Cognitive and Functional Impairment in Chinese Elderly with Late-onset Depression

華裔老年晚發性抑鬱症患者的認知和功能缺損研究

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Abstract

Objectives: To investigate cognitive and functional impairment in Chinese elderly subjects with late-onset depression.

Methods: Subjects with late-onset depression and who were clinically non-demented were recruited. Their cognitive and functional scores were compared with those of cognitively normal elderly controls and elderly persons with mild cognitive impairment. Functional ability was assessed by the Disability Assessment for Dementia score. Various cognitive domains were assessed including global cognitive function, delayed episodic memory, working memory, and categorical verbal fluency test.

Results: A total of 105 depressed subjects and 324 non-depressed controls (149 normal elderly controls and 175 with mild cognitive impairment) were recruited. The depression group had significantly poorer performance in all cognitive assessments compared to the normal elderly control group. The depression group had a similar cognitive profile to those with mild cognitive impairment, except that its subjects had slightly better performance in the Categorical Verbal Fluency Test, delayed recall testing, and the Chinese version of the Alzheimer’s Disease Assessment Scale–Cognitive subscale test. Depressed subjects had significantly lower functional scores in instrumental activities of daily living than the non-depressed, normal elderly controls, and those with mild cognitive impairment.

Conclusions: Our results demonstrate that Chinese elderly with late-onset depression had cognitive impairments in multiple domains similar to those encountered in the age- and sex-matched non-depressed controls with mild cognitive impairment. However, their functional performance was significantly poorer than that in these controls. This study provided extensive characterisation of the range and depth of cognitive and functional impairments in elderly patients with late-onset depression.

Key words: Age of onset; Cognition disorders; Depression
Introduction

Given that the personal and public burdens of both depression and cognitive impairment are likely to increase along with the ageing population, it is important for mental health professionals to better understand the characteristics of cognitive impairment in depression, as well as how to detect and treat it.

There is increasing recognition that cognitive impairment occurs in geriatric depression, and that its presentation is heterogeneous. Most research has found that depressed individuals tend to have worse performance relative to non-depressed comparison groups on a number of neuropsychological measures. The most consistent deficits occur in the areas of processing speed; effortful tasks involving selective attention, response inhibition, and performance monitoring (i.e. executive functions); and the acquisition and retrieval of new information (i.e. episodic memory). Neurocognitive deficits involving executive dysfunction are common when the episode of depression occurs in late life. Some research suggests that memory deficits may be more focally affected among older individuals with a history of recurrent depression beginning earlier in life.

Studies involving multiple cognitive domains found that 33 to 50% of depressed individuals have clinical levels of cognitive impairment. The presence of depression (particularly in late-onset cases) should raise the possibility of screening for cognitive impairment as part of a long-term approach to care.

Depression has considerable influence on functional impairment and disability. The relationship between disability and depression is complex and probably bidirectional. In a systematic review of variables predicting functional decline in community-dwelling older adults, depression was one of the key risk factors. Impairment in activities of daily living (ADL) is likely an underappreciated feature of depression and one that has important effects on dementia outcomes. Functional impairment may also be a marker for adverse outcomes. Among depressed individuals, self-reported impairments in instrumental activities of daily living (IADL) are associated with more pervasive cognitive impairment and persistence of impairment after depression remits. Thus, evidence of functional impairment among individuals with depression may be a warning sign of individuals who are at risk for cognitive decline and that this risk may be lowered by effective identification and treatment.

In Hong Kong, there is a paucity of studies on the cognitive and functional profiles of subjects with late-onset depression. Our study aimed to investigate cognitive and functional impairment in Chinese elderly subjects with late-onset depression. We hypothesised that such elderly had impairment in cognition and IADL compared with non-depressed age- and education-matched controls. The corresponding findings could provide more information to characterise the clinical presentation of late-onset depressive syndromes.

Methods

Sample

Depressed Subjects

Patients aged ≥ 60 years who fulfilled the DSM-IV criteria for major or minor depression were recruited from psychiatric outpatient clinics and the inpatient psychiatric unit. The onset of the first depressive episode was aged ≥ 50 years.

Each depressed subject was evaluated by a qualified psychiatrist to establish eligibility for inclusion in the study and a clinical diagnosis, and to assess clinical staging based on the Clinical Dementia Rating (CDR) scale. Subjects with a global CDR score of 0 or 0.5 were recruited.

