mean ZBI: 3.8 ± 2 at follow-up, $P < .001$). In unadjusted analyses, ZBI tended to be higher for patients whose MMSE decreased of at least 3 points between the visits. ZBI increased over time when IADL decreased (P value for within-patient effect <.001), while it remained stable when the IADL increased. ZBI increased when NPI increased. After mutual adjustment for change of MMSE, IADL, NPI, and etiologies, increase of ZBI over time remained significant when MMSE decreased at least 3 points between baseline and follow-up, when IADL decreased, and when NPI increased of at least 4 points.
Conclusions: In a study population of patients with SCD or NCD at all stages, concomitant decrease of cognitive performance, increase of functional impairment, and increase neuropsychiatric symptoms over time were independently associated with increased caregiver burden. The identification of risk factors associated with an increased caregiver burden over time may allow a better evaluation of the impact of specific interventions on cognitive, behavioral, and functional dimensions of NCD on caregivers.
Trial registration: ClinicalTrials.gov NCT02825732.

The authors declare no conflicts of interest.

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http://dx.doi.org/10.1016/j.jamda.2016.07.003
1525-8610/

The presence of an informal caregiver contributes to home support for patients with progressive neurocognitive disorders (NCDs) and may delay nursing home transfer.[1] However, informal caregivers are frequently exposed to health comorbidities, especially affective disorders.[2] In addition, the large part of cost of care for patients with NCD is supported by informal caregivers. According to a previous study conducted in the United States, the annual cost of informal care of patients with dementia was $18,385 per patient, 34% of which was for caregiving time and 66% for caregiver's loss of earnings.[3] In a study conducted in the North of Europe, informal care cost, estimated by the caregiver time spent with patient, was on average $20,285 per patient with Alzheimer disease (AD), although authors cautioned that the costs vary across countries.[4]

Previous cross-sectional studies have shown that caregiver burden increases with the degree of severity of symptoms related to cognitive impairment of their relatives, as well as with the severity of patients' comorbidities.[5–9] Cognitive and functional impairment, as well as behavioral disorders, were shown to be associated with higher caregiver burden independent of cognitive impairment etiology.[7] Yet, longitudinal studies describing the evolution of caregiver burden and the risk factors associated with this evolution remain scarce and focused on specific etiologies such as AD or on patients with dementia.[10–13] In a previous study conducted in Spain and published in 2014, the authors showed that caregiver burden, measured with the Zarit Burden Interview (ZBI), increased slightly during the 3 years of follow-up and that neuropsychiatric symptoms and functional impairment of patients with probable AD were associated with increased caregiver burden.[10] In the same country, another study found that caregiver burden improved slightly during 12 months of follow-up, for caregivers of patients with moderate to severe AD.[13] In this study, behavioral impairment was the factor the most related to caregiver burden compared with functional or cognitive decline.

In a previous cohort study conducted in Australia among patients with dementia, the caregiver burden increased at 36 months of follow-up and behavioral disorders, rapid functional decline, and use antipsychotics and antidepressants were found as significant predictors of increased caregiver burden.[11] In another study conducted in Germany, the caregiver burden measured with the Caregiver Burden Interview remained stable over 2 years of follow-up, whereas the severity of the symptoms (functional impairment and behavioral disturbances) in patients with dementia increased over the same period of observation.[12] Nevertheless, no previous longitudinal study included patients with subjective cognitive decline (SCD), defined as the presence of a subjective cognitive complaint with unimpaired performance on the objective neuropsychological evaluation.[14]

In this context, it is interesting to investigate this objective among patients with SCD or at various stages of NCD (as measured by The Diagnostic and Statistical Manual of Mental Disorders, 5th ed. [DSM-V] and whatever the etiologies) who are followed at a memory center. This improves the understanding of the conditions and risk factors linked to caregiver burden and make it possible to plan specific interventions aimed at supporting caregivers.[15]

This study goals were to assess the relationship between the evolution of symptoms of patients with cognitive complaint, measured twice successively, at minor and major stages of NCD, as well as among patients with SCD, and the evolution of caregiver burden, assessed with the short version of the ZBI, in a cohort study conducted in a memory center.

