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Research report

Clinical manifestations of geriatric depression in a memory clinic: Toward a proposed subtyping of geriatric depression

Carol Dillon *, Gerardo Machnicki, Cecilia M. Serrano, Galeno Rojas, Gustavo Vazquez, Ricardo F. Allegri

Memory Research Center, Department of Neurology, Hospital General Abel Zubizarreta, Buenos Aires, Argentina

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ABSTRACT

Background: As the older population increases so does the number of older psychiatric patients. Elderly psychiatric patients manifest certain specific and unique characteristics. Different subtypes of depressive syndromes exist in late-life depression, and many of these are associated with cognitive impairment.

Materials and methods: A total of 109 depressive patients and 30 normal subjects matched by age and educational level were evaluated using a neuropsychiatric interview and an extensive neuropsychological battery. Depressive patients were classified into four different groups by SCAN 2.1 (schedules for clinical assessment in Neuropsychiatry): major depression disorder (n: 34), dysthymia disorder (n: 29), subsyndromal depression (n: 28), and depression due to mild dementia of Alzheimer's type (n: 18).

Results: We found significant associations ($p<.05$) between depressive status and demographic or clinical factors that include marital status (OR: 3.4, CI: 1.2–9.6), level of daily activity (OR: 5.3, CI: 2–14), heart disease (OR: 12.5, CI: 1.6–96.3), and high blood cholesterol levels (p:.032). Neuropsychological differences were observed among the four depressive groups and also between depressive patients and controls. Significant differences were observed in daily life activities and caregivers' burden between depressive patients and normal subjects.

Conclusion: Geriatric depression is associated with heart disease, high cholesterol blood levels, marital status, and daily inactivity. Different subtypes of geriatric depression have particular clinical features, such as cognitive profiles, daily life activities, and caregivers' burden, that can help to differentiate among them.

Limitations: The cohort referred to a memory clinic with memory complaints is a biased sample, and the results cannot be generalized to other non-memory symptomatic cohorts.

1. Introduction

Progress in different aspects of general science and medical studies has led to an increase in the elderly population during the last decades. The older population is increasing all over the world, and so is the number of older psychiatric patients who manifest certain specific and unique characteristics. Most psychiatrists are trained to diagnose and treat young patients with 'functional' disorders and thus may find it difficult to evaluate a typical elderly patient (Engedal et al., 2010; Fountoulakis et al., 2003; Madhusoodanan et al., 2010; Millán-Calenti et al., 2010).

Depressed mood is one of the 'core' symptoms of depression at any age. This symptom, however, may not be as prominent in many elderly depressives. Other symptoms like somatic complaints, loss of appetite, fatigue, and cognitive disorders are more prevalent in geriatric depression (Alexopoulos, 2005; Fountoulakis et al., 2003). Up to 15% to 20% of older adults have significant depressive symptoms, and it is estimated that as many as 45% of persons age 85 and older have significant cognitive impairment and dementia

* Corresponding author at: Memory Research Center, Department of Neurology, Hospital General Abel Zubizarreta, Nueva York 3952. Buenos Aires, Argentina. Tel./fax: +54 114503 4117.
E-mail address: drcaroldillon@yahoo.com.ar (C. Dillon).

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(Tannock and Katona, 1995). Major depression declines while other depression syndromes increase with advancing age (Romanoski et al., 1992). In the elderly, various subtypes of geriatric depression exist, such as dysthymic disorder, major depression disorder, subsyndromal depression, depression due to a general medical condition, late-onset depression, substance-induced depression, bipolar I disorder (most recent episode depressed), adjustment disorder with depressed mood, minor depressive disorder, etc. (Alexopoulos, 2005).

Depression is common in older persons, and as the number of older people increases throughout the world, depression is becoming a major public health problem, not only because of the personal suffering that it causes, but also because of its related morbidity and excess mortality (Bagulho, 2002; Miu and Chan, 2011). The estimation of the frequency of depression in old age exhibits a great variability due to the sample involved, the definition of depression, the methodology used, and the experience of the evaluator. When compared with depression in the youth, the rate of treatment for depression in old age is significantly minor (Gallo and Lebowitz, 1999). Only 10% of elderly patients who need treatment actually receive it (Gallo and Lebowitz, 1999).

