INTERNATIONAL JOURNAL OF GERIATRIC PSYCHIATRY
Int J Geriatr Psychiatry 2003; **18**: 479–485.
Published online in Wiley InterScience (www.interscience.wiley.com). **DOI**: 10.1002/gps.869

Apathy and cognitive performance in older adults with depression

Denise Feil[1]*, Jill Razani[2], Kyle Boone[3] and Ira Lesser[3]

[1]*UCLA/VA Greater Los Angeles Health Care System, California, USA*
[2]*California State University, Northridge, California, USA*
[3]*Harbor-UCLA Medical Center, California, USA*

SUMMARY

Objectives Recent studies have linked apathy to frontal lobe dysfunction in persons with dementia, but few studies have explored this relationship in older, depressed persons without dementia. We examined the association between apathy and cognitive function in a group of older persons with major depression using standardized neuropsychological tests. We hypothesized that presence of apathy in depression is associated with poorer frontal executive performance.
Methods We analyzed data from 89 older adults with major depression. We defined apathy using four items from the Hamilton Psychiatric Rating Scale for Depression which reflect the clinical state of apathy, including 'diminished work/interest,' 'psychomotor retardation,' 'anergy' and 'lack of insight.'
Results Apathy most strongly correlated with two verbal executive measures (Stroop C and FAS), a nonverbal executive measure (Wisconsin Card Sorting Test—Other Responses), and a measure of information processing speed (Stroop B). Apathy was not associated with age, sex, education, medical illness burden, Mini-Mental State Examination score and Full Scale IQ score. Stepwise regression analyses of significant cognitive tests showed that apathy alone or apathy plus depression severity, age, or education accounted for a significant amount of the variance.
Conclusions The results of this study provide support for an apathy syndrome associated with poorer executive function in older adults with major depression. Copyright © 2003 John Wiley & Sons, Ltd.

KEY WORDS — executive function; cognition; apathy; geriatric depression; motivation; emotions; neuropsychological tests; Stroop C; Wisconsin Card Sorting

INTRODUCTION

Elderly persons are thought to be at particular risk for an apathy-executive-depressive syndrome because of vulnerability of frontal-subcortical pathways in the aging brain (Alexopoulos *et al.*, 1997). The neuropsychological deficits of an apathy syndrome in geriatric depression are hypothesized to be executive in nature, but the precise relationship between executive dysfunction, geriatric depression and apathy remains unclear.

Depression in the elderly has been associated with both apathy and a range of cognitive deficits including executive dysfunction (Marin *et al.*, 1994; Boone *et al.*, 1995; Bassuk *et al.*, 1998; Yaffe *et al.*, 1999). A small number of studies suggest that apathy is a distinct syndrome in non-demented elderly with depression, and may indicate presence of more neuropsychological impairments and cerebrovascular disease disrupting prefrontal systems (Marin *et al.*, 1994; Alexopoulos *et al.*, 1997).

Apathy has already been identified in dementia as a distinct syndrome from depression, present in

* Correspondence to: Dr D. Feil, UCLA/VA Greater Los Angeles Health Care System 11301 Wilshire Boulevard, 116-AF, Building 500, Room 3416, Los Angeles, CA 90073, USA. Tel: 310-478-3711 Ext. 48480. Fax: 310-268-4181. E-mail: dfeil@mednet.ucla.edu

Contract/grant sponsor: Hartford Foundation, the National Institute of Mental Health; contract/grant number: MH43960.
Contract/grant sponsor: General Clinical Research Center, NIH Division of Research Resources; contract/grant number: RR-00425.