Methods

Study Design, Setting, and Follow-Up

This observational and monocenter study was based on an outpatient cohort, extracted from a patient medical record database at the Clinical and Research Memory Centre of Lyon (Charpennes Hospital, University Hospital of Lyon, France). Repeated measurements were collected at 2 successive visits of patients, in routine care, at the memory center between the November 1, 2011 and June 30, 2014.

Study Population

The study population included the dyad of patient-caregiver for patients who have undergone a memory visit with a neurologist or a geriatrician. Patients visited the memory center after a cognitive complaint, either expressed by themselves or by one of their relatives. Patient characteristics visiting the memory center have been described previously in a cross-sectional study.[6,7] Inclusion criteria were patients with a cognitive complaint, either expressed by the patient or one of their relatives, at any stage of disease (SCD, mild or major NCD), patients living in the community, and having an informal caregiver who completed the questionnaire to assess the caregiver burden at 2 successive visits.

Written information regarding the collection of individual data was provided to the patient and caregivers. Authorization for handling personal data has been granted by the French Data Protection Authority (CNIL: Commission Nationale de l'Informatique et Libertés): June 08, 2010, number of registration: 10–18. The study has been registered in the register ClinicalTrials.gov with the number NCT02825732.

Data Collection

All patient and caregiver data were reported in an electronic case report form, using the software Cristalnet, developed by the Centre Régional Informatique Hospitalière des Alpes and the computer and software service of the University Hospital of Grenoble, Grenoble, France. The data were entered in the electronic case report form by trained medical and paramedical staff, at every patient visit. Follow-up visit was planned within the usual monitoring time frame of patients at the memory center, typically 12 months after the first consultation. The delay between the consultations may vary according to the need of care and management of the patient's health.

Primary Outcome: Caregiver Burden Change

The caregiver burden change was assessed using 2 repeated measures of the validated short version of the ZBI.[16,17] The short version of ZBI score ranged from 0 (no burden) to 7 (higher burden). This score is corresponding to the sum of the answers to 7 questions to which the caregivers answered "never" (0 point), "sometimes" (0.5 point), or "nearly always" (1 point). As described previously, the answers were first self-reported by the informal caregiver in a questionnaire sent to their home before the patient's consultation at the memory center.[6,7] The questionnaires were then verified by a nurse in an interview with the caregiver during the patient visit.

Patient's Characteristics Collected at Baseline

The following patient's characteristics were collected at baseline during the routine care visits: age, sex, the current living situation of the patient including living at home with a spouse, at home with relatives, alone at home with relatives in the neighborhood, alone at home without relatives in the neighborhood, or unspecified other living situation. The relationship between the patients and their caregivers was recorded as (1) spouse, (2) child, stepchild, or grandchild, (3) brother, sister, niece or nephew, or (4) other unspecified caregiver.

Patient Characteristics Collected at Baseline and Follow-Up

The overall cognitive performance, the functional autonomy level, and the Behavioral and Psychological Symptoms of Dementia (BPSD), representing main symptoms and the degree of severity of the NCDs in link with AD and related disorders, were assessed by a nurse at each visit of the patients accompanied by their informal caregiver. In detail, the cognitive performance was assessed using the Mini-Mental State Examination (MMSE) and the functional autonomy level was assessed with the Instrumental Activities of Daily Living (IADL) scale, as recommended by the French National Authority for Health and in accordance to the French AD data bank.[18–21] The French version of MMSE was previously validated for the detection of cognitive impairment using the DSM-III criteria.[22] The IADL assessed 8 instrumental activities: ability to use the telephone, shopping, food preparation, housekeeping, laundry, mode of transportation, responsibility for own medications, and ability to handle finances. The score ranging from 0 (dependent) to 8 (independent).[23,24] The BPSD were assessed using the Neuropsychiatric Inventory (NPI), which was previously validated.[25,26] This NPI evaluates 10 behavioral domains including delusions, hallucinations, agitation/aggression, depression/dysphoria, anxiety, elation/euphoria, apathy/indifference, disinhibition, irritability/lability, aberrant motor behavior, and 2 neurovegetative troubles: sleep/night-time behavioral disorders and appetite/eating disorders. A higher overall NPI score (maximum 144) indicates more severe behavioral disorders.

