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Executive functions in elderly men

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Abstract The executive function deficit is greater in depressed patients with cardiovascular disease than in depressed patients without cardiovascular disease. Late-life depression is said to have a vascular etiology and would worsen the executive function. A cross-sectional design was used for this study. The study was done in outpatient clinics of Kaohsiung Veterans General Hospital and National Cheng Kung University Hospital, Taiwan. Three hundred thirty-five older elderly men (>75 years old) were chosen as study participants, some military veterans and some not. The mini-mental state examination was used to exclude those suspected of dementia, the Mini-International Neuropsychiatric Interview to screen those undergoing a current major depressive episode, and the revised Geriatric Depression Scale Short Form to measure the severity of depression. Specialist physicians obtained past histories of medical illnesses

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through chart reviews, history taking, and health examinations. Elderly men with major depression comorbid with cardiovascular disease had worse executive functions. Executive function impairment is greater in elderly men diagnosed with major depression comorbid with cardiovascular disease than in those without cardiovascular disease.

Keywords Elderly men · Cardiovascular comorbidity · Major depression · Executive function

Introduction

The aging society has become a common phenomenon worldwide. More than 10% of the total population in Taiwan has consisted of elderly persons (≥65 years old) since 2007. A significant growing number of the old-old population older elderly (>75 years old), 42.1% of older population (≥65 years old) were also noted (Ministry of the Interior Statistical Information Service et al. 2006). Military veterans account for one sixth of these elderly (Veterans Affairs Commission EY et al. 2004) and have unique characteristics. When the Chinese civil war ended in 1949, many of the nationalist armed forces relocated from mainland China to Taiwan. After resigning from the armed forces, many of these men remained in Taiwan and the majority never married (Weng 1999). Their languages, habits, and value systems were different from those of local people, which made it difficult for them to develop new social networks and get jobs in Taiwan (Lu 1998). In addition, because they have more medical disabilities, are more vulnerable to depression, and are more dependent on social support than are the younger elderly (60–74 years old) (Blelsky 1990), their symptomatic expressions are complex and contribute to their increased vulnerability in Taiwan. However, because current knowledge about and studies on the medical comorbidities and psychiatric illnesses of elderly patients are limited, it is a challenge for physicians to identify them early and precisely.

Depression is the leading cause of geriatric psychiatric problems and increases with age in the Han Chinese old elderly population in Taiwan (Chou and Chi 2005). Between 1% and 4% of the elderly have major depressive disorder (Blazer 2003), and its prevalence in the elderly older than 85 years is twice that in those 70 years old (Palsson et al. 2001). In Taiwan, the prevalence of depression in the elderly is 39.2% in psychiatric hospitals and 29.5% in the community (Lin et al. 2004). The high prevalence of major depression seems to be a significant risk factor of suicide in the very elderly (Conwell et al. 2002).

In addition, most of the depressed elderly are comorbid with physical illness, cognitive impairment, disability, or social isolation (Alexopoulos et al. 2002). In addition, some medical illnesses, such as cardiovascular comorbidities, are associated with depression (Eastwood et al. 1989). There is imaging evidence to support that specific cardiovascular lesions are related to late-onset depression (Krishnan 1991). Depression in the elderly is also more likely to increase the risk of type II diabetes mellitus (DM) and hypertension (Brown et al. 2004). The deficits in executive functioning measured by the Wisconsin Card Sorting Task (WCST) may be the result of damage to the frontal–subcortical circuits of the brain (Campbell et al. 2001), a series of discrete pathways supporting executive cognitive functions (Mega and Cummings 1994). This region is particularly vulnerable to ischemic injury because of its relatively long, small diameter, penetrating branches deriving from the anterior and middle cerebral arteries (Campbell et al. 2001). Moreover, dysregulation between the prefrontal cortex and the limbic system has been implicated in the pathogenesis of major depressive disorder (Davidson et al. 2002) and might be associated with decreased cognitive functioning (Elderkin-Thompson et al. 2009). In summary, both depression and cardiovascular disease may both be associated with frontal lobe dysfunction and an increased risk for the development of cognitive impairment (Elderkin-Thompson et al. 2009; Gianaros et al. 2006; Hoshi et al. 2010). Moreover, the management and prognosis of underlying medical illnesses can be affected by major depression. Therefore, the association between depression and cardiovascular diseases have been reported and suggested for clinicians, who are urged to take it into account while the aging becomes important gradually.