Lack of recognition of depression by the patient and the medical staff in the context of multiple physical problems could make depression in the elderly insidious (Alexopoulos, 2005; Engedal et al., 2010; Gallo and Lebowitz, 1999; Millán-Calenti et al., 2010). Because of the great variety of diseases and socioeconomic problems, many clinicians conclude that depression is the normal consequence of these problems, an explanation that is also shared by patients (Gallo and Lebowitz, 1999).

2. Aims

This research aimed to study different depressive syndromes in geriatric patients who consult or are referred to a memory clinic in order to determine their distinctive clinical manifestations.

3. Materials and methods

A cross-sectional analytical study was performed. The study took place in a memory clinic from a Buenos Aires community-based outpatient hospital, the Hospital General Zubizarreta (public health system).

3.1. Study population

A total of 109 depressive patients with cognitive complaints and 30 controls (those lacking signs and symptoms of depression or cognitive impairment) from the general population, matched by age and educational level (age 6.3 +/− 8.28 years, educational level 9.8 +/− 4.3 years), were recruited.

3.2. Inclusion criteria

Included in the study were patients who consulted or were referred to our Memory Clinic, presenting depressive symptoms that were due to psychiatric causes or were related with mild dementia of Alzheimer's type (CDR 1: mild dementia; CDR: Clinical Dementia Rating Scale; Morris, 1993), who were more than 55 years old but less than 80 years old, and with a Hamilton Depression Scale rating >9 points and Beck Depression inventory >9.

3.3. Exclusion criteria

Patients with drug or alcohol abuse, with moderate or severe dementia by the CDR (2 = moderate dementia or 3 = severe dementia) (Morris, 1993), and with schizophrenia or schizoaffective disorder were excluded from the study.

3.4. Screening procedure

Depressive patients were divided into four different groups according to DSM IV (APA, 2000) and ICD 10 (1990) criteria with the SCAN 2.1 (WHO: World Health Organization) schedules for clinical assessment in neuropsychiatry.

SCAN is a set of instruments and manuals aimed at assessing, measuring, and classifying psychopathology and behavior associated with the major psychiatric disorders in adult life. It can be used for clinical, research, and training purposes, and was developed within the WHO framework. SCAN has a bottom-up approach where no diagnosis-driven frames are applied in grouping the symptoms. Each symptom is assessed in its own right. SCAN has a proven stability. The method used is that of a semi-structured standardized clinical interview, with cross-examination of the subject. Rating is done on the basis of matching the answers of the respondent against the definitions of the symptoms in the Glossary, which is an integral part of SCAN. All the symptoms and signs and classification items are defined in this Glossary, which is largely based on the phenomenology of Jaspers. With SCAN the interviewer decides what to rate on the basis of the subject's information, always bearing in mind the definitions and rating rules (Wing et al., 1990).

The study participants were grouped as follows:

Group 1: major depression disorder (MDD) (n: 34)
Group 2: dysthymia disorder (DD) (n: 29)
Group 3: subsyndromal depression (SSD) (n: 28)
Group 4: depression due to dementia (DdD): only mild Alzheimer dementia; CDR 1 (Clinical Dementia Rating Scale) were recruited (n: 18)
Group 5: controls (C) (n: 30)
Screen failures: 11 patients

All of the recruited patients were assessed using a semi-structured neuropsychiatric interview. Different psychiatric scales were used, including the Beck Depression Scale, the Hamilton Depression Scale, and the Hamilton Anxiety Scale.

Patients and normal controls were matched by age, education, and overall cognitive status using the Mini Mental State Examination (MMSE) (Folstein et al., 1975).