The changes over time of MMSE, IADL, and NPI were considered using the absolute difference of the 2 repeated measures, as well as the tertiles of each absolute difference.

Diagnosis stage and etiologies of the patients were determined by the neurologist by a clinical examination and a neuropsychological evaluation performed by a clinical neuropsychologist. Mild and major NCD were identified using the DSM-V classification.[15] The disease stage of mild cognitive impairment (also considered as mild NCD) and dementia (also considered as major NCD) in AD was established on the basis of the McKhann and the Albert criteria.[27,28] The etiologies were identified as follows: AD, AD with cerebrovascular component, vascular dementia (NINDS-AIREN [National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherche et l'Enseignement en Neurosciences] criteria), Lewy body disease, and frontotemporal dementia. The other etiologies were grouped together in the category (others related disorders) because of small number of patients: 1 patient with Parkinson disease, 5 patients with other dementia and pathologies leading to a progressive cognitive impairment (including chronic hydrocephalus, progressive supranuclear palsy, corticobasal degeneration, and unclassified dementia), 4 patients with psychiatric disorders (including psychoses, anxious disorder, isolated depression disorder, recurrent depressive disorder, bipolar disorder, and unclassified psychiatric disorders), and 9 patients with others disorders [including other neurologic diseases, such as tumor, aneurysm, head injury, and organic brain disorder related to the pathology (eg, metabolic deficiency)].[27–31] Patients with isolated cognitive complaint without cognitive disorders according to the standard neuropsychological evaluation were also included and considered as patients having SCD.[14] The change of diagnosis stage or etiologies was expressed using a dummy variable (0: no change, 1: change).

Statistical Analysis

Patients characteristics were described at baseline and follow-up with means ± standard deviation or frequencies (percentage) as appropriate. Imputation of missing data of MMSE, IADL, and NPI at follow-up was performed using linear regression models.

Proportions and means were compared between baseline and follow-up using paired MacNemar test or paired *t*-test.

The relationships between characteristics of patients, evolution of their symptoms (MMSE, IADL, and NPI), and change of caregiver burden during follow-up was assessed using a general linear model for repeated measures. ZBI change (dependent variable) was modelized using the 2 repeated measures, whereas MMSE, IADL, and NPI change (explanatory variables) were modelized using the absolute difference of their 2 repeated measures, as well as tertiles of the absolute difference of each variable. Interaction between patient symptoms was assessed in the model. Three test statistics were presented (ie, (1) the within-patient effect which shows whether there is a linear trend of mean ZBI between baseline and follow-up for each tertile; (2) the between-patient effect, which shows whether there is a significant difference of mean ZBI between the tertiles; and (3) the interaction between time effect and the tertiles that shows whether the evolution of ZBI is different in each tertile). The model was performed without adjustment and with adjustment for all the variables, which were significantly associated with ZBI and its evolution. In addition, scatterplots with locally weighted scatterplot smoothing were performed to show the relationship (regression) between the change of each variable: MMSE, IADL, NPI, and ZBI. The coefficient of regressions (b) and their statistical significance were reported. Statistical tests were 2-tailed, and *P* values less than .05 were considered to be statistically significant. Analyses were performed using SPSS v 19.0 for Windows (SPSS Inc, Chicago, IL).