The elderly usually have executive function disabilities in planning, initiating, shifting, working memory, and so on (Lockwood et al. 2002). Moreover, chronic illness, such as cardiovascular diseases, hypertension, heart disease, and DM were reported to be associated with executive dysfunction (Lowe et al. 1994; Schillerstrom et al. 2005). Both depression and cardiovascular diseases are risk factors for cognitive impairment (Austin et al. 2001; Barnes et al. 2006), but the various neuropsychological mechanisms underlying late-life depression can lead to different patterns of cognitive impairment (Crocco et al. 2010). Based on these findings, physicians may be able to find occult depression or cardiovascular disease by carefully evaluating the patient's cognitive functions. However, whether these symptoms are caused just by underlying cardiovascular diseases or are related to depression is unclear. In this study, we tried to clarify to what extent the executive function would be impaired in older elderly men with major depression with or without the comorbidity of cardiovascular disease. In addition, investigated and discuss whether the depression or cardiovascular disease or both are crucial in executive dysfunction.

Methods

Participants and procedures

This study was approved by the institutional review board of National Cheng Kung University Hospital. Participants were recruited from newly admitted residents of the Taiwan National Veterans' Care Homes in Tainan and Kaohsiung. They had voluntarily applied for residency in these home care centers because they were living alone, in poor health, lacking family and social support, or physically handicapped. The majority were ambulatory, physically capable, and able to provide for their own daily needs with no assistance from others. Only a few were physically disabled and required a wheelchair, cane or other ambulatory equipment, or needed other assistance.

Three hundred thirty-five residents, who had completed health examinations between 2004 and 2008 at clinics affiliated with the Veterans' Care Home, volunteered for this study. The study procedures were fully explained, and written informed consent was obtained from all.

The inclusion criteria were: (1) 75 years old or older, (2) male gender, (3) able to speak Mandarin or Taiwanese, and (4) capable of verbal communication. For the group with late-life depression (LLD), those with a diagnosis of current major depressive disorder were recruited. For the group with cardiovascular disease (CVD), medical measures were completed by a physician based on the interviews and medical chart review. Those with hypertension, diabetes, coronary heart disease, cigarette smoking, atrial fibrillation, and left ventricular hypertrophy were classified as patients with CVD. Patients in the LLD+CVD group were diagnosed as having a current depressive disorder and cardiovascular disease. The exclusion criteria were factors that might interfere with the presentation of depressive symptoms: (1) a history of dementia or suspected dementia, (2) a current diagnosis of psychiatric disorders other than current major depressive disorder, (3) currently using antipsychotics or mood stabilizers, or (4) current substance abuse.

All participants were interviewed by an attending psychiatrist for an initial evaluation, and then by psychiatrists and psychologists using the mini-mental state examination (MMSE), the Geriatric Depression Scale (GDS), and the Mini-International Neuropsychiatric Interview (MINI). All the patients with major depression in their depressive symptom-free stage were given an antidepressant and a small dose of benzodiazepines. To increase inter-rater reliability, all the interviewers were intensively trained on how to use the interview instruments, and all the interviewers were closely supervised by two of the authors (RBL and YKY). All demographic data, medical charts, and histories of medical illnesses were reviewed, and then the results of the participants' health examinations were analyzed. All participants were divided into four groups: healthy controls (HC), patients with CVD, patients with late-life major depression (LLD), and patients with major depression comorbid with cardiovascular diseases (LLD+CVD).

Measurements

We used the 30-item Chinese version of the MMSE (Guo et al. 1988) with a standardized norm to screen the participants. For those who had less than 2 years of education, the cutoff point score was 12/13; for those who had 3–9 years of education, the cutoff point score was 21/22; and for those who had more than 10 years of education, the cutoff point score was 23/24.

