

# FRONTAL FUNCTION, DISABILITY AND CAREGIVER BURDEN IN ELDERLY PATIENTS WITH MAJOR DEPRESSIVE DISORDER

Hui-Mei Chen,<sup>1,2</sup> Shu-Ying Hou,<sup>3,4</sup> Yi-Chun Yeh,<sup>3</sup> Chiung-Yi Chang,<sup>3</sup> Ju-Yu Yen,<sup>3,5,6</sup>  
Chih-Hung Ko,<sup>3,5</sup> Cheng-Fang Yen,<sup>3,5</sup> and Cheng-Sheng Chen<sup>3,5,6</sup>

<sup>1</sup>Department of Occupational Therapy, College of Health Science, and

<sup>5</sup>Department of Psychiatry, <sup>6</sup>Graduate Institute of Medicine, College of Medicine, Kaohsiung Medical University, and Departments of <sup>2</sup>Rehabilitation, <sup>3</sup>Psychiatry and

<sup>4</sup>Nursing, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan.

Caregivers of patients with late-life major depressive disorder experience a significant level of general caregiver burden. Disability in patients is possibly one of the origins of caregiver burden. Frontal lobe dysfunction might be the source of disability. This study investigated if frontal lobe dysfunction (body level) of patients with late-life major depressive disorder was associated with their disability (individual level), and if it led to a high level of caregiver burden (societal level). Thirty-four unselected pairs of caregivers and their family members with late-life major depressive disorder were recruited. Frontal Assessment Battery and Timed Instrumental Activities of Daily Living (TIADL) were used to assess patients' frontal function and disability, and Caregiver Burden Inventory was used to measure caregiver burden. Frontal Assessment Battery correlated with TIADL ( $r=-0.47$ ;  $p<0.006$ ). TIADL score was also associated with two subscales of the Caregiver Burden Inventory: social ( $r=0.38$ ,  $p=0.026$ ) and time-dependent ( $r=0.37$ ,  $p=0.033$ ). This study supported the hypothesis that frontal lobe dysfunction in elderly patients with depression is associated with their disability in instrumental activities of daily living. Disability is related to social and time-dependent aspects of caregiver burden. Further studies to examine proposed cognitive interventions are suggested to reduce patient disability and caregiver burden.

**Key Words:** caregiver burden, depression, disability, elderly, frontal function  
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Major depressive disorder is one of the most common mental disorders among the elderly [1,2], and can cause severe health problems [3]. It presents with a diverse range of symptoms. Besides depressive symptomatology, substantial numbers of patients with late-life major depressive disorder present with cognitive impairment [4,5], among which, at related to frontal

lobe function is the most common [6–8]. Furthermore, elderly patients with depression and cognitive impairment are at about a 2-fold higher risk of developing dementia later compared with those without cognitive impairment [9]. As with dementia, elderly patients with depression experience greater disability, particularly in the aspect of instrumental activities of daily living (IADL) [10,11]. Impairment in IADL is proposed as a treatment target to improve outcome of late-life depression [10].

Caregiver burden for the elderly is a major public health issue and it has been suggested that it should be evaluated as part of comprehensive geriatric assessment [12]. It is composed of multiple dimensions



ELSEVIER

Received: Mar 2, 2010 Accepted: May 21, 2010  
Address correspondence and reprint requests to:  
Dr Cheng-Sheng Chen, Department of Psychiatry,  
Kaohsiung Medical University, 100 Tz-You 1<sup>st</sup>  
Road, San-Ming Area, Kaohsiung 80708, Taiwan.  
E-mail: sheng@kmu.edu.tw

including physical, emotional, developmental, social burdens, and time dependence [13]. Etiology includes patients' conditions and caregivers' characteristics. Additionally, functional decline has been shown as the major predictor of caregiver burden. Specific functional limitation, such as IADL, could result in high levels of burden for caregivers of non-depressed patients with cognitive impairment [14]. For all cognitive domains, frontal system behavioral functioning has an impact on daily functioning to a greater extent than do memory changes [15]. One previous study reported that caregivers of patients with late-life depressive disorder experience a moderate-to-high level of general caregiver burden [16]. Although family caregivers of patients with late-life depression experience a greater burden than family caregivers of patients without late-life depression [16,17], most relevant research regarding caregiver burden has focused on dementia. The understanding of correlates of caregiver burden and late-life depression is relatively limited, thus it is worthwhile to examine if a similar picture exists with regard to the relationship between disability and frontal dysfunction with caregiver burden, to improve the efficacy of depression treatment.