Results

Description of the Study Population at Baseline and Follow-Up

The study population included 222 patients (62.9% female), with an average age of 80 years old at inclusion (Table 1). A majority of the patients lived at home with their spouse (61.7%). The informal caregiver who have accompanied the patient at the memory center was the spouse in 43% of cases and the child/stepchild or grandchild in 37% of cases. There were 8.1%, 4%, and 5.9% of missing data at follow-up for MMSE, IADL, and NPI, respectively. Once the missing data were replaced by imputation procedure, the means of MMSE, IADL, and NPI were not significantly different between the sample with or without the missing data. The maximum follow-up time was 30 months, and the average follow-up time was 12.6 ± 6 months (Table 2). The comparison of patient characteristics showed significant change between baseline and follow-up for the diagnosis stage and etiologies, MMSE, IADL, and ZBI. Patients were more frequently at major NCD

Table 1
Patients Characteristics at Baseline (n = 222)

Variables	n % or Mean ± SD	
Age (years) - mean ± SD	80.0 ± 7.1	
Sex		
Female	139	62.9%
Male	83	37.4%
Current lifestyle		
At home with spouse	137	61.7%
At home with relatives	14	6.3%
At home, alone, with relatives in the neighborhood	54	24.3%
At home, alone, without relatives in the neighborhood	9	4.1%
Unspecified	8	3.6%
Relationship between patient and informal caregiver		
Spouse	95	42.8%
Child/stepchild/grandchild	83	37.4%
Brother/sister/niece/nephew	10	4.5%
Other unspecified caregiver	34	15.3%

SD, standard deviation.

Table 2
Comparison of Patient Characteristics Collected at Baseline and Follow-Up

Variables	Baseline		Follow-Up		*P* Value*
	n % or Mean ± SD		n % or Mean ± SD		
Time between measurements (in months) - mean ± SD	12.60 ± 6.42				
Classification of cognitive stages					<.001
SCD	36	16.2%	19	8.6%	
NCDs					
Mild NCD	75	33.8%	65	29.3%	
Major NCD	111	50.0%	138	62.2%	
Diagnosis etiology					.04
AD	129	58.1%	132	59.5%	
AD with cardiovascular component	29	13.1%	32	14.4%	
Vascular dementia	15	6.8%	16	7.2%	
Lewy body disease	9	4.1%	9	4.1%	
Frontotemporal dementia	4	1.8%	4	1.8%	
Other related disorders (other dementia, Parkinson disease, psychiatric disorders)	19	8.6%	19	8.6%	
Diagnosis not yet established	17	7.7%	10	4.5%	
MMSE					<.001
>20	112	50.5%	87	39.2%	
≥10 and ≤20	93	41.9%	95	42.8%	
<10	17	7.7%	40	18.0%	
MMSE	19.59 ± 6.20		17.58 ± 7.00		<.001
IADL	3.83 ± 2.22		2.76 ± 2.03		<.001
NPI	17.55 ± 16.34		18.50 ± 15.48		.40
ZARIT	3.17 ± 1.96		3.80 ± 1.90		<.001

*P value for difference between baseline and follow-up: unadjusted paired McNemar test for proportions comparison, and paired *t*-test for means comparison.

stage at the second visit compared with the first visit (ie, 62.2% vs 50.0%, respectively, $P < .001$). There was a significant decrease of MMSE and IADL between the 2 visits, meaning reduction of overall cognitive performance and functional abilities. The NPI tended to increase between baseline and follow-up, showing a tendency of increased behavior disturbance, but the difference was not significant. The ZBI score increased during the time between the 2 visits (mean ZBI: 3.2 ± 2 at baseline, mean ZBI: 3.8 ± 2 at follow-up, $P < .001$), reflecting a higher caregiver burden over time.