The Chinese version of the MINI was used to evaluate current major depressive episodes and other psychiatric diagnoses (Sheehan et al. 1998). The diagnostic criteria of the MINI are based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. The revised Chinese GDS was used to measure the severity of depression. The Chinese versions of the MINI and the GDS have been validated (Liao et al. 2000; Mui 1996).

Neuropsychological assessments

The WCST measures the ability to perform certain types of executive functions, including categorization, abstraction reasoning, maintain set, set switching, strategic planning, and modulate impulsive responding (Mohlman 2005). The test requires that certain cognitive functions be intact, for example, attention, working memory, and visual processing. Participants are required to try out different rules in order to find a correct method for sorting the cards. The test used cards that had to be sorted into piles in front of four stimulus cards. The participants were instructed to infer the matching principle from the feedback provided: “correct” or “incorrect,” depending on whether they guessed the rule correctly or not. The cards could be matched by number (1, 2, 3, or 4); color (yellow, green, blue, or red); or shape of the symbols (star, triangle, circle, or cross). The rule is applied for a run of trials and then changed without warning (Mei 1998). The inter-rater liability is 0.88–0.93, within-rater reliability is 0.91–0.96, and test–retest reliability is 0.57. Performance on the WCST was scored in terms of the total number of errors, perseverative errors, conceptual level response, number of categories completed (NCC), and trials to complete the first category (TCC) (Alexopoulos et al. 2005; Elderkin-Thompson et al. 2006; Elderkin-Thompson et al. 2004; Naismith et al. 2003, 2006; Nakano et al. 2008; Yuan et al. 2008).

Trail making test

The trail making test (TMT) (Lezak et al. 2004; Reitan 1958; Spreen and Strauss 1991) is a visuomotor task that consists of two parts; in part A, the participant was asked to draw lines to connect consecutively numbered circles on one worksheet, and then, in part B, to connect the same number of consecutively numbered and lettered circles by alternating between the two sets.

The instruction for both parts was to perform the test as correctly and as quickly as possible. The examiner has to point out errors made by the test as they occur so that the test can always complete the test without errors and the scoring can be based on time alone (Lezak et al. 2004). The time required to complete each task represents the relevant score. In contrast to part A, part B involves frequent switching between two mental sets. Because visual search and general motor speed are relevant for both parts of the test, calculating the difference in scores between parts A and B minimizes these interfering effects. The TMTB-A score is, therefore, well established as an instrument to assess executive functions with special emphasis on set shifting. While some researchers use the TMTB/A ratio for the same purpose (Arbuthnott and Frank 2000), a large-scale (n=285) comparative assessment of the two scores yielded better discriminatory power of the TMTB-A score with respect to the detection of performance differences between young and elderly tests (Drane et al. 2002).

Results

Demographic data

All participants in the study were male. Their mean age was 81.23±4.20, mean education level was 5.05±4.65, and mean MMSE score was 24.43±2.82. There were no significant differences in age between groups (F=1.13, p=0.34). Education levels (F=5.34, p=0.001) and MMSE scores (F=2.92, p=0.03) were significantly different, however. The post hoc showed that the CVD group had a significantly higher level of education (p=0.001) and MMSE score (p=0.045) than did the LLD+CVD group. The LLD and LLD+CVD groups had higher GDS scores than did the HC and CVD groups (p<0.0005) (Table 1).

Neuropsychological data

A significant difference in educational level as well as in the MMSE score were found among the four groups, and an effect of education in WCST was reported (Boone et al. 1993). Multiple analysis of covariate analysis was used to analyze differences in WCST and TMT scores (education levels and MMSE scores were controlled as covariate variables). The

Table 1 Demographic data

	Groups				Statistics	
	HC (n=45)	CVD (n=157)	LLD (n=43)	LLD+CVD (n=90)	F (p value)	Post hoc
Age (years)	81.41±3.89	81.02±4.22	80.53±3.28	81.80±4.67	1.13 (0.34)	–
Education (years)	5.23±4.01	5.93±5.14	4.79±3.98	3.53±3.98	5.34 (0.001)	CVD>LLD+CVD (p=0.001)
MMSE score	24.73±3.03	24.78±2.55	24.35±2.57	23.72±3.16	2.92 (0.03)	CVD>LLD+CVD (p=0.045)
GDS	2.25±1.87	2.44±1.31	7.47±1.81	6.83±2.60	121.43 (<0.0005)	LLD, LLD+CVD>HC, CVD (p<0.0005)