Received 2 January 2003
Accepted 11 March 2003

Alzheimer subjects with and without depression (24% and 13%, respectively; Starkstein *et al.*, 2001). An apathy-executive syndrome has been identified in Alzheimer's disease, vascular and subcortical dementias (Cummings and Benson, 1988; Starkstein *et al.*, 1993). In one study of cortical and subcortical dementias, apathy, rather than depression, was associated with greater cognitive deficits (Levy *et al.*, 1998). Similarly, a study of Alzheimer's Disease found that frontal executive deficits were associated with apathy rather than with depression (Kuzis *et al.*, 1999). The Alzheimer's patients with apathy displayed not only more verbal memory and naming deficits, but also more executive skill deficits in set shifting and verbal fluency than those without apathy.

No study has specifically addressed the relationship between apathy and cognition in non-demented, older persons with major depression using extensive neuropsychological tests. The purpose of the present study is to determine whether apathy is associated with poorer cognitive performance on formal neuropsychological tests in a sample of older, non-demented persons with major depression. We hypothesize that there is a relationship specifically between apathy and frontal-systems tasks, in support of an apathy-dysexecutive function syndrome in geriatric depression.

METHODS

Participants

A total of 89 subjects with complete records were selected from the NIMH database of 95 subjects aged 50 to 85 years with major depression (Lesser *et al.*, 1996). The remaining six subjects did not have complete health measures. The 89 subjects did not differ statistically from the original study subjects on age, education, sex and Hamilton Depression Rating Scale (Ham-D) scores. A full description of the selection criteria and participant characteristics is provided elsewhere (Boone *et al.*, 1995; Lesser *et al.*, 1996). All participants met criteria for major depression in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III-R; American Psychiatric Association, 1987) based on the Structured Clinical Interview (SCID) for DSM-III-R (Spitzer and Williams, 1986). Subjects completed physical and neurological examinations, EKG, laboratory examinations, including complete blood count, electrolytes, liver and kidney function, thyroid function tests, and magnetic resonance imaging (MRI). Subjects entered into the study did not have major medical, laboratory or MRI abnormalities.

Apathy and depression measure

All participants were administered the 21-item Ham-D Scale (Williams, 1988). Apathy was measured using a four-item apathy measure developed and validated by Marin *et al.* (1991, 1993). This measure includes the items 'loss of interest,' 'psychomotor retardation,' 'loss of energy,' and 'loss of insight' from the Ham-D Scale, with potential scores ranging from 0 to 10 (Marin *et al.*, 1991). Marin found that these four items most strongly correlated with the Apathy Evaluation Scale (Marin *et al.*, 1993).

Cognitive assessment

Trained clinicians administered a comprehensive, $2^1/_2$ hour neuropsychological test battery to all participants. Below is a list of the specific cognitive domains sampled, the tests used to assess these domains, and the specific outcome measures.

Overall intelligence:

- Intellectual skills were assessed with the Satz-Mogel format of the Wechsler Adult Intelligence Scale-Revised (WAIS-R; Adams *et al.*, 1984). This abbreviated version of the standard WAIS-R includes all 11 subscales. For the current study, three outcome measures were used for analyses: Full Scale IQ (FSIQ), Verbal IQ (VIQ), and Performance IQ (PIQ).

Attention:

- Digit Span subtest scaled score of the WAIS-R was also calculated and used as an outcome measure of attentional skills.

Information processing speed:

- The Comalli Stroop Test (Mitrushina *et al.*, 1999) was used to measure verbal information processing speed. This test assesses the participant's ability to rapidly read words (Part A) and name colors (Part B). Time in seconds for Part A and time in seconds for Part B are the outcome measures in the statistical analyses.
- Digit Symbol subtest from WAIS-R was used as a nonverbal measure of information processing speed. This test assesses participants' ability to copy symbols that correspond to numbers as quickly as possible in 90 seconds.

Language skills:

- The Boston Naming Test (Kaplan *et al.*, 1983) is designed to assess confrontational naming ability.

The outcome measure used in the analyses is the total number of line drawings named by participants out of a possible 60.