Association Between Change of Cognitive Performance, Functional Autonomy Level and BPSD, and Change of ZBI

Unadjusted analyses showed that ZBI increased significantly over time regardless of the tertile change of MMSE (Table 3). Caregiver burden tended to be higher for patients whose MMSE decreased of at least 3 points between baseline and follow-up. ZBI increased over time when IADL decreased between the 2 visits (*P* value for within-patient effect of <.001), whereas it remained stable when the IADL increased. Finally, ZBI increased when NPI increased, showing higher caregiver burden related to increase of behavioral disorders. Of note, ZBI tended to decrease when NPI decreased of at least 4 points, but the statistical significance was not reached. Interaction in pairs between tertiles of change of MMSE, IADL, and NPI were not significant. After mutual adjustment for change of MMSE, IADL, NPI, and for etiologies at baseline, the increase of ZBI over time remained significant for a MMSE decrease of at least 3 points between baseline and follow-up, an IADL decrease of at least 1 point, and a NPI increase of at least 4 points.

Scatterplots showed no significant linear relationship between change of MMSE and change of ZBI ($b = -0.3$, $P = .32$) (Figure 1). There was a significant linear relationship between changes of IADL, NPI, and

Table 3
Association Between Change Over Time of MMSE, IADL, and NPI and Change of ZBI

Variables	Models Without Adjustment*						Model With Adjustment†		
	ZBI at Baseline Mean ± SD	ZBI at Follow-Up Mean ± SD	*P* Value for Within-Patient Effect	Mean ZBI Between Baseline and Follow-Up	*P* Value for Between-Patient Effect	*P* Value for Interaction	*P* Value for Within-Patient Effect	*P* Value for Between-Patient Effect	*P* Value for Interaction
Change over time (tertiles of absolute difference)									
Change of MMSE									
<−3 points	3.14 ± 2.03	4.29 ± 1.81	<.001	3.72 ± 1.67	.24	<.02	.001	.35	.09
Between −3 points and 0	3.06 ± 2.07	3.41 ± 1.88	.045	3.23 ± 1.83			.40		
≥0 points	3.30 ± 1.80	3.78 ± 1.93	.02	3.54 ± 1.62			.11		
Change of IADL									
<−2 points	2.68 ± 1.97	4.17 ± 1.89	<.001	3.42 ± 1.63	.89	<.001	.006	.72	.003
Between −2 points and 0	3.03 ± 1.87	3.87 ± 1.78	<.001	3.45 ± 1.68			<.001		
≥0 points	3.56 ± 1.99	3.55 ± 2.03	.98	3.56 ± 1.80			.50		
Change of NPI									
<−4 points	3.91 ± 1.96	3.78 ± 1.94	.58	3.84 ± 1.69	.03	<.001	.52	.09	<.001
Between −4 and +5 points	2.78 ± 1.76	3.40 ± 1.88	.001	3.09 ± 1.64			.01		
≥5 points	2.88 ± 1.96	4.17 ± 1.84	<.001	3.52 ± 1.74			<.001		

*Association between each variable (tertile of absolute change of MMSE, IADL and NPI) and change of ZBI.
†All variables (tertile of absolute change of MMSE, IADL, and NPI) were modeled together in the same model, and etiologies contributed significantly in the model. Age, sex, current lifestyle relationship between patients and their caregivers, diagnosis stage, and the change of diagnosis between baseline and follow-up did not contribute significantly to the model.

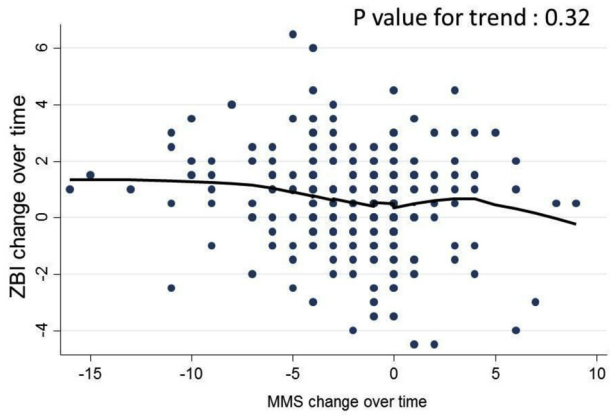

Fig. 1. Scatterplots of the relationship between change of MMSE and change of ZBI.