Data are means±SD

SD standard deviation, *CVD* elderly men with cardiovascular disease, *LLD* elderly men with late-life depression, *LLD+ CVD* elderly men with late-life depression comorbid with cardiovascular disease, *GDS* Geriatric Depression Scale

WCST scores were significantly different between groups. The post hoc analysis showed that overall, the HC group had the highest WCST scores, and that the LLD+CVD group had the lowest WCST and TMT scores. However, no significant differences were found between the CVD and LLD groups or between the LLD and LLD+CVD groups (Table 2). There were no significant differences in the TMT-A and TMT-B (because of their poorly sustained attention, only 195 participants completed the TMT-B) scores between groups.

Discussion

The association between depression and cognitive impairment agrees with previous studies (Austin et al. 1992; Merriam et al. 1999). Cardiovascular risk factors, such as hypertension and diabetes, are associated with poorer neuropsychological functioning as well as with increased rates of cognitive decline (Elias et al. 2004; Sims et al. 2008). In addition, the depressed elderly with executive dysfunction are more likely to have cardiovascular comorbidity (Rapp

Table 2 Comparison of executive functions among four groups of elderly men

	HC (n=45)	CVD (n=157)	LLD (n=43)	LLD+CVD (n=90)	MANCOVA (F, p value)	Post hoc[a]
TNE	58.84±25.62	69.11±19.02	74.91±14.14	78.47±17.43	F=10.43, p<0.0005	HC>CVD>LLD+CVD, HC>LLD
PE	38.18±22.81	41.25±22.40	40.63±19.84	49.64±25.22	F=2.78, p=0.04	HC>LLD+CVD, CVD>LLD+CVD
CLR	47.80±25.06	37.54±21.34	31.65±18.72	24.81±20.31	F=11.85, p<0.0005	HC>CVD>LLD+CVD, HC>LLD
NCC	3.07±1.96	1.86±1.57	1.19±1.16	0.73±1.04	F=26.17, p<0.0005	HC>CVD>LLD, LLD+CVD
TCFC	41.82±42.03	55.69±46.32	76.69±44.58	88.67±48.27	F=13.59, p<0.0005	HC>LLD, HC>LLD+CVD
TMT-A	112.20±83.87	124.59±77.38	120.19±36.63	140.40±74.22	F=1.07, p=0.36	–
TMT-B	245.29±140.02	268.98±112.07	261.81±63.72	303.97±108.74	F=1.81, p=0.15	–

Data are means±standard deviation (SD).

MANCOVA multiple analysis of covariate analysis, *CVD* elderly men with cardiovascular disease, *LLD* elderly men with late-life depression, *LLD+ CVD* elderly men with late-life depression comorbid with cardiovascular disease, *TNE* total number of errors, *PE* perseverative errors, *CLR* conceptual level response, *TCC* trials to complete the first category

[a] The direction shows the performance from better to worse.

et al. 2005). However, whether the executive dysfunction is caused by depression or cardiovascular disease is unclear.

We found that the LLD+CVD group had the worst performance among the four groups, which is consistent with previous reports (Elderkin-Thompson et al. 2009; Gianaros et al. 2006; Hoshi et al. 2010) that the depressed elderly with executive function deficits often have cardiovascular disease. However, a significant difference was found between the CVD and LLD groups, which implied the influence of late-life depression rather than cardiovascular comorbidity in the elderly. Although only the NCC Index was reported, for the other indices of the WCST, the CVD group performed significantly better than did the LLD+CVD group, but there was no difference between the LLD and LLD+CVD groups. It could be that depression and cardiovascular disease may have a similar pathogenesis, such as neuroendocrine, inflammatory process, autonomic dysregulation, platelet abnormalities, unhealthy behaviors, and certain vulnerability genes (Hoshi et al. 2010; Carney et al. 2002; McCaffery et al. 2006) all of which may lead to executive function deficits (Oxenkrug 2007) and to a cumulative effect of comorbidity on the degree of cognitive deficit (Sheline et al. 2006; Smith et al. 2007).