Constructional skills:

- The Rey-Osterrieth Complex Figure (Osterrieth, 1944) was used as the visual-construction measure. This test is designed to assess the participant's ability to copy a complex line design. The Osterrieth (Boone *et al.*, 1993) scoring method was used so that participants were given full or partial credit for accurate drawing and placement of 18 details of the design. A total score out of a possible 36 was used as the outcome measure.

Verbal Memory:

- The Logical Memory (LM) subtest Wechsler Memory Scale/Wechsler Memory Scale—Revised (WMS/WMS-R; Wechsler, 1974, 1987), in which participants are to recall story details immediately and 30-min later, was used as the measure of verbal memory. The percentage of the story details retained after a 30-min delay was used as the outcome measure for analyses (i.e. 30-min delay/immediate delay).

Nonverbal Memory:

- The Visual Reproduction subtest of the Wechsler Memory Scale/Wechsler Memory Scale—Revised (WMS/WMS-R; Wechsler, 1974, 1987), in which participants are to reproduce designs immediately and 30-min later, was employed as a measure of visual memory. The percentage of the information retained after a 30-min delay was used as the outcome measure for analyses (i.e. 30-min delay/immediate delay).
- The Rey-O Complex Figure Delayed Recall is used as a second measure of visual memory. Participants are asked to reproduce a complex figure from memory 3 min after it is copied. As with the copy portion of the test, the Osterrieth (Boone *et al.*, 1993) scoring method was used.

Executive ability:

- The Comalli Stroop Test (Part C; Mitrushina *et al.*, 1999) is designed to assess a participant's ability to inhibit over learned responding. Participants were presented with color names (red, blue, and green) printed in different colored ink (red, blue and green) and their task was to inhibit reading responses and instead to name the color of the ink in which the words were printed. Time in seconds taken to complete this task was used as the outcome measure.
- Wisconsin Card Sorting Test (WCST; Heaton *et al.*, 1993). This is a complex test of cognitive flexibility and reasoning ability. Participants were required to match stimulus cards to four key cards. The cards could be matched based on three abstract principles: color, shape, or number. This test measures the ability to efficiently sort when the 'rules' of the task are ambiguous. The outcome measures from this test were: number of accurate categorical sorts, perseverative (repetitive) responses, total errors, percentage of conceptual level responses, and 'other' responses (sorting strategies other than color, form, or number).
- The Controlled Oral Word Association Test ('FAS' or COWA for letters F, A, and S; Benton and Hamsher, 1976). This is a test of the participant's ability to produce words starting with the letters F, A, and S in one minute per letter. The total number of words produced for all three letters was used as the outcome measure.

Medical and stroke risk measures

Medical illness burden was assessed by physician chart review using the Cumulative Index Rating Scale modified for geriatrics (CIRS-G), a reliable and validated scale that measures the medical burden in each organ system (Miller *et al.*, 1992). This scale consists of 13 variables, one for each organ system. The organ system for 'psychiatric' was eliminated due to preselecting subjects with major depression. The CIRS-G index was calculated by dividing the total score by the total number of organ system categories (12 for this study). One physician rated all subjects.

Statistical analyses

We used descriptive statistics and chi-square analysis for demographic, medical and psychiatric variables. The 19 cognitive outcome measures (description of each measure provided above) were individually correlated with the apathy (Ham-D Apathy), total depression (Ham-D), and health status (CIRS-G Index) measures, and the demographic variables of age and education. Individual stepwise regression analyses were performed on neuropsychological measures that significantly correlated with apathy to determine whether apathy uniquely accounted for test score variance over and above that accounted for by depression, health status, age, and education. Given the numerous analyses, we adjusted the alpha level (i.e. Type I error) to 0.01.

