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Frontal lobe function in elderly patients with Alzheimer's disease and caregiver burden

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Abstract

Background

The understanding of the relationships between caregiver burden and the degree of behavioural deficits in patients with Alzheimer's disease (AD) is relatively limited. Thus, it is worthwhile to examine the correlations between the various relevant factors to improve the efficacy of care for patients with AD. The aim of this study was to investigate the specific contributions of frontal lobe dysfunction in AD patients to caregiver burden, controlling for other predictor variables.

Methods

Participants comprised 30 pairs of caregivers and patients with AD. The Zarit Burden Interview (ZBI) and Frontal Assessment Battery (FAB) were used to measure the caregiver burden and patients' frontal function, respectively. To investigate the contribution of frontal lobe dysfunction on the caregiver burden, hierarchical regression equations with steps incorporating additional predictor variables were fitted. We also performed a correlation analysis between the individual subdomains of ZBI and the predictor variables.

Results

Our study suggests that the degree of frontal lobe dysfunction in AD patients predicts their caregiver burden after controlling for other factors of daily functional limitations and neuropsychiatric symptoms. When considering the dimensions of caregiver burden, daily functional limitations and neuropsychiatric symptoms affected caregivers' psychosocial burden, whereas frontal lobe dysfunction affected caregivers' burden due to the increase in the dependency of the patients.

Conclusion

Our findings indicate the necessity of developing interventions focused not only on psychosocial burdens as shown in previous studies but also on the excessive dependency of the patients due to frontal lobe dysfunction to both ameliorate the disabilities of the patients and reduce the caregiver burden.

Key words: Alzheimer's disease; caregiver burden; dementia; frontal lobe function

Introduction

The majority of patients with Alzheimer's disease (AD) and related disorders are cared for at home by family members.[1, 2] Offering care for patients with dementia has a significant effect on the caregivers' emotional and physical health burdens. Caregivers have a higher risk of anxiety, depressive and sleep disorders, decreased quality of life, and the increased risk of cardiovascular morbidity and mortality.[2-8] Therefore, understanding the factors that contribute to caregiver burden is important for the realisation of more effective psychosocial interventions aimed at improving the caregivers' quality of life.

Caregiver burden for the elderly consists of multiple dimensions, including time dependence and physical, emotional, developmental, and social burdens.[9] The functional decline of the patients is the main predictor of the caregiver burden. The limitation of specific functions, such as the instrumental activities of daily living, increases the burden on caregivers of patients with dementia.[10] Across all cognitive domains, frontal system behavioural functioning has a larger influence on daily functioning than memory dysfunction.[11, 12] Previous studies have indicated that frontal system behavioural problems of demented patients are predictive of caregiver burden after controlling for dementia severity and caregiver depression.[13, 14]

However, the understanding of the association between caregiver burden and behavioural dysfunction in AD patients is still relatively limited, and it is necessary to examine the relationships in detail to improve the efficiency of the care of patients with AD. This study investigated the contribution of frontal lobe dysfunction on caregiver burden. The Frontal Assessment Battery (FAB) was used to assess patients' frontal function,[15] and the Zarit Burden Interview (ZBI) was used to measure caregiver burden.[16] Our aim in this study was to acquire a better understanding of the details of the frontal lobe dysfunction in AD patients related to the level of caregiver burden. Our overarching aim is to contribute to the development of interventions planned to relieve the distress of the caregiver.

Methods

Subjects

Participants comprised 30 pairs of caregivers and AD patients with mild to moderate dementia. They were recruited from geriatric psychiatric outpatient clinics at a university hospital. All patients were diagnosed with probable AD using the criteria of the National Institute on Aging and the Alzheimer's Association.[17] Patients were excluded if they had any neurodegenerative disease other than AD (e.g. dementia with Lewy bodies, Parkinson's disease, or Huntington's disease, etc.). Additionally, we excluded subjects with significant hearing or visual impairments that rendered interviews difficult. Each caregiver met the following inclusion criteria: 1) was a relative of the patient; 2) was familiar with the patient's daily activities; and 3) agreed to be interviewed. This study protocol was approved by the Institutional Review Boards of the university hospital and was performed in accordance with the Declaration of Helsinki (as revised in Brazil, 2013).

Measures

Caregiver burden was measured by the ZBI,[16] which consists of 22 items that are self-administered (scores range from 0–88). A higher score represents a higher burden.