Nevertheless, although the four groups performed significantly differently on the WCST, there were no significant differences in the performance of TMT tasks, which indicated that there were no differences in attention between the four groups of elderly men in our study. Attention deficits are reported (Rapp et al. 2005) in the depressed elderly, but neither the severity of those deficits nor the comorbidity with cardiovascular disease were evaluated. In addition, while the TMT tasks assess attention and visuomotor processing speed, they also demand mental flexibility (Reitan 1958). The participants in our study were more than 75 years old, and some had cardiovascular disease, which may have influenced their task performance. In addition, although the participants wore glasses, most of them had bad corrected eyesight, which also may have influenced their performance in tasks that demand speed.

We found evidence that cardiovascular comorbidities worsened the executive function in the LLD groups; however, there was no significant difference in executive function performance between the CVD and LLD groups. It could be that both depression and cardiovascular disease are associated with frontal lobe dysfunction and the development of cognitive impairment (Elderkin-Thompson et al. 2009; Gianaros et al. 2006; Hoshi et al. 2010). In addition, the subtypes and the severity of cardiovascular disease could be other confounding factors, a possibility that needs confirmation. Moreover, the CVD group had more education than did the other three groups, which might be the reason for their slower decline in cognitive performance than the LLD+CVD, but this needs further investigation. The effect of education on WCST scores was reported to be non-significant (Shan 2008), but the authors did not take the illiterate elderly into account when calculating the norm. In addition, the education effect on the WCST for the illiterate elderly with depression or cardiovascular disease deserves further investigation. Moreover, only older men were studied in our study, which prevents its findings from being generalized to all elderly groups. Further, because in the present study only the WCST and TMT were used to measure executive function and inconsistent impairment were found for the both tests, we are unable to generalize our findings on executive impairment in the depressed elderly with comorbid cardiovascular disease.

Depression that occurs in late life is often considered to be an "organic model" of depression (Baldwin and Tomenson 1995) and a major health problem that causes executive function dysfunction. Psychiatrists often pay more attention to this type of depression because it frequently could be a secondary disorder associated with a treatable underlying medical illness. Identifying the risk factors of cardiovascular disease in those with depression and discriminating the dysfunctional executive function between depression and cardiovascular disease may provide evidence of an organic etiology for depression; such symptoms should prompt psychiatrists to conduct additional examinations to check for possible cardiovascular illnesses.

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References

Alexopoulos GS, Buckwalter K, Olin J, Martinez R, Wainscott C, Krishnan KR (2002) Comorbidity of late life depression: an opportunity for research on mechanisms and treatment. Biol Psychiatry 52:543–558

Alexopoulos GS, Kiosses DN, Heo M, Murphy CF, Shanmugham B, Gunning-Dixon F (2005) Executive dysfunction and the course of geriatric depression. Biol Psychiatry 58:204–210

Arbuthnott K, Frank J (2000) Trail making test, part B as a measure of executive control: validation using a set-switching paradigm. J Clin Exp Neuropsychol 22:518–528

Austin MP, Ross M, Murray C, O'Carroll RE, Ebmeier KP, Goodwin GM (1992) Cognitive function in major depression. J Affect Disord 25:21–29

Austin MP, Mitchell P, Goodwin GM (2001) Cognitive deficits in depression: possible implications for functional neuropathology. Br J Psychiatry 178:200–206

Baldwin RC, Tomenson B (1995) Depression in later life. A comparison of symptoms and risk factors in early and late onset cases. Br J Psychiatry 167:649–652

Barnes DE, Alexopoulos GS, Lopez OL, Williamson JD, Yaffe K (2006) Depressive symptoms, vascular disease, and mild cognitive impairment: findings from the Cardiovascular Health Study. Arch Gen Psychiatry 63:273–279

Blazer DG (2003) Depression in late life: review and commentary. J Gerontol A Biol Sci Med Sci 58:249–265

Blelsky J (1990) The psychology of aging: theory, research, and intervention. Brooks/Cole, Pacific Grove California

Boone KB, Ghaffarian S, Lesser IM, Hill-Gutierrez E, Berman NG (1993) Wisconsin Card Sorting Test performance in healthy, older adults: relationship to age, sex, education, and IQ. J Clin Psychol 49:54–60