Vascular risk factors and co-morbidities such as high blood pressure, high blood cholesterol level, cigarette smoking, stroke, diabetes, and heart disease were assessed. Additionally, the sociological risk factors of depression, such as marital status (married or non-married) and level of activity (active: patients who work or have planned activities; or inactive: patients with no activities at all) were evaluated.

Each patient underwent an extensive neuropsychological battery to evaluate the following areas of cognitive ability:

Orientation: MMSE (Folstein et al., 1975).
Attention: Digit span (forward and backward) (Wechsler, 1988); Trail making test "A" (Reitan, 1958).
Language: Boston naming test (BNT) (local version adapted by Allegri et al., 1997), Semantic fluency (SF) (Benton et al., 1983), Verbal fluency (VF) (Benton et al., 1983).
Memory: Signoret memory battery (Signoret and Whiteley, 1979): episodic memory, immediate logic memory (ILM), delayed logic memory (DLM); verbal serial learning (VSL), delayed serial memory (DSM), cued recall (CR), recognition (Recog); Buschke selective reminding test, free recall (BSRT fr); Buschke selective reminding test, cued recall (BSRT cr) (Buschke, 1973).
Visuospatial abilities: Clock drawing test (Freedman et al., 1994).
Executive functions: Trail making test "B" (Reitan, 1958), VF (Benton et al., 1983).
Quality of life: Determined by two scales: Lawton and Brody (1969) self-maintaining and instrumental activities of daily living scale (reported by the relative) and Zarit and Zarit (1990) caregivers' burden interview. Caregivers' burden and daily life activities are variables that indirectly affect the health-related quality of life (Machnicki et al., 2009a).

Written informed consent was obtained from each subject after the subject had been given a full explanation of the study. The research was performed in accordance with the ICH Good Clinical Practice guidelines, the latest revision of the 1964 Helsinki Declaration (last amended in Seoul 2008), and the Buenos Aires Government Health Authorities.

4. Data analysis

Demographic variables for both populations (patients and controls) as well as the results of neuropsychiatric and neuropsychological general global tests were expressed as means, standard deviation, and medians. Quantitative variables were compared using ANOVA. Pairwise comparisons involving each depressive group versus the controls (four comparisons per neuropsychiatric test) were corrected for multiplicity using the Dunnet test. Pairwise comparisons of each depression group with the other groups and controls were corrected for multiplicity using the Scheffé method. In both cases, the overall probability of type I error for each clinical test involving multiple groups was held at 5%. The relationship between qualitative variables was compared by the chi-square test. Variables associated with depression were analyzed using odds ratios (OR) with 95% confidence intervals (95% CI). Data were analyzed using the SPSS 14 (2006) statistical package.

5. Results

5.1. Demographic data

There were no significant differences in age and educational level among the five groups. Table 1 shows significant cognitive level (MMSE) differences ($p<.05$) between the DdD and the other depressive groups (MDD, DD, SSD) and between DdD and normal controls.

5.2. Variables associated with depression (family and personal history)

5.2.1. Depressives versus control

Table 2 shows significant differences ($p<.05$) in marital status (OR: 3.4, CI: 1.2–9.6), level of activity (OR: 5.3, CI: 2–14), heart disease (OR: 12.5, CI: 1.6–96.3), and high cholesterol level between depressive patients and normal controls.

5.2.2. Depressive groups (DMM, DD, SSD, DdD)

Significant differences ($p=.034$) were found only in level of activity among the different depressive groups (DMM, DD, SSD, DdD) (Table 2).

5.2. Neuropsychological battery

5.2.1. Comparisons versus controls

All depressive groups demonstrated cognitive impairment compared with normal controls.

Table 1
Demographic data.