Patients' frontal lobe functions were assessed with the FAB.[15] It is a brief bedside cognitive and behavioural battery for the assessment of frontal lobe function, is relatively easy to administer, and has good validity and reliability.[18] The FAB consists of six subtests that comprise conceptualisation, mental flexibility, motor programming, sensitivity to interference, inhibitory control, and environmental autonomy. The total score is 18, and higher scores indicate better frontal functioning.

Patients' cognitive dysfunction was evaluated using the Mini-Mental State Examination (MMSE),[19] and the neuropsychiatric symptoms were assessed with the Neuropsychiatric Inventory (NPI).[20] Depression was assessed with the 15-item Geriatric Depression Scale (GDS).[21] Finally, functional capabilities were assessed using the Physical Self-Maintenance Scale (PSMS),[22] consisting of six different items: toilet, feeding, dressing, grooming, physical ambulation, and bathing. Each item was scored from 0 (no impairment) to 4 (severe impairment), allowing for a total range of 0–24 points.

Statistical Analyses

Pearson correlation analyses were performed to investigate the relationships between ZBI scores and each patient characteristic and each measurement of the FAB, MMSE, NPI, PSMS, and GDS scores. Multivariate linear regression analyses were performed using a stepwise approach and included all the characteristics that were found to be significant in the correlation analysis. Estimates were adjusted for all the characteristics that remained significant at the final step. To investigate the relationship between frontal lobe dysfunction in the patient and perceived caregiver burden, hierarchical regression equations with steps incorporating predictor variables were fitted. Scores on the measures of the significant effects other than FAB were added in the first step to control for other predictor variables. FAB scores were added in the final step. Further, we conducted a second hierarchical regression analysis to investigate the specific domains of frontal dysfunction contributing to caregiver burden. Total scores on the ZBI served as the outcome variable in the regression analysis.

To investigate the relationship between the dimensions of caregiver burden and frontal lobe dysfunction and other significant predictor variables, we performed a partial correlation analysis between the individual subdomains of the ZBI and predictor variable, after controlling for other predictor variables.

Burden due to the three factors of psychosocial, dependency, and guilt was calculated as the mean of the three separate factors.[23] Psychosocial burden subscales included: 4, feels embarrassed; 5, feels angry; 6, relative affects relationships with others in negative way; 9, feels strained; 11, does not have privacy; 12, social life has suffered; 13, feels uncomfortable about having friends over; 16, unable to take care of relative much longer; 17, lost control of life; 18, wishes to leave the care to someone else; 19, feels uncertain; and 22, feels burdened. Dependency burden subscales included: 1, relative asks for more help than he/she needs; 2, not enough time for oneself due to time with relative; 3, stressed trying to balance care and family/work responsibilities; 8, relative is dependent; 10, health has suffered because of involvement with relative; 14, are the only one that relative depends on; and 15, not enough money to take care of relative. Guilt burden included: 7, afraid what the future holds for your relative; 20, should be doing more for your relative; and 21, could do a better job in caring for relative.

A P value < 0.05 was considered statistically significant. The multiplicity of the statistical analyses was considered to avoid type I errors. SPSS version 22.0 was used for all descriptive and correlational analyses.

Results

The characteristics of the patients and their associations with scores on the ZBI are presented in Table 1. Patients' sex, age, and educational level were not associated with the scores for the ZBI. The score of the caregiver burden was associated with frontal lobe dysfunction, as assessed by the score on the FAB, in addition to the cognitive and behavioural problems shown in the scores on the MMSE, NPI, and PSMS. When the significant variables associated with the ZBI were modelled together in a stepwise regression model, the NPI, PSMS, and FAB scores remained significant, whereas the MMSE score was not significant anymore.

To determine the relative contributions of neuropsychiatric symptoms, physical activity in daily life, and frontal lobe dysfunction on caregiver burden, we used an hierarchical regression analysis with the total score on the ZBI as the dependent variable. We entered variables in the following order: NPI, PSMS, and FAB scores. Results of the hierarchical regression analyses are presented in Table 2. NPI scores significantly accounted for the variance in the ZBI scores. PSMS scores added in the second step accounted for a significant increase in the variance of the ZBI scores. As predicted, FAB scores, added in the final step, accounted for a significant increase in the variance in the ZBI scores under the control of the NPI and PSMS scores.

We conducted a second hierarchical regression analysis to investigate the specific domains of frontal dysfunction contributing to caregiver burden (Table 3). The NPI scores and PSMS scores were entered, followed by the FAB subscale scores. Examination of individual predictors in these models indicated that the FAB subscale of conflicting instructions were significantly predictive of the ZBI scores.