The International Classification of Functioning, Disability and Health (ICF) is the framework of the World Health Organization for measuring health and disability [18]. ICF is a classification of health-related domains, including body, individual and societal perspectives [19]. It can be used in clinical practice to construct and facilitate a feasible framework for problem-solving in disease processes [20]. Based on the ICF, we wanted to investigate if frontal lobe dysfunction (body level) of patients with late-life depression was associated with their IADL (individual level). Furthermore, we wished to establish if patients' disability (individual level) led to a high level of caregiver burden (societal level). We hypothesized that frontal lobe dysfunction was correlated with disability in IADL in late-life depression and, in turn, such disability led to higher caregiver burden.

## **METHODS**

### ***Subjects***

Thirty-four unselected pairs of caregivers and their elderly family members with major depressive disorder were recruited from geriatric psychiatric outpatients

at a university teaching hospital during a 1-year study period. Caregivers were included if they were in charge of caring and spent at least one-third of the time caring for patients in the past month of our study. Inclusion criteria for the patients were: (1) age  $\geq 60$  years; (2) a diagnosis of major depressive disorder based on the Diagnostic and Statistical Manual of Mental Disorders, 4<sup>th</sup> edition (DSM-IV)[21]; (3) good ambulatory function in basic daily living; and (4) no dementia and a score of less than 24 on the Mini-Mental State Examination. Exclusion criteria were any other DSM-IV Axis I diagnosis, or clinical history of major neurological illness. The protocol was approved by the Institutional Review Board of Kaohsiung Medical University. All participants gave informed consent.

### ***Measures***

Depression severity and cognitive dysfunction were evaluated using the 17-item Hamilton Rating Scale for Depression (HRSD) [22] and the Mini-Mental State Examination [23], respectively. Frontal Assessment Battery (FAB) is a brief bedside cognitive and behavioral battery for assessment of frontal lobe functions [24]. It was relatively easy to administer and had good validity and reliability [25]. FAB consists of six subtests that comprise conceptualization, mental flexibility, motor programming, sensitivity to interference, inhibitory control, and environmental autonomy. The total score is 18, and higher scores indicate better frontal functioning. A trained study nurse performed the FAB for each study participant. Timed Instrumental Activities of Daily Living (TIADL) has been developed to assess ability to perform IADL well [26]. TIADL measured basis of performance, rather than self-report or informant-report. All tasks addressed the following five IADL domains: communication, finance, cooking, shopping, and taking of medications. All tasks made use of actual everyday objects, not enlarged or pictured stimuli, except for communication and drug use. These two domain tasks were modified by graphical patterns (telephone book and drug containers) instead of written words in common representation. All tasks were time-limited. If the subject did not complete the task within this time period, testing on that item was terminated. The three-level scoring of each item was: (1) task was completed correctly within the time limit without error; (2) task was completed within the time limit with minor errors; and (3) task was either not completed in the time limit or completed

with major errors. The Caregiver Burden Inventory (CBI) was a 24-item, caregiver report measure of burden [27]. Each item used a five-point Likert scale that ranged from 0 (not at all descriptive) to 4 (very descriptive). It had five subscales, including time dependence, developmental, physical, social, and emotional burdens. It took 10–15 minutes to administer. We used the Chinese version of CBI, which has been validated [28].

### Statistical analysis

Independent Student's *t* test was used to assess the significance of differences in scores on continuous variables with two groups. Pearson's correlations between two continuous variables were examined. Partial correlations were used to examine correlations between two continuous variables, controlling for confounding factors. A *p* value <0.05 was considered statistically significant.