	MDD	DD	SSD	DdD	Controls	*p*
Patients (n)	34	29	28	18	30	
Age (years)	64.1 ± 7.4	66.7 ± 9.1	66.4 ± 9.7	71.2 ± 7.6	65.1 ± 6.7	ns
Educational level (years)	9.82 ± 3,6	8.9 ± 4.6	9.7 ± 5.2	8.5 ± 3.7	11.7 ± 3.7	ns
MMSE	27.2 ± 3.1	26.8 ± 3.4	27.1 ± 2.1	23 ± 4.5	29.0 ± 1.0	DMC versus control<.0001 DMC versus MDD<.0001 DMC versus DD=.001 DMC versus SSD<.0001

Notes
Values expressed are mean ± standard deviation (SD).
Significant differences: $p<.05$. NS: non-significant differences ($p>.05$).
MDD: major depression disorder.
DD: dysthymia disorder.
SSD: subsyndromal depression.
DdD: depression due to dementia.
ns: not significant at .05 level.
MMSE: Mini Mental State Examination.

Table 2
Variables associated with depression.

Variables	Depressives versus controls				Depressive groups				
	Depressive N:109	Controls N:30	p *	OR (CI)	MDD N:34	DM N:29	SSD N:28	DdD N:18	p *
Level of activity (inactive/active)	60/43	6/23	0.001	5.3 (2–14.2)	20/11	11/15	14/14	15/3	0.034
Marital status (not married/married)	45/61	5/23	0.017	3.3 (1.19–9.6)	16/17	10/17	14/14	5/13	ns
High blood pressure level (yes, no)	51/58	10/20	ns		14/20	11/18	15/13	11/7	ns
Diabetes (yes, no)	12/97	1/29	ns		5/29	3/26	2/26	2/16	ns
High blood cholesterol level (yes, no)	53/56	8/22	0.032	0	19/15	15/14	11/17	8/10	ns
Heart disease (yes, no)	33/76	1/29	0.002	12.5 (1.6–96.3)	10/24	12/17	8/20	3/15	ns
Neurological disease (yes, no)	10/99	1/29	ns		2/32	3/26	2/26	3/15	ns
Concomitant disease (yes, no)	69/37	16/13	ns		69/37	16/13	16/13	16/13	ns
Heavy smoking (yes, no)	34/75	9/21	ns		11/23	6/23	10/18	7/11	ns
Family history of depression (yes, no)	57/44	21/16	ns		18/13	13/14	13/14	13/3	ns
Hypothyroidism (yes, no)	19/88	1/28	ns		5/28	6/22	3/25	5/13	ns
Gender (female, male)	82/27	19/11	ns		27/7	23/6	20/8	12/6	ns

Notes
* Chi square.
MDD: major depression disorder.
DD: dysthymia disorder.
SSD: subsyndromal depression.
DdD: depression due to dementia.
ns: not significant at 0.5 level.

The DdD group showed statistically significant differences ($p<.05$) in all the cognitive domains: memory (cortical profile: severe impairment in learning (verbal serial learning), failure to recall (delayed serial recall and cued recall), and failure in recognition), language (severe impairment, typical of cortical profiles), visuospatial abilities, executive functions, and attention in comparison with normal controls (Table 3 and Fig. 1).

The MDD group demonstrated significant differences in memory (subcortical profile: poor learning and failure to recall (delayed serial recall) with good cued recall and recognition), executive functions, and language with normal controls (Table 3 and Fig. 1).

The DD group had significant differences ($p<.05$) with controls in memory (subcortical profile), attention, executive functions, and language (Table 3 and Fig. 1).

The SSD group presented significant differences with controls in memory (subcortical profile), language, and executive functions (Table 3 and Fig. 1).

Table 3
Neuropsychological Battery: comparisons versus controls.