In the correlation analysis between the three factors of the ZBI and the FAB, NPI, and PSMS measures (Table 4), the scores of the NPI and PSMS were mainly associated with the factor of psychosocial burden, whereas the FAB scores showed a correlation with the caregivers’ burden due to the dependency of the patients. The FAB subscale of conflicting instructions was significantly predictive of both the psychosocial and dependency factors of the ZBI scores.

Discussion

We found that frontal lobe dysfunction, daily functional limitations, and neuropsychiatric symptoms in AD patients were significantly correlated to higher caregiver burden. As predicted, the frontal lobe dysfunction of AD patients predicted their caregiver burden after controlling for the other factors of daily functional limitations and neuropsychiatric symptoms.

The observed significant contribution of daily functional limitations and neuropsychiatric symptoms on caregiver burden is consistent with previous findings demonstrating that behavioural disturbance in the patient is one of the strongest contributors to caregiver burden.[13, 24-28] Further, our study suggests that the degree of frontal lobe dysfunction in AD patients predicts their caregiver burden. Behavioural problems related to the frontal system have been shown to be particularly burdensome.[13, 14] Additionally, the level of distress associated with being a caregiver for a patient with behavioural variant frontotemporal dementia (bvFTD) is higher than for caregivers of patients with AD, possibly because frontal system behavioural problems are usually more prominent in FTD than AD.[29-33] Our finding of the significant contribution of frontal lobe dysfunction replicates these previous results. Furthermore, our findings extend the previous findings: we demonstrate that this relationship between caregiver burden and frontal lobe dysfunction remains after accounting for the variability of daily functional limitations and neuropsychiatric symptoms of the AD patients.

When considering the subscales of FAB, our findings indicated that “conflicting instructions (sensitivity to interference)” was predictive of burden, whereas other subscales were less burdensome to caregivers. The task of conflicting instructions challenges self-regulation in a behavioural interference paradigm by instructing patients to execute one action in response to the observation of a different action, thereby requiring the inhibition of imitative response tendencies.[34-36] Patients with this dysfunction tend to display unintended imitative responses.[37] Although previous research suggests that objective measures of cognition are less reliably associated with burden,[14] the current study demonstrated that deficient self-regulation in a behavioural interference task is a strong predictor of caregiver burden.

Caregiver burden has various dimensions. When considering the dimensions of caregiver burden, the daily functional limitations and neuropsychiatric symptoms of the patients significantly affected their caregivers’ psychosocial burden. Previous studies of patients with dementia also have demonstrated that the patients’ disabilities, including impairments in orientation, communication, financial, and transportation skills, are major predictors of the time-dependent burden.[10, 38] The current results imply that the patients' functional disabilities and neuropsychiatric symptoms directly relate to psychosocial burden including time pressures and the caregivers' feelings of being psychosocially isolated. The caregiver is required to take over the patients' everyday tasks, managing the neuropsychiatric symptoms, thereby creating the greatest time demand and level of psychosocial isolation. Our results indicate that interventions to address problems of psychosocial burdens have the potential to be particularly helpful in reducing carer burden of patients with daily functional limitations and neuropsychiatric symptoms.

In addition, frontal lobe dysfunction was shown to affect caregivers' burden due to the increased dependency of the patients in addition to the psychosocial burden. The caregivers' feeling of the excessive dependency of the patients may be induced by the patients' poor self-regulation in the behavioural interference paradigm. These findings indicate the clinical importance of implementing interventions for reducing caregiver burden that are focused not only on their psychosocial burden, but also on the excessive dependency of the patients due to frontal lobe dysfunction. In clinical settings, interventions designed to improve caregiver understanding of the specific changes in the patient's dependency may be beneficial. Specifically, well-designed psychoeducational interventions could help to reduce caregivers' burdens by helping them understand the changes inherent to frontal lobe dysfunction.[39] This will allow caregivers to adjust their expectations, leading to acceptance of the diagnosis and helping them overcome the difficulties of the situation.[29]

This study had some limitations. First, in contrast to epidemiologic data that rests on large population studies, our data of 30 individuals recruited from the geriatric psychiatric outpatients clinic at a university hospital are not based on random sampling selection. Second, this was a cross-sectional survey and not a longitudinal follow-up study, which limits the ability to make causal inferences from this study. Finally, a more sophisticated frontal function measure, in addition to the FAB, is recommended in future studies. Neuroimaging technology is one such sophisticated alternative method for defining frontal lobe function.[12] The findings of our pilot study need confirmation with further studies using a prospective design, larger sample size, and a more precise measure of frontal function to address these issues.