## RESULTS

The sociodemographic and clinical data of the patients and their caregivers are presented in the Table. Nearly half of the caregivers were female; the average age was

55.1 ± 15.1 years; average educational level was 12.2 ± 4.4 years; 82.4% were married; 44.1% were spouses; and 55.9% were parents. For the patients, 79.4% were in remission. Mean FAB score in patients was 13.9 ± 2.5, and mean TIADL score was 11.9 ± 1.9. Severity of caregiver burden represented by CBI revealed a total score of 16.1 ± 16.2; 2.8 ± 3.7 in the physical burden subscale; 3.6 ± 5.1 in the developmental burden subscale; 1.3 ± 1.9 in the emotional burden subscale; 2.5 ± 3.1 in the social burden subscale; and 5.9 ± 5.8 in the time burden subscale.

For the patients, there was no difference in total score for TIADL between sexes (male *vs.* female = 11.5 ± 1.3 *vs.* 12.1 ± 2.2; *t* = -0.9; *p* = 0.40). Total score for TIADL did not correlate with age (*r* = 0.22; *p* = 0.21), and HRSD (*r* = 0.16; *p* = 0.36), but it was inversely associated with educational level (*r* = -0.58; *p* < 0.001). After controlling for education and age, there was an association between total score for TIADL and FAB (*r* = -0.47; *p* < 0.006).

We further examined the correlates of caregiver burden with respect to characteristics of caregivers and patients' disabilities. Caregivers' sex, age and educational level were not associated with total scores for CBI and its subscales. Offspring of caregivers seemed

**Table.** Demographic and clinical characteristics of caregivers and patients with late-life major depressive disorder\*

	Caregivers ( <i>n</i> = 34)	Elders with major depressive disorder ( <i>n</i> = 34)
Sex, female	16 (47.1)	22 (64.7)
Age (yr)	55.1 ± 15.1 (18–80)	71.6 ± 5.8 (61–84)
Education (yr)	12.2 ± 4.4 (0–22)	6.2 ± 5.7 (0–16)
Marital status		
Married	28 (82.4)	25 (73.5)
Single/widowhood	6 (17.6) <sup>†</sup>	9 (26.5) <sup>‡</sup>
Relationships with patients		
Spouse	15 (44.1)	–
Offspring	19 (55.9)	–
Caregiver burden	16.1 ± 16.2	–
Physical burden	2.8 ± 3.7	–
Developmental burden	3.6 ± 5.1	–
Emotional burden	1.3 ± 1.9	–
Social burden	2.5 ± 3.1	–
Time burden	5.9 ± 5.8	–
Remitted state	–	27 (79.4)
HRSD	–	5.9 ± 5.5 (0–21)
FAB	–	13.9 ± 2.5 (8–18)
TIADL	–	11.9 ± 1.9 (10–16)

\*Data presented as *n* (%) or mean ± standard deviation (range); <sup>†</sup>included one widow and five single; <sup>‡</sup>nine widow. HRSD = Hamilton Rating Scale for Depression; FAB = Frontal assessment battery; TIADL = Timed Instrumental Activities of Daily Living.

to score higher for total CBI score than did spouse caregivers ( $20.7 \pm 15.3$  vs.  $10.4 \pm 15.9$ ;  $p=0.06$ ), especially in the subscale of time dependence burden ( $7.8 \pm 5.8$  vs.  $3.6 \pm 5.1$ ;  $p=0.04$ ) and social burden ( $3.5 \pm 3.3$  vs.  $1.1 \pm 2.2$ ;  $p=0.02$ ). Patients' total scores for HRSD were not associated with total scores for CBI and its subscales. TIADL score was also associated with social and time-dependent subscales of CBI ( $r=0.25$ ,  $p=0.15$  for total score;  $r=-0.02$ ,  $p=0.93$  for physical;  $r=0.12$ ,  $p=0.51$  for developmental;  $r=0.13$ ,  $p=0.46$  for emotional;  $r=0.38$ ,  $p=0.026$  for social; and  $r=0.37$ ,  $p=0.033$  for time-dependent subscales) after adjustment for the relationship variable (Figure).

## DISCUSSION

The principal finding of this study was that frontal lobe dysfunction in depressed patients was associated with their lack on ability in IADL. Furthermore, this inability in depressed patients increased their caregiver burden regardless of the caring relationship.