Table 1. Demographic, psychiatric and medical characteristics of 89 depressed, older adults

Variable	Analysis		
	Mean	Range	Standard deviation
Sex 52% Female	—	—	—
Age (years)	62	50–85	8.08
Education (years)	15	10–30	3.09
Full Scale IQ	111	83–142	14.58
Hamilton Depression Rating Scale	20	11–40	5.00
Hamilton Depression Apathy Scale	4.5	2–9	1.46
Cumulative Illness Rating Scale Index-Geriatrics	0.36	0–10	0.20
Mini-Mental State Examination	29	25–30	1.35

RESULTS

Subjects were nearly equally divided in gender and averaged 15 years of education with mean Full Scale IQ scores within the high average range (Table 1). Age ranged from 50 to 85 years old, with a mean of 62 years. MMSE scores were between 25 and 30 for all study subjects.

As shown in Table 2, results of the bivariate correlation analyses revealed no significant relationships between Ham-D Apathy and neurocognitive measures of intelligence, attention, language, verbal and nonverbal memory, or visual-constructional ability. Significant relationships were found between Ham-D apathy and WCST—Other Responses, a nonverbal executive score, and Stroop B, a measure of processing speed, with greater apathy associated with worse performance. In addition, near-significant relationships were found between Ham-D Apathy and Stroop C and FAS, both verbal executive measures.

Total Ham-D scores were significantly correlated with two information processing speed measures (Stroop A and B), and were nearly significantly correlated with Stroop C, Performance IQ and Full Scale IQ. CIRS-G Index did not significantly correlate with any cognitive measure. Age was negatively associated with some measures of processing speed, verbal and visual memory, and select executive skills (rapid response inhibition, mental flexibility/conceptual ability), while education was positively associated with Verbal IQ, Full Scale IQ, visual spatial ability, visual memory, and some executive skills (word generation, mental flexibility/conceptual ability).

To differentiate the role of apathy on cognitive performance from that of depression and demographic factors, we performed a series of stepwise regression analyses. These analyses were performed only with those four cognitive measures that were correlated

Table 2. Cognitive tests that were correlated at *p*-value of 0.05 or lower with apathy, depression, age and education

			Pearson correlations							
			Ham-D apathy[a]		Ham-D Total[b]		Age		Education	
Cognitive variable	Mean	SD	R	*p*-value	R	*p*-value	R	*p*-value	R	*p*-value
Full Scale IQ	117	15	—		−0.230	0.032	—		0.459*	<0.0001
Verbal IQ	111	15	—		—		—		0.540*	<0.0001
Performance IQ	108	15	—		−0.247	0.021	—		—	
Stroop A	47	10	—		0.347*	0.001	0.265	0.014	—	
Stroop B	67	16	0.277*	0.010	0.444*	0.000	0.234	0.030	—	
Digit Symbol	7.5	2.4	—		—		−0.444*	0.000	—	
Boston Naming	54	6	—		—		−0.272	0.011	0.235	0.030
Rey Ostereith C	33	4	—		—		—		0.325*	0.002
Logical Memory Percent Retention	71	15	—		—		−0.432*	0.000	—	
Visual Reproduction Percent Retention	62	30	—		—		−0.330*	0.002	—	
Rey Osterrieth Delayed Recall	15	6.3	—		—		−0.227*	0.035	0.279*	0.009
Stroop C	140	53	0.241	0.025	0.232	0.032	0.428*	0.000	—	
WCST Categories Retained	4.1	2.1	—		—		−0.233	0.030	0.254	0.018
WCST Perseveration	30	27	—		—		—		−0.248	0.024
WCST Other Responses	1.9	4.6	0.345*	0.001	—		—		—	
WCST Conceptual Level	56	25	—		—				0.308*	0.005
WCST Number of Errors	41	27	—		—		—		−0.306*	0.005
Verbal Fluency (FAS)	36	13	−0.218	0.043	—		—		0.280*	0.009

[a]Hamilton Depression Scale items 7, 8, 13 and 17.
[b]Hamilton Depression Scale total score.