In conclusion, our study suggests that frontal lobe dysfunction in AD patients predicts their caregiver burden after controlling for other factors of daily functional limitations and neuropsychiatric symptoms. When considering the dimensions of caregiver burden, daily functional limitations and neuropsychiatric symptoms affected caregivers' psychosocial burdens, whereas frontal lobe dysfunction affected caregivers' burden due to the increase in the dependency of the patients. Given these correlations, further studies should examine interventions focused on the excessive dependency of the patients due to frontal lobe dysfunction to ameliorate the specific disabilities of patients and reduce caregiver burden.

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Disclosure statement

The authors have no potential conflicts of interest to disclose.

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Table 1. Characteristics of patients and association with the Zarit Burden Interview

Variables	Mean ± SD or Frequency (%)	Range	r (*P*) †
Age (years)	73.0 ± 9.8	46-89	-0.22 (0.24)
Sex			
Male	8 (26.7%)	-	
Female	22 (73.3%)	-	-0.06 (0.75)
Education (years)	11.8 ± 2.4	9-16	0.09 (0.63)
Measurements			
Zarit Burden Interview	12.6 ± 6.2	1-38	
Frontal Assessment Battery	13.8 ± 3.7	4-18	-0.67 (<0.001)**
Mini-Mental State Examination	22.9 ± 3.2	13-26	-0.39 (0.03)*
Neuropsychiatric Inventory	2.7 ± 3.9	0-16	0.57 (0.001)**
Physical Self-Maintenance Scale	1.0 ± 1.8	0-7	0.55 (0.002)*
Geriatric Depression Scale	4.2 ± 4.0	0-13	0.13 (0.51)

*$P < 0.05$; **$P < 0.001$

† Results of Pearson correlation analyses performed to investigate the relationships between ZBI scores and each patient's characteristics and measurements.

Table 2. Hierarchical Regression Model Relating Burden to Neuropsychiatric Inventory, Physical Self-Maintenance Scale, and Frontal Assessment Battery

Hierarchical Step	Predictor Variables	Adjusted R^2	Change Statistics		
			ΔR^2	ΔF	Sig. ΔF
1	Neuropsychiatric Inventory	0.30	0.32	13.2	0.001**
2	Physical Self-Maintenance Scale	0.49	0.20	11.3	0.002*
3	Frontal Assessment Battery	0.55	0.08	5.12	0.032*

Total $R^2 = 0.60$, $F(3, 26) = 12.95$, $P < 0.001$; $*P < 0.05$; $**P < 0.001$

Table 3. Hierarchical Multiple Regression Analysis Relating Burden to Frontal Assessment Battery Subscales

Step	Predictor Variables	β	ΔR^2	*P*
1	Neuropsychiatric Inventory	0.36	0.32	0.01*
2	Physical Self-Maintenance Scale	0.30	0.20	0.04*
3†	FAB: Similarities	-0.04	0.19	0.79
	FAB: Verbal fluency	-0.10		0.48
	FAB: Motor sequence	0.23		0.13
	FAB: Conflicting instructions	-0.34		0.02*
	FAB: Go, No go	-0.21		0.18

†No patients showed the dysfunction of the subscale of FAB: Prehension behaviour

*$P < 0.05$; FAB = Frontal Assessment Battery

Table 4. Partial correlations between three factors of the Zarit Burden Interview and predictor variables [r(P)]†

Variables	Psychosocial	Dependency	Guilt
NPI	0.65 (< 0.001)*	0.12 (0.54)	0.16 (0.42)
PSMS	0.63 (< 0.001)*	0.12 (0.55)	0.39 (0.04)
FAB	-0.37 (0.06)	-0.48 (0.01)*	-0.07 (0.73)
FAB: Similarities	-0.18 (0.35)	-0.30 (0.12)	0.009 (0.96)
FAB: Verbal fluency	-0.18 (0.37)	-0.27 (0.16)	-0.19 (0.34)
FAB: Motor sequence	-0.13 (0.50)	02 (0.93)	0.27 (0.16)
FAB: Conflicting instructions	-0.50 (0.007)*	-0.53 (0.004)*	0.28 (0.15)
FAB: Go, No go	-0.13 (0.50)	-0.42 (0.03)	0.18 (0.35)

†Other predictor variables are covariated.

*$P < 0.0166$ (0.05/3); FAB = Frontal Assessment Battery, NPI = Neuropsychiatric Inventory, PSMS = Physical Self-Maintenance Scale