	MDD	DD	SSD	DdD	Controls
Memory					
Immediate logic memory	**5.6 ± 2.8**	**5.3 ± 2,4**	**5.2 ± 2.1**	**2.6 ± 1.8**	7.7 ± 2.1
Delayed logic memory	**5.3 ± 3.0**	**4.6 ± 2.0**	**4.9 ± 2.2**	**1.9 ± 1.8**	7.4 ± 2.1
Verbal serial learning	**7.5 ± 2.3**	**7.5 ± 2.1**	**7.4 ± 2.1**	**4.9 ± 1.7**	9.4 ± 1.4
Delayed serial memory	**6.1 ± 2.5**	**5.6 ± 2.8**	**5.2 ± 2.5**	**2.3 ± 2.4**	8.1 ± 1.5
Cued recall	**8.4 ± 3.2**	**8.8 ± 3.1**	**8.5 ± 3.5**	**5.5 ± 3.1**	11.1 ± 1.0
Recognition	10.5 ± 2.1	10.6 ± 2.3	10.8 ± 1.5	**8.2 ± 3.3**	11.7 ± 0.4
Buschke Memory battery (Immediate memory).	6.5 ± 1.8	6.7 ± 2.0	6.5 ± 1,4	**4.0 ± 2.6**	7.5 ± 1.0
Buschke Memory battery (Cued memory)	7.1 ± 1	7.2 ± 1.5	7.1 ± 0.8	**5 ± 2.7**	7.6 ± 0.8
Language					
Boston Naming Test	**45.8 ± 6.8**	**46.2 ± 7.7**	**44.5 ± 7.2**	**37.4 ± 10.1**	51.6 ± 4
Semantic Fluency	**14.4 ± 4**	**14.6 ± 5.3**	**13.7 ± 4**	**9.7 ± 3.5**	19.6 ± 6
Executive function					
Verbal fluency	**11.5 ± 4.7**	**11.6 ± 5**	**10.5 ± 4.8**	**6.7 ± 3.4**	15.5 3.8
Trail Making Test "B"	**213.9 ± 144**	**226.7 ± 148**	**205.6 ± 137**	**310.9 ± 166**	109.8 ± 41.6
Attention					
Trail Making Test "A"	66.8 ± 34.7	69.3 ± 42.8	68.4 ± 25.4	**109 ± 54**	48.6 ± 16.6
Digit Span (forward)	5.3 ± 1	4.9 ± 1.2	5.1 ± 1	5.1 ± 1	6 ± 1
Digit Span (backward)	3.8 ± 1	**3.4 ± 0.9**	3.6 ± 1.1	3.1 ± 1	4.4 ± 1
Visuospatial abilities					
Clock Drawing Test	6 ± 1.3	5.3 ± 2.2	6 ± 1.5	**3.8 ± 2.5**	6.5 ± 1

Note: Groups with statistically significant differences versus controls are shown in bold. The overall type I error for all comparison involving a variable was set at 5%. Dunnet's test was used to adjust for multiplicity.

5.2.2. Comparisons among all groups

Several differences among depressive subgroups were revealed in multiple comparisons. Immediate and delayed serial memory, verbal serial learning, and delayed serial memory and cued recall showed three distinctive subgroups: DdD (group 1); SSD, DD, and MD (group 2); and controls (group 3). In some of these comparisons the grouping was unambiguous (such as for immediate logic memory and verbal serial learning), but in other cases some of the patient groups were assigned to more than one subgroup as there was no statistical power to rule out alternative ordering of the patient subgroups. The only differences for recognition, BSRTfr and BSRTcr, were between DdD and all the other groups. The language and executive function tests showed three groups that frequently involved assignment to more than one subgroup for a given patient segment. The attention variables showed a difference between DdD and the rest of the groups (except for the backward digit span); the clock drawing test also differentiated between the DdD and all the other groups (Table 3 and Fig. 1).

5.3. Neuropsychiatric interview

Significant differences (simultaneous $p = .05$) were observed in the Hamilton and Beck depression scales and the Hamilton Anxiety scale when depressive groups (MDD, DD, SSD, DdD) were compared with normal controls.