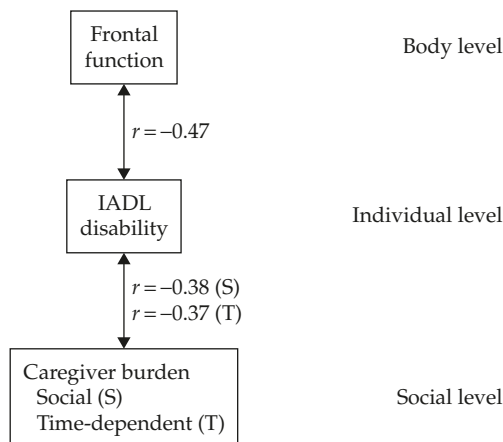
One major methodological consideration in this study was the use of performance-based IADL measurement rather than traditional self-reported or informant-reported methods. One weakness of traditional methods is that caregivers' level of burden might interfere with their judgment or perception of patients' disability level. For example, caregivers' perceptions tend to align the patients' functional status with their own burden level and the psychological distress caused by caring for the patient [14]. Also, patients with subtle

disability might not be apparent because they compensate for their disability with a change in either the frequency or method of doing an activity. Therefore, traditional methods are not sensitive enough to detect any subtle changes.

Conversely, performance-based measures are thought to be more sensitive to change in disease status than are self-report instruments [29]. In our study, TIADL allowed the examiner to observe the performance directly. Although TIADL takes longer to carry out, it is thought to be a more objective and suitable tool than the conventional self-reported or informant-observed assessments. Thus the use of performance-based measures of functional capacity allows investigators and clinicians to examine objectively the relationship between caregivers' burden and observed functional performance among cognitively impaired patients.

Various symptoms or impairments related to depression can lead to disability. A previous study has illustrated that some depressive symptoms, such as anxiety, depressive ideation, psychomotor retardation and weight loss, are significantly associated with disability in depressive disorder [10]. We did not find any association between depression severity and disability in this study. The reason for the lack of association might have been the high rate of remission among our study participants. The depression symptomatology was not severe enough to cause disability. Clinically, depressive symptoms can be relieved by antidepressant treatment. However, frontal dysfunction is considered to be a persistent impairment in late-life depression, even in patients in remission [30].

Our result that frontal impairment was related to disability was similar to previous findings that symptoms and cognition associated with striato-frontal dysfunction contribute to disability in depressed elderly patients [15,31]. The results imply that frontal lobe dysfunction in patients with late-life major depressive disorder erodes their ability to understand which tasks are necessary or how to approach the accomplishment of these tasks. Nevertheless, the fact that frontal lobe dysfunction was associated with IADL restriction seemed to be regardless of diagnosis. A study that has examined non-depressive subjects with mild cognitive impairment also has found that disability in IADL is significantly associated with cognitive performance, and mainly related to executive functioning [32]. Combining our results with others previously obtained,



**Figure.** Relationships between frontal lobe function, disability and caregiver burden in late-life major depressive disorder in remission.



we propose that any neuropsychiatric diseases that are linked to striato-frontal dysfunction are related to high levels of disability in IADL.

Caregiver burden has various dimensions. In the present study, disability in IADL affected caregivers' time dependence and social burdens, but not other burdens. Previous studies of patients with dementia also have demonstrated that patients' disability, including impairments in orientation, communication, financial, and transportation skills, are major predictors of the time-dependent burden [14,33]. The current results imply that patients' functional disabilities directly relate to time pressures and caregivers' feelings of being socially isolated. The caregiver is required to take over the patients' everyday tasks, thereby creating the greatest time demand. Social burden in this study can be explained by over half of the participants being offspring of the patients. Members of the younger generation ought to have their own social life instead of undertaking care tasks.

These findings have clinical implications in that an intervention focused on frontal lobe dysfunction might be beneficial in reducing disability. Although amelioration of depressive symptoms with antidepressant treatment can reduce caregiver burden [16], in this study, we found that frontal lobe impairment related to depressive disorder contributed to disability as well. Frontal lobe dysfunction in late-life depression is not only linked to treatment resistance [34], but also worse outcomes, such as recurrence of depression [7], disability, and further development of dementia [35].