Controls

The control subjects were recruited from a population-based epidemiology study of cognitive impairment in elderly conducted from October 2005 to July 2006. The subjects had been assessed by an experienced psychiatrist and were neither clinically demented nor depressed. All of the subjects were ≥ 60 years with no history or current depression. Control subjects with CDR of 0 were classified as cognitively normal controls (NC). Control subjects with CDR of 0.5 and delayed recall test score of > 1.5 standard deviation (SD) below the mean of the NC were classified as having mild cognitive impairment (MCI). All controls were age- and education-matched with the depressed subjects.

We excluded subjects and controls with any prior history of degenerative neurological disorder, dementia, cortical strokes, severe or unstable physical illness, and prior or current substance / alcohol abuse. Subjects that had electroconvulsive therapy in the past 3 months were also excluded. The psychiatrists explained the procedure and obtained informed consent from the participants or their caregivers. The entire study was approved by the Joint CUHK-NTEC Clinical Research Ethics Committee of the Chinese University of Hong Kong.

Assessments

All subjects underwent a comprehensive psychiatric, cognitive, and functional assessment. Depression was diagnosed according to the DSM-IV criteria, and symptom severity was rated using the Montgomery-Asberg Depression Rating Scale (MADRS) and the Hamilton Depression Rating Scale (HDRS).

Cognitive Tests

Global cognitive assessment was estimated using the Cantonese version of the Mini-Mental State Examination and the Chinese version of the Alzheimer’s Disease Assessment Scale–Cognitive subscale (ADAS-Cog). To test for episodic memory, subjects were also examined using a 10-minute delayed recall of a word list from the ADAS-Cog. Digit span and visual span tests were carried out to test attention and working memory. The Category
Verbal Fluency Test (CVFT) was performed as a test of executive function. In the CVFT, subjects were asked to generate exemplars in the categories of animals, fruit, and vegetables within 1 minute. Combined scores were then computed.\(^{19}\)

**Disability Assessment for Dementia Scale**
The Disability Assessment for Dementia (DAD) scale is a validated measure of ADL designed specifically for use in patients with dementia.\(^{16}\) The Chinese version of the DAD scale has been validated in Chinese subjects.\(^{20}\) Each test item is considered by the cognitive processing involved as being an initiation item, a planning and organisation item, or a performance item. Of the 47 items, 14 are assigned as initiation items, 15 as planning and organisation items, and 18 as performance items. The DAD score is expressed as a percentage, with higher scores indicating better functioning. Apart from the total DAD score, the scores for basic and IADL domains, the initiation, planning and organisation, and performance scales can also be analysed.

**Statistical Analyses**
Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS 17.0; SPSS Inc., Chicago [IL], US). The demographic data, cognitive scores and functional scores between groups were analysed using analysis of variance with Bonferroni correction. The significance level was set at \(p < 0.05\). The Chi-square statistics was used to compare frequencies of the categorical demographic data. \(Z\) scores of the cognitive and functional scores were calculated with reference to the mean scores of the NC group.

**Results**
The whole sample consisted of 429 subjects; 105 subjects belonged to the depression group and 324 to the non-depressed controls. There were 149 subjects in NC group and 175 in MCI group. In all, there were 175 male and 254 female subjects.

The demographic characteristics of the subjects are summarised in Table 1. The depression and NC groups were matched in terms of age and education level. The mean (± SD) age was 74 ± 6 years and the mean (± SD) duration of education was 3.6 ± 3.9 years. The depression group had a significantly higher female-to-male ratio. In the depression group, the respective mean (± SD) MADRS and HDRS scores were 23 ± 9 and 18 ± 8. The mean depressive scores reflected that they had mild-to-moderate depression.

**Cognitive Profiles**
The depression group showed significant cognitive impairment compared to the NC group in all cognitive tests including global cognitive function, delayed recall memory, working memory, and CVFT. The depression group had more prominent impairment in episodic memory than for other cognitive domains, as reflected in the \(Z\) scores (Fig 1). The depression group had significantly better performance than the MCI group in the ADAS-Cog, delayed recall test, and CVFT. The MCI group had more prominent impairment in episodic memory and verbal fluency compared to the NC group. Of 105 depressed subjects, 61 (58%) had a global CDR of 0.5, 51 (47%) had a delayed recall test score of > 1.5 SD below the mean of the NC group. Details of the cognitive profiles are shown in Table 2.