Brown ES, Varghese FP, McEwen BS (2004) Association of depression with medical illness: does cortisol play a role? Biol Psychiatry 55:1–9

Campbell 3rd JJ, Coffey CE (2001) Neuropsychiatric significance of subcortical hyperintensity. J Neuropsychiatry Clin Neurosci 13:261–288

Carney RM, Freedland KE, Miller GE, Jaffe AS (2002) Depression as a risk factor for cardiac mortality and morbidity: a review of potential mechanisms. J Psychosom Res 53:897–902

Chou K-L, Chi I (2005) Prevalence and correlates of depression in Chinese oldest-old. Int J Geriatr Psychiatry 20:41–50

Conwell Y, Duberstein PR, Caine ED (2002) Risk factors for suicide in later life. Biol Psychiatry 52:193–204

Crocco EA, Castro K, Loewenstein DA (2010) How late-life depression affects cognition: neural mechanisms. Curr Psychiatry Rep 12:34–38

Davidson RJ, Pizzagalli D, Nitschke JB, Putnam K (2002) Depression: perspectives from affective neuroscience. Annu Rev Psychol 53:545–574

Drane DL, Yuspeh RL, Huthwaite JS, Klingler LK (2002) Demographic characteristics and normative observations for derived-trail making test indices. Neuropsychiatry Neuropsychol Behav Neurol 15:39–43

Eastwood MR, Rifat SL, Nobbs H, Ruderman J (1989) Mood disorder following cerebrovascular accident. Br J Psychiatry 154:195–200

Elderkin-Thompson V, Thomas MA, Binesh N et al (2004) Brain metabolites and cognitive function among older depressed and healthy individuals using 2D MR spectroscopy. Neuropsychopharmacology 29:2251–2257

Elderkin-Thompson V, Mintz J, Haroon E, Lavretsky H, Kumar A (2006) Executive dysfunction and memory in older patients with major and minor depression. Arch Clin Neuropsychol 21:669–676

Elderkin-Thompson V, Hellemann G, Pham D, Kumar A (2009) Prefrontal brain morphology and executive function in healthy and depressed elderly. Int J Geriatr Psychiatry 24:459–468

Elias MF, Sullivan LM, D'Agostino RB et al (2004) Framingham stroke risk profile and lowered cognitive performance. Stroke 35:404–409

Gianaros PJ, Greer PJ, Ryan CM, Jennings JR (2006) Higher blood pressure predicts lower regional grey matter volume: consequences on short-term information processing. Neuroimage 31:754–765

Guo N-W, Liu H-C, Wong P-F et al (1988) Chinese version and norms of the mini-mental status examination (full text in Mandarin). J Rehabil Med Assoc 16:52–59

Hoshi T, Yamagami H, Furukado S et al (2010) Serum inflammatory proteins and frontal lobe dysfunction in patients with cardiovascular risk factors. Eur J Neurol 17:1134–1140

Krishnan KR (1991) Organic bases of depression in the elderly. Annu Rev Med 42:261–266

Lezak MD, Howieson DB, Loring DW (2004) Neuropsychological assessment, 4th edn. Oxford University Press, New York

Liao SC, Lee YJ, Liu SK, Lee MB (2000) Acute stress syndromes in patients at an emergency medical station after a major earthquake. Taiwanese Journal of Psychiatry 14:31–40

Lin I-C, Yu S-M, Chang H-J (2004) A survey of depression and its related factors of the institutionalized and non-institutionalized elderly in Hsin-Tien City. Taiwan Journal of Family Medicine 14:81–93

Lockwood KA, Alexopoulos GS, van Gorp WG (2002) Executive dysfunction in geriatric depression. Am J Psychiatry 159:1119–1126

Lowe LP, Tranel D, Wallace RB, Welty TK (1994) Type II diabetes and cognitive function. A population-based study of Native Americans. Diab Care 17:891–896

Lu X (1998) Social mobility and social resources on military-dependents' village: field research of a veteran community. Unpublished Master thesis, Tunghai University, Taichung