Accordingly, frontal dysfunction is proposed to be a target for intervention. Our study group has previously investigated the effectiveness of cognitive interventions on frontal dysfunction among elderly patients with subjective cognitive complaints [36]. Among these interventions, cognitive stimulation strategy involves group activities and discussion to enhance cognitive and social functions. In general, professional guidance is less necessary in the cognitive stimulation program. In the future, this program could be examined to minimize the impact of frontal lobe dysfunction in late-life major depressive disorder, and in turn, indirectly to reduce disability in IADL. Finally, it could be helpful for decreasing caregiver burdens.

This study had some limitations. First, the small sample size hindered the possibility of multivariate testing to control for the potential confounder effect from medical burden. However, our study participants

showed no significant impairment in basic activities of daily living. The medical burden was supposed not to interfere with caregiver burden in this study. Also, we did not apply for  $p$  value adjustment for multiple comparisons because of the small sample size, which could have increased type I error. Our preliminary findings therefore need confirmation with further studies with a larger sample size. Second, the cross-sectional design also limited the ability to make causal inferences in this study. Finally, a more sophisticated frontal function measure, besides FAB, is advised in further studies. Neuroimaging technologies should be an alternative and superior method for defining frontal lobe function and might be expected to find a more robust relationship between frontal function and disability. Further studies with a prospective design, larger sample size, and a more precise frontal function are needed to address these issues.

In conclusion, our study suggests that frontal lobe dysfunction is related to inability in IADL among patients with late-life major depressive disorder. This inability is related to the social and time-dependent aspects of caregiver burden. Given these correlations, further studies are suggested to examine proposed interventions that involve frontal lobe function to ameliorate the inability of patients and reduce the caregiver burden.

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# 重度憂鬱症老年人之額葉功能、失能與其照顧者負荷

陳惠媚<sup>1,2</sup> 侯叔英<sup>3,4</sup> 葉怡君<sup>3</sup> 張瓊怡<sup>3</sup> 顏如佑<sup>3,5,6</sup> 柯志鴻<sup>3,5</sup> 顏正芳<sup>3,5</sup> 陳正生<sup>3,5,6</sup>

高雄醫學大學<sup>1</sup> 健康科學院 職能治療學系<sup>5</sup> 醫學院醫學系 精神學科<sup>6</sup> 醫學院 醫學研究所

高雄醫學大學附設醫院<sup>2</sup> 復健科<sup>3</sup> 精神科<sup>4</sup> 護理部

老年重度憂鬱症照顧者有顯著的照顧負荷，病人的失能可能是造成照顧者負荷的起因之一。額葉功能之運作障礙可能是失能的來源。此研究的目的主要在研究老年重度憂鬱症患者的額葉功能障礙（身體層面）是否與其失能（個體層面）有關，且進而引起高的照顧負荷（社會層面）。研究對象為 34 對老年重度憂鬱症患者與其照顧者，使用額葉評估測驗（Frontal Assessment Battery, FAB）與定時工具性日常生活活動量（Timed Instrumental Activities of Daily Living, TIADL）工具分別測量患者之額葉功能與失能狀態；使用照顧者負荷量表（Caregiver Burden Inventory, CBI）評估患者之照顧者的照顧者負荷。結果顯示 FAB 與 TIADL 達相關性（ $r = -0.47$ ； $p < 0.006$ ），TIADL 分數與 CBI 中兩個分項目呈相關性，分別為社會性負荷（ $r = -0.38$ ； $p = 0.026$ ）與時間倚賴負荷（ $r = 0.37$ ； $p = 0.033$ ）。本研究結果支持老人重度憂鬱症患者的額葉功能與其失能程度是逆相關，其失能狀態進而影響照顧者在社會性與時間倚賴之負荷。未來可以進一步驗證是否使用認知治療介入來降低失能程度與照顧者負荷。

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通訊作者：陳正生醫師

高雄醫學大學附設醫院精神科

高雄市三民區自由一路 100 號