**Functional Performance**
The depression group had poorer functional performance than the NC and MCI groups in terms of IADL. As reflected by the \(Z\) scores, the impairment was more prominent for the motivation, as well as organisation and planning subscores (Fig 2). There were no significant differences in basic ADL between depression and NC groups. Details are also shown in Table 3.

**Discussion**
This study provided a characterisation of the cognitive and functional profiles in Chinese elderly with late-onset depression. Depressed subjects showed cognitive impairments affecting episodic memory, working memory, executive functions and global functions compared to the age- and education-matched NC group. Consistent with

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* Comparison between normal control and depression groups, as well as mild cognitive impairment and depression groups.
dementia, are slowed processing speed, deficits in executive function and memory. Executive function dysfunction and/or slowed processing speed (both putative indices of frontostriatal dysfunction) mediate other cognitive weaknesses in geriatric depression, including poor visual the literature, impairment was found to affect multiple cognitive domains, including episodic memory, executive functioning, and processing speed. The most consistent cognitive deficits observed in depressed patients, who do not meet criteria for early dementia, are slowed processing speed, deficits in executive function and memory. Executive function dysfunction and/or slowed processing speed (both putative indices of frontostriatal dysfunction) mediate other cognitive weaknesses in geriatric depression, including poor visual cognitive impairments in depression and mild cognitive impairment (MCI) groups. Abbreviations: CMMSE = Cantonese version of the Mini-Mental State Examination; CVFT = Category Verbal Fluency Test; and ADAS-Cog = Alzheimer’s Disease Assessment Scale–Cognitive subscale.

Figure 2. Profiles of functional impairment in depression and mild cognitive impairment (MCI) groups. Abbreviations: DAD = Disability Assessment for Dementia scale; and IADL = instrumental activities of daily living.
spatial skills and episodic memory. A recent study found that the effect of slowed processing speed on executive function deficits was greater than that on memory deficits, though its effect was not sufficient to explain deficits in other domains that exist in parallel. The cognitive deficits in geriatric depression may stem from a diversity of structural brain changes. Late-onset depression is associated with pathology in subcortical and deep white matter structures and more frequently occurs with cognitive impairment, typically with prominent features of executive dysfunction that reflect underlying disruption of frontostriatal circuits.

It has been suggested that compared to other cognitive domains, measures of executive function may have good prognostic value with regard to responsiveness to treatment, whereas measures of global cognitive function and memory identify patients ‘at risk’ of dementia.

Our results suggest that it is difficult to differentiate between control subjects with MCI and depressed subjects on the basis of their neuropsychological profiles. Zihl et al. also reported similar neuropsychological profiles for attention, memory, and executive functions in MCI and in depression.

Although the depressed subjects had less severe cognitive impairment than the age- and education-matched community controls with MCI, they showed more marked functional impairment. This might imply that late-onset depression is associated with additional functional impairment, independent of the cognitive impairment in older persons with MCI. Functional disability may result from depressive symptoms such as fatigue or apathy, which are reflected in their lower motivation, planning, and organisational scores. Lack of interest and motivation, depressive mood, compounded by behavioural abnormalities resulting from executive dysfunction, may well account for functional disability in elderly subjects with late-onset depression.

The strengths of the present study are: (1) recourse to a heterogeneous geriatric patient group to maximise the
generalisability of findings; and (2) inclusion of a large
sample of elderly control subjects to account for age-related
cognitive change. Regarding limitations, we have difficulty
performing a comprehensive neuropsychological battery
to assess all the community control subjects, particularly
the executive tests and the tests for information processing
speed. Moreover, our control sample had relatively low
education levels and had difficulty completing the more
complex executive tests. Any future study should entail
more detailed tests into attention and information processing
speed, so as to delineate age-related and mood-related
cognitive dysfunction.

In conclusion, late-onset depression affects mood,
cognition and functional ability in the elderly. Depression
with cognitive deficits showed broad-based cognitive
impairment, similar to that in community elderly with
multi-domain MCI. However, late-onset depression was
associated with impairment in initiation, organisation and
planning of IADL, which was out of proportion to the
cognitive deficit.

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