5.3.1. Comparisons among all groups

With regard to depressive groups, SSD demonstrated significant differences ($p < .05$) with the other depressive

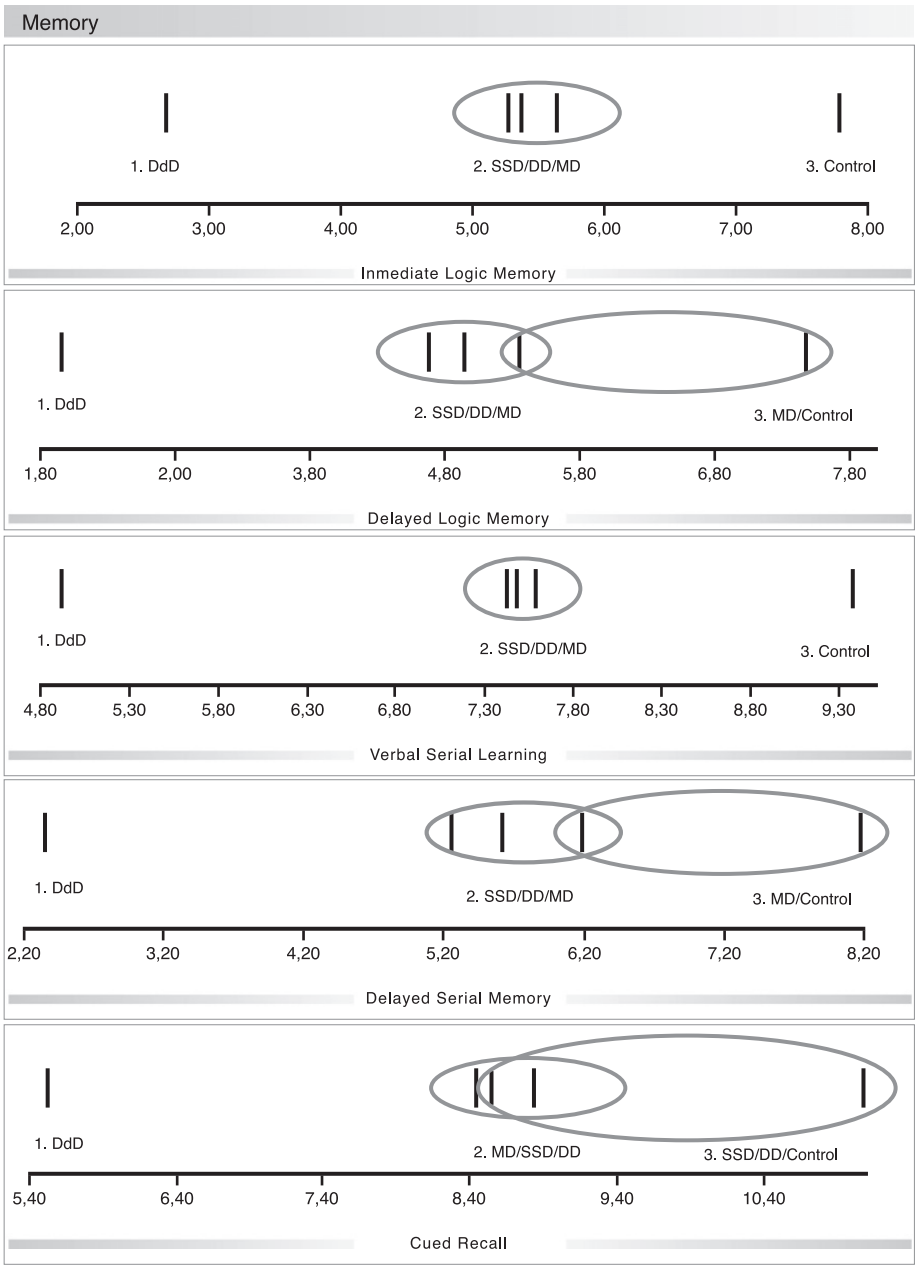


Fig. 1. Neuropsychiatric tests: homogeneous groups emerging from multiple comparisons (95% simultaneous confidence intervals).