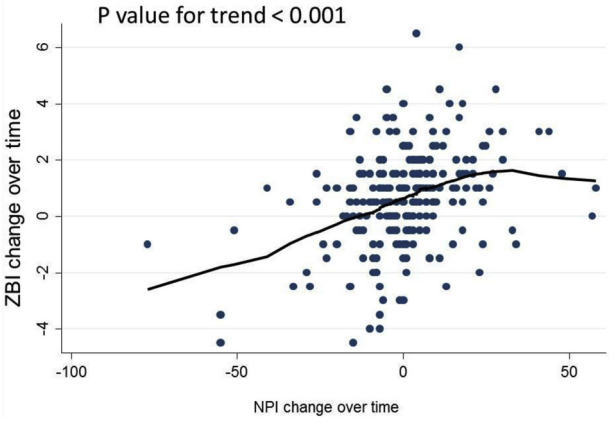

Fig. 3. Scatterplots of the relationship between change of NPI and change of ZBI.

ZBI (respectively: b-IADL = −0.3, <0.001, b-NPI = 0.03, $P < .001$) (Figures 2 and 3).

Discussion

In a study population of patients with memory complaint, in the context of a SCC or in mild or major NCD, increase of caregiver burden during an average period of 12.6 months is associated independently with decrease of cognitive performance, increase of functional impairment, and increase of neuropsychiatric symptoms over time, after adjustment for the etiologies. Likewise, whatever the baseline characteristics of the patients, the worsening of their symptoms over time contribute to increase caregiver burden. More precisely, the use of tertiles has allowed to identify patients for whom evolution of symptoms during an average period of 12.6 months is related to increased caregiver burden (ie, a MMSE decrease of at least 3 points, a IADL decrease of at least 1 point, and a NPI increase of at least 4 points). While the relationship between evolution of the patients symptoms and evolution of the caregiver burden appears to be linear, the determination of these threshold may be interesting in a clinical point of view. Nevertheless, they remain specific of this population study and in absence of standard thresholds, it would be interesting to perform the same analysis in other study population.

This study is also going a step further than previous studies that have focused specifically on patients with AD or dementia, by expanding the scope of to patients with a SCD and patients at different stages of memory disorders.[10,11] This study conducted in a memory center offers an overview of the real situation faced by patients' caregivers. Thereby, in this study, the different etiologies and stages of cognitive decline or NCD do not appear to change the relationship between evolution of the symptoms of the patients and evolution of caregiver burden. In terms of relationship between evolution of patient symptoms and caregiver burden, the following comparison with previous findings can be performed. In Conde-Sala et al,[10] behavioral and functional impairment over time was associated with an increase of caregiver burden, assessed with the ZBI, whereas the MMSE change did not contribute significantly to caregiver burden change among patients with AD. In Brodaty et al,[11] among patients with dementia, behavioral symptoms and functional decline contributed to increase the caregiver burden, whereas cognitive performance was not related to caregiver burden. Overall, previous results about the relationship between either change over time of symptoms of the patients, or the symptoms measured once at baseline and caregiver burden point in the same direction than those of the present study, whereas the study population are different, as well as the scales used to measure patient characteristics and caregiver burden. In the present study, caregiver burden is assessed using the short version of the ZBI, which appears more suitable for current practice, and which has not been used previously to study the change over time of caregiver burden and its risk factors. The present result reinforces the clinical value of this shortened scale dedicated to caregiver burden.

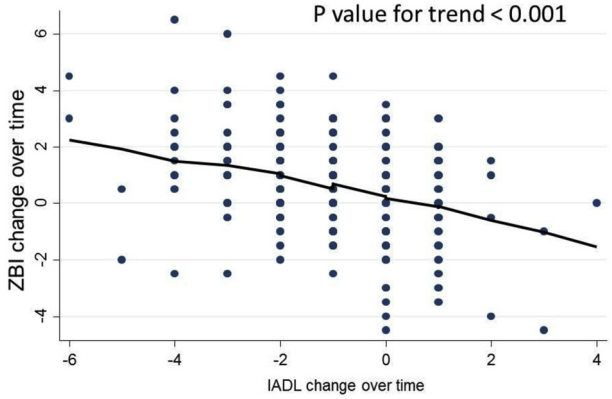

Fig. 2. Scatterplots of the relationship between change of IADL and change of ZBI.