Table 3. Stepwise regression analysis with apathy, depression severity, medical illness burden, age, and education as predictors

Cognitive variables	Variables entered	R^2	*p*-value
F, A, S	Education	0.074	0.009
(Verbal fluency)	Apathy	0.070	0.010
		0.147 (total)	
Stroop B	Ham-D Total	0.219	< 0.001
(Processing speed)	Age	0.046	0.022
	Apathy	0.043	0.028
		0.308 (total)	
Stroop C	Age	0.171	< 0.001
(Verbal executive)	Apathy	0.100	0.001
		0.271 (total)	
WCST 'Other Responses' (Nonverbal executive)	Apathy	0.13	0.001

with apathy at a significant level or approaching significance. As shown in Table 3, results of the regression analyses showed that apathy, in addition to depression and demographic variables, accounted for a significant amount of score variance on two verbal executive tests (FAS and Stroop C), and one test of information processing speed (Stroop B). In addition, apathy alone accounted for a significant amount of test score variance on a nonverbal executive task (WCST—Other Responses).

DISCUSSION

These results demonstrate that apathy, as measured by the four-item Hamilton Depression Scale apathy measure (Marin, 1996), correlated primarily with cognitive tasks in the executive domain, and secondarily with measures of information processing speed. When contrasted with Ham-D scores, age, and education, apathy alone was a significant predictor of performance on a nonverbal executive test (WCST—Other Responses). In addition, apathy was a secondary predictor after the contribution of age on a verbal executive test (Stroop C), was a secondary predictor after the contribution of education on a verbal fluency measure (FAS), and contributed unique predictor power after age and depression on an information processing speed measure (Stroop B). Overall, the findings indicate that apathy was more strongly related to executive performance than was depression severity, while the latter may be more related to processing speed than apathy.

The current findings indicate that the cognitive pattern of older adults with apathetic depression is one of frontal systems dysfunction. Skills such as flexible thinking, abstract reasoning, word generation, and information processing speed decrease as apathy increases. Other cognitive domains such as attention, memory, language, visual-spatial skills, and intelligence do not seem to be affected by presence of apathy.

The clinical profile of executive deficits, apathy and depression in older adults may indicate presence of brain lesions in frontal-subcortical regions from cerebrovascular disease, Alzheimer's disease, Parkinson's disease, head trauma and other frontal-subcortical neuro-degenerative diseases (Starkstein *et al*., 1993; Marin, 1996; Salloway *et al.*, 1996; Alexopolous *et al.*, 1997; Cummings and Benson, 1998; Levy *et al.*, 1998; Gallarda, 1999; Richard, 2000; Andersson, 1999). Starkstein *et al.* (1993) found that cerebrovascular lesions involving the posterior limb of the internal capsule were most often associated with major depression and apathy in patients with stroke and Marin *et al.* (1994) found an association with left hemisphere stroke suggesting that there may be a vulnerable area of the brain for development of an apathy-depression syndrome.

The frontal-subcortical pathways are mediated by serotonergic and endogenous monoaminergic release, which are involved in the regulation of motivated behavior, mood and cognitive function (Levy *et al.*, 1998; McAllister, 2000). Treatment of apathy with medications that target dopaminergic, serotonergic, noradrenergic and adrenergic release such as methylphenidate, amphetamine, bromocriptine, amantadine, selegiline, bupropion and other antidepressents have met with some success in case reports and clinical trials (Muller and von Cramon, 1994; Marin *et al.*, 1995; Van Reekum *et al.*, 1995; Watanabe *et al.*, 1995; Taragano *et al.*, 2001). The cholinesterase inhibitors have also been found to improve apathy in patients with Alzheimer's disease (Dubois *et al.*, 1999; Mega *et al.*, 1999; Cummings, 2000). Treatment of associated executive dysfunction has proven more elusive in depressed patients and several studies have demonstrated that presence of executive dysfunction in depression predicts poorer depression course and treatment response (Alexopoulos *et al.*, 2000; Dunkin *et al.*, 2000); however, drugs such as dopamine-3 agonists may hold promise for treatment of the dysexecutive syndrome (Alexopoulos, 2001).