McCaffery JM, Frasure-Smith N, Dube MP et al (2006) Common genetic vulnerability to depressive symptoms and coronary artery disease: a review and development of candidate genes related to inflammation and serotonin. Psychosom Med 68:187–200

Mega MS, Cummings JL (1994) Frontal-subcortical circuits and neuropsychiatric disorders. J Neuropsychiatry Clin Neurosci 6:358–370

Mei C-J (1998) Neuropsychology. Gui-Guan Press, Taipei

Merriam EP, Thase ME, Haas GL, Keshavan MS, Sweeney JA (1999) Prefrontal cortical dysfunction in depression determined by Wisconsin Card Sorting Test performance. Am J Psychiatry 156:780–782

Mohlman J (2005) Does executive dysfunction affect treatment outcome in late-life mood and anxiety disorders? J Geriatr Psychiatry Neurol 18:97–108

Monthly Bulletin of Interior statistics: Population by 5-year Age Group (2006) Ministry of the Interior Statistical Information Service, http://www.vac.gov.tw/cxls/index.asp?pno=510. Accessed 10 August, 2010

Mui AC (1996) Geriatric Depression Scale as a community screening instrument for elderly Chinese immigrants. Int Psychogeriatr 8:445–458

Naismith SL, Hickie IB, Turner K et al (2003) Neuropsychological performance in patients with depression is associated with clinical, etiological and genetic risk factors. J Clin Exp Neuropsychol 25:866–877

Naismith SL, Hickie IB, Ward PB, Scott E, Little C (2006) Impaired implicit sequence learning in depression: a probe for frontostriatal dysfunction? Psychol Med 36:313–323

Nakano Y, Baba H, Maeshima H et al (2008) Executive dysfunction in medicated, remitted state of major depression. J Affect Disord 111:46–51

Oxenkrug GF (2007) Genetic and hormonal regulation of tryptophan kynurenine metabolism: implications for vascular cognitive impairment, major depressive disorder, and aging. Ann NY Acad Sci 1122:35–49

Palsson SP, Ostling S, Skoog I (2001) The incidence of first-onset depression in a population followed from the age of 70 to 85. Psychol Med 31:1159–1168

Rapp MA, Dahlman K, Sano M, Grossman HT, Haroutunian V, Gorman JM (2005) Neuropsychological differences between late-onset and recurrent geriatric major depression. Am J Psychiatry 162:691–698

Reitan R (1958) Perceptual and motor skills. Percept Mot Skills 8:271–276

Schillerstrom JE, Horton MS, Royall DR (2005) The impact of medical illness on executive function. Psychosomatics 46:508–516

Shan IK, Chen YS, Lee YC, SU TP (2008) Adult normative data of the Wisconsin Card Sorting Test in Taiwan. J Chin Med Assoc. 71:517–522

Sheehan DV, Lecrubier Y, Sheehan KH et al (1998) The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry 59 Suppl 20:22–33, quiz 34-57

Sheline YI, Barch DM, Garcia K et al (2006) Cognitive function in late life depression: relationships to depression severity, cerebrovascular risk factors and processing speed. Biol Psychiatry 60:58–65

Sims R, Madhere S, Callender C, Campbell A Jr (2008) Patterns of relationships between cardiovascular disease risk factors and neurocognitive function in African Americans. Ethn Dis 18:471–476

Smith PJ, Blumenthal JA, Babyak MA et al (2007) Cerebrovascular risk factors, vascular disease, and neuropsychological outcomes in adults with major depression. Psychosom Med 69:578–586

Spreen O, Strauss E (1991) A compendium of neuropsychological tests: administration, norms and commentary. Oxford University Press, New York

Statistical Yearbook of Interior (2004) Veterans Affairs Commission EY (2004). http://sowf.moi.gov.tw/stat/year/list.htm. Accessed 8 June, 2010

Weng Z (1998) The Domicile Difference of Marital Distribution for Total Population in Taiwan Area in 1990, Master, National Chengchi University, Taipei

Yuan Y, Zhang Z, Bai F et al (2008) Abnormal neural activity in the patients with remitted geriatric depression: a resting-state functional magnetic resonance imaging study. J Affect Disord 111:145–152