In this study population, caregiver burden increased significantly over time no matter what the patient characteristics were. This result is concordant with previous findings, among patients with AD or dementia.[10,11] In contrast, others studies have found that caregiver burden may not systematically increase over time for patients with dementia or AD.[12,13] In Berger et al,[12] caregiver burden assessed by the Caregiver Burden Interview remained stable over 2 years; severe caregiver depression appeared to decrease, showing that caregiver situation, in terms of these aspects, did not degrade during evolution of patient symptoms. However, these authors found associations similar to our results (ie, severity of dementia, functional impairment, and behavioral disturbance increased caregiver burden). Another study found that caregiver burden assessed with ZBI improved slightly between baseline and 12 months for caregivers of patients with moderate to severe AD.[13] These authors also found that behavioral impairment was the most related factor to caregiver burden compared with functional or cognitive decline. The difference of change over time of caregiver burden observed between studies may be due to the fact that the observations made are not at the same phase of caregiver burden change. We assume that there may be a specific phase when caregiver burden increases, in particular when the patient functional abilities decline, and the behavioral symptoms are more frequent, which may increases stress among caregivers and requires more support from caregivers. After

that phase, caregivers may get used to the situation and learn how to cope with it better. This is what previous authors have argued and have called the adaptation hypothesis.[32] Another possible explanation may be that caregivers, as well as patients, are taken in charge through pharmacologic and nonpharmacologic therapies, in a different way between studied population, which may have an impact on the estimation of the burden change. Caregivers characteristics may also differ between studies, and previous findings have shown that these characteristics may impact the level of caregiver burden, such as sex, age, and the relationship between patients and caregivers.[33] Finally, the management of patients and their symptoms may differ between countries and years, which could also explain that caregivers are facing different situations that do not represent the same burden.[33]

In this study, worsening of health symptoms related to memory disorders of the patients is observed, such as overall cognitive and functional impairment and increase of behavioral and neuropsychiatric symptoms, which are in accordance with the evolution of symptoms among patients with NCDs, and which are also used as diagnosis criteria to identify diagnosis stage.[12,34,35]

Several limitations of this study should be noted. The characteristics of the caregivers, such as sex, educational level, or age, are not included in the analysis because it was not possible to collect them in current practice. These caregiver characteristics may impact level of burden. As shown in previous findings, caregivers with higher educational level, female caregivers, and young caregivers may experience a higher burden.[33,36] Nevertheless, one can note that results differ between studies in terms of these potential effects.[6,10,37] Change over time was measured using 2 repeated measures; more repeated measures may be useful to highlight more specific variations.

The analysis were performed among patients for whom the measures of caregiver burden were available. A selection bias cannot, therefore, be excluded, and the reasons why some caregivers did not respond to the ZBI were not collected.

Conclusions

The worsening of the 3 main categories of symptoms related to NCDs (ie, cognitive, behavioral, and functional impairment) increase caregiver burden, independent of any cognitive disorder stage and etiology. This study conducted in a memory center allows to improve the understanding of the link between the evolution of patient symptoms and the increased caregiver burden, which may allow medical staffs to better detect and manage the situation faced by caregivers. Although the generalization of these findings remain limited, this study provides ample evidence pleading for the assessment and management of caregiver well-being at the same time as the evolution of patient symptoms at all stages of cognitive impairment, in clinical practice, and student and professional training. In addition, future interventions designed to delay the evolution of patient symptoms in link with NCD should include the target of decrease the caregiver burden to positively impact the dyad patient-caregiver.

Acknowledgments

The authors would like to thank Dr Michel Kossovsky and Camille Schiffler for their assistance in the research.

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