In addition to psychopharmacologic treatment, non-pharmacologic interventions may be of some benefit, but there is little research on how apathy affects daily living and health outcomes (Fogel, 1994). One study by Steffens *et al.* (1999) found that depression, cognitive deficits, and apathy were each associated with disability on instrumental activities of daily living. Another study found that the apathy

in AD was associated with poorer activities of daily living (Starkstein *et al.*, 2001). Certain interventions that help caregivers cope with functional impairments associated with executive skill loss, apathy and depression may be beneficial (Haupt, 1999), but more research is needed to characterize the relationship of apathy, depression and executive dysfunction with the environment.

This study's strengths include the relatively large number of depressed, older subjects with formal neuropsychological testing in each cognitive domain. A weakness is that the study's apathy measure was extracted from the Ham-D scale. In order to account for the expected correlation between the apathy measure and the total depression score, we included total Ham-D score in our stepwise regression analyses and found that apathy accounted for the variance on executive tests better than depression severity. Another weakness of the apathy measure is that it gave a limited range of scores (0–10). This could be improved in future studies by using an apathy measure such as the AES which employs a wider range of scores (Marin *et al.*, 1993).

In conclusion, these findings confirmed our hypothesis that apathy in depression is associated primarily with executive function, and lends support for an apathy-dysexecutive syndrome in depressed, nondemented, older adults. Whether older, depressed adults with apathy are at a higher risk of dementia merits further study. Clinically, older, depressed adults with apathy symptoms may be at higher risk for executive dysfunction as well as functional impairments. Presence of apathy may indicate the need for a neuropsychiatric evaluation including frontal-executive function tests. Distinctive pharmacotherapeutic agents and environmental interventions may be warranted to treat depression characterized by apathy and dysexecutive function.

ACKNOWLEDGEMENTS

This research was supported in part by the Hartford Foundation, the National Institute of Mental Health Grant Number MH43960 to Dr. Ira Lesser, and General Clinical Research Center Grant RR-00425 from the NIH Division of Research Resources. This study was conducted at the Research and Education Institute of Harbor UCLA Medical Center.

REFERENCES

Adams RL, Smigielski J, Jenkins RL. 1984. Development of a Satz-Mogel short form of the WAIS-R. *J Consulting Clin Psychol* **52**: 908.

Alexopoulos GS. 1998. In reply to Letter to the Editor. *Arch Gen Psychiatry* **55**: 844–845.

Alexopoulos GS, Meyers BS, Young RC, *et al*. 1997. 'Vascular depression' hypothesis. *Arch Gen Psychiatry* **54**: 915–922.

Alexopoulos GS, Meyers BS, Young RC, *et al*. 1993. The course of geriatric depresion with 'reversible dementia.' *Am J Psychiatry* **150**: 1693–1699.

Alexopoulos GS. 2001. The depression-executive dysfunction syndrome of late life. *Am J Geriatr Psychiatry* **9**: 22–29.

Alexopoulos GS, Meyers BS, Young RC, *et al.* 2000. Executive dysfunction and long-term outcomes of geriatric depression. *Arch Gen Psychiatry* **57**: 285–290.

Andersson S, Krogstad JM, Finset A. 1999. Apathy and depressed mood in acquired brain damage: relationship to lesion localization and psychophysiological reactivity. *Psychol Med* **29**: 447–456.

Bassuk SS, Berkman LF, Wypij D. 1998. Depressive symptomatology and incident cognitive decline in an elderly community sample. *Arch Gen Psychiatry* **55**: 1073–1081.

Benton AL, Hamsher K, de S. 1976. *Multilingual Aphasia Examination*. University of Iowa: Iowa City.

Boone KB, Lesser IM, Miller BL, *et al.* 1995. Cognitive functioning in older depressed outpatients: relationship of presence and severity of depression to neuropsychological test scores. *Neuropsychology* **9**: 390–398.

Boone KB, Lesser IM, Hill-Gutierrez E, *et al.* 1993. Rey-Osterrieth Complex Figure performance in healthy, older adults: relationship to age, education, sex, and IQ. *The Clinical Neuropsychologist* **7**: 22–28.

Bramford KA, Caine ED. 1988. Does benign senescent forgetfulness exist? *Clin Geriatr Med* **4**: 897–916.

Comalli PE, Wapner S, Werner H. 1962. Interference effects of Stroop Color-Word Test in childhood, adulthood, and aging. *J Genetic Psychol* **100**: 47–53.

Cummings JL. 2000. Cholinesterase inhibitors: a new class of compounds. *Am J Psychiatry* **157**: 4–15.

Cummings JL, Benson DF. 1988. Psychological dysfunction accompanying subcortical dementias. *Ann Rev Med* **39**: 53–61.

Dubois B, McKeith I, Orgogozo JM, *et al*. 1999. A multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy, tolerability and safety of two doses of metrifonate in patients with mild-to-moderate Alzheimer's disease: the MALT study. *Int J Geriatr Psychiatry* **14**: 973–982.

Dunkin JJ, Leuchter AF, Cook IA, *et al.* 2000. Executive dysfunction predicts nonresponse to fluoxetine in major depression. *J Affect Disord* **60**: 13–23.

Fogel BS. 1994. The significance of frontal system disorders for medical practice and health policy. *J Neuropsychiatry Clin Neurosci* **6**: 343–347.

Fones CS. 1998. Letter to the Editor: distinguishing apathy syndromes from vascular depression. *Arch Gen Psychiatry* **55**: 844.

Gallarda T. 1999. Alzheimer's disease and depression. *Encephale* **25**: 14–18.

Haupt M. 1999. The course of behavior disorders and their psychosocial treatment in patients with dementia. *Z Gerontol Geriatri* **32**: 159–166.

Heaton RK, Chelune GJ, Talley JL, *et al.* 1993. *Wisconsin Card Sorting Test Manual—Revised and Expanded.* Psychological Assessment Resources: Odessa, FL.

Kaplan E, Goodglass H, Weintraub S. 1983. *Boston Naming Test*. Lea & Febiger: Philadelphia, PA.

Katz IR. 1998. Diagnosis and treatment of depression in patients with Alzheimer's disease and other dementias. *J Clin Psychiatry* **59**(Suppl.): 38–44.

Kuzis G, Sabe C, Tiberti F, *et al*. 1999. Neuropsycholgoical correlates of apathy and depression in patients with dementia. *Neurology* **52**: 1403–1407.

Lesser IM, Boone KB, Mehringer CM, *et al*. 1996. Cognition and White Matter Hyperintensities in older depressed patients. *Am J Psychiatry* **153**: 1280–1287.

Levy ML, Cummings JL, Fairbanks LA, *et al*. 1998. Apathy is not depression. *J Neuropsychiatry Clin Neurosci* **10**: 314–319.

Marin RS. 1996. Apathy: concept, syndrome, neural mechanisms, and treatment. *Semin Clin Neuropsychiatry* **1**: 304–314.

Marin RS, Biedrzycki RC, Firinciogullari S. 1991. Reliability and validity of the apathy evaluation scale. *Psychiatry Res* **38**: 143–162.

Marin RS, Firinciogullari S, Biedrzycki RC. 1994. Group differences in the relationship between apathy and depression. *J Nerv Ment Dis* **182**: 235–239.

Marin RS, Firinciogullari S, Biedrzycki RC. 1993. The sources of convergence between measures of apathy and depression. *J Affect Dis* **28**: 117–124.

Marin RS, Fogel BS, Hawkins J, *et al*. 1995. Apathy: a treatable syndrome. *J Neuropsychiatry Clin Neurosci* **7**: 23–30.

McAllister TW. 2000. Apathy. *Semin Clin Neuropsychiatry* **5**: 275–282.