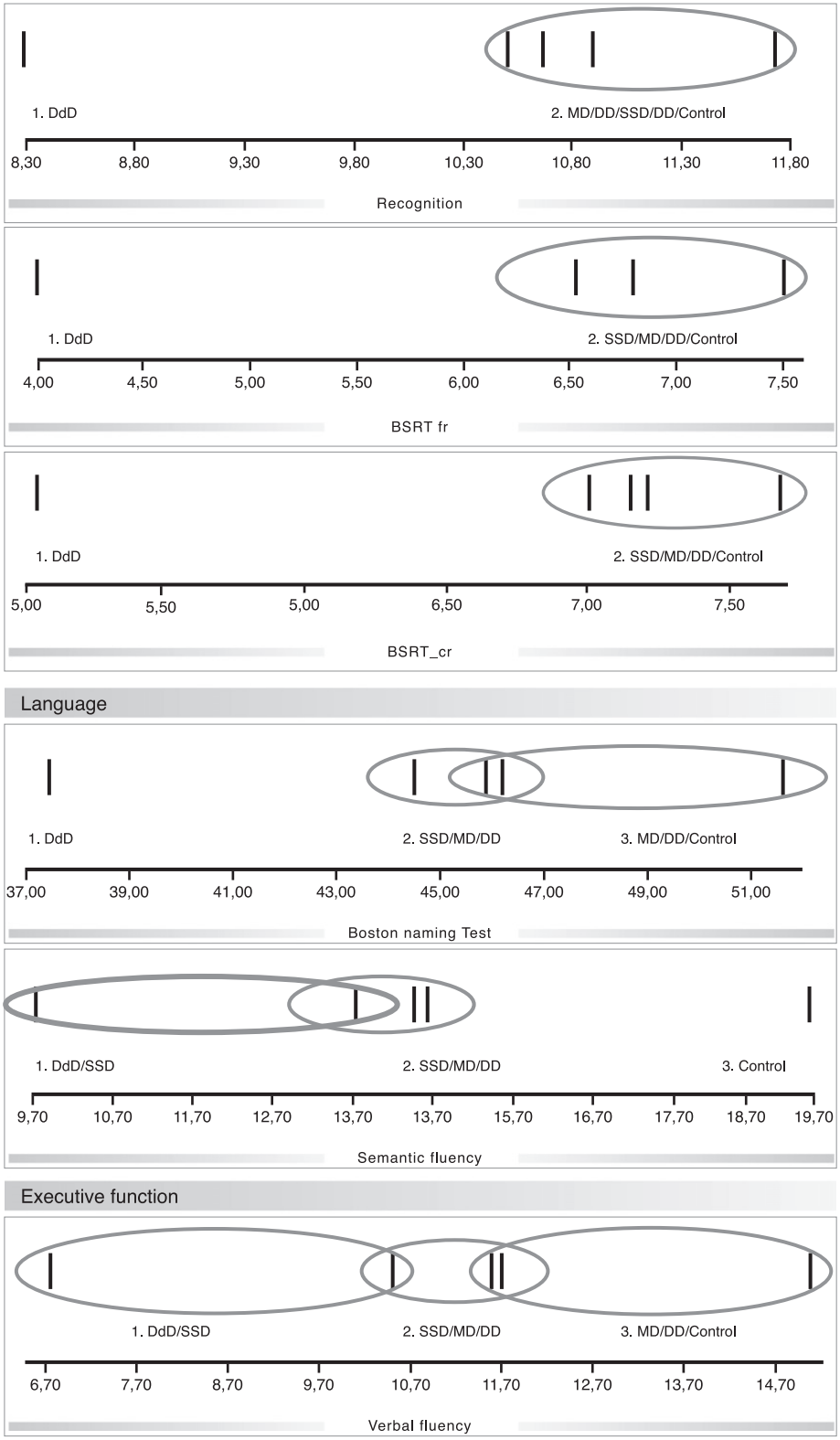


Fig. 1 (*continued*).

groups (MDD, DD, and DdD) in Beck Depression Inventory scores (Fig. 2).

5.4. Quality of life

5.4.1. Caregivers' burden