Mega MS, Masterman DM, O'Connor SM, *et al*. 1999. The spectrum of behavioral responses to cholinesterase inhibitor therapy in Alzheimer disease. *Arch Neurol* **56**: 1388–1393.

Meyer JE, Meyer KR. 1992. *A Training Manual for the Clinical Scoring of the Rey-Osterrieth Complex Figure and the Recognition Subtests*. Published by John E. Meyers, Marian Health Center, Department of Psychology, Sioux City, Iowa.

Miller MD, Paradis CF, Houck PR, *et al.* 1992. Rating chronic medical illness burden in geropsychiatric paractice and research: application of the Cumulative Illness Rating Scale. *Psychiatry Res* **41**: 237–248.

Milner B. 1970. Disorders of learning and memory after temporal lobe lesions in man. *Clinical Neurosurgery* **19**: 299–321.

Mitrushina M, Boone K, D'Elia L. 1999. *Handbook of Normative Data and Neuropsychological Assessment*. Oxford University Press: New York.

Muller U, von Cramon DY. 1994. The therapeutic potential of bromocriptine in neuropsychological rehabilitation of patients with acquired brain damage. *Prog Neuropsychopharmacol Biol Psychiatry* **18**: 1103–1120.

Osterrieth PA. 1944. Le test de copie d'une figure complexe. *Archives de Psychologie* **30**: 206–356.

Richard IH. 2000. Depression in Parkinson's disease. *Curr Treat Options Neurol* **2**: 263–274.

Salloway S, Malloy P, Kohn R, *et al*. 1996. MRI and neuropsychological differences in early and late life onset geriatric depression. *Neurology* **46**: 1567–1574.

Saulthouse TA. 1985. *A Theory of Cognitive Aging*. Elsevier: New York.

Spitzer RL, Williams JBW. 1986. *Structured Clinical Interview for DSM-III-R (SCID)*. New York State Psychiatric Institute, Biometrics Research: New York.

Starkstein SE, Fedoroff JP, Price TR, *et al*. 1993. Apathy following cerebrovascular lesions. *Stroke* **24**: 1625–1630.

Starkstein SE, Petracca G, Chemerinski E, *et al*. 2001. Syndromic validity of apathy in Alzheimer's disease. *Am J Psychiatry* **158**: 872–877.

Steffens DC, Hays JC, Krishnan KR. 1999. *Am J Geriatr Psychiatry* **7**: 34–40.

Taragano FE, Allegri R, Vicario A, *et al*. 2001. A double blind, randomized clinical trial assessing the efficacy and safety of augmentaing standard antidepressant therapy with nimodipine in the treatment of 'vascular depression'. *Int J Geriatr Psychiatry* **16**: 254–260.

Van Reekum R, Bayley M, Garner S, *et al*. 1995. N of 1 study: amantadine for the amotivational syndrome in a patient with traumatic brain injury. *Brain Inj* **9**: 49–53.

Warrington EK. 1984. *Recognition Memory Test*. NFER-Nelson: Windsor, UK.

Watanabe MD, Martin EM, Deleon OA, *et al*. 1995. Successful methylphenidate treatment of apathy after subcortical infarcts. *J Neuropsychiatry Clin Neurosci* **7**: 502–504.

Wechsler D. 1974. *Wechsler Memory Scale Manual*. The Psychological Corporation: San Antonio, TX.

Wechsler D. 1981. *Wechsler Adult Intelligence Scale—Revised Manual*. The Psychological Corporation: NY, USA.

Wechsler D. 1997. *Wechsler Adult Intelligence Scale—Third Edition*. The Psychological Corporation: San Antonio, TX.

Williams JBW. 1988. A structured interview guide for the Hamilton depression rating scale. *Arch Gen Psychiatry* **45**: 742–747.

Yaffe K, Blackwell T, Gore R, *et al*. 1999. Depressive symptoms and cognitive decline in nondemented elderly women: a prospective study. *Arch Gen Psychiatry* **56**: 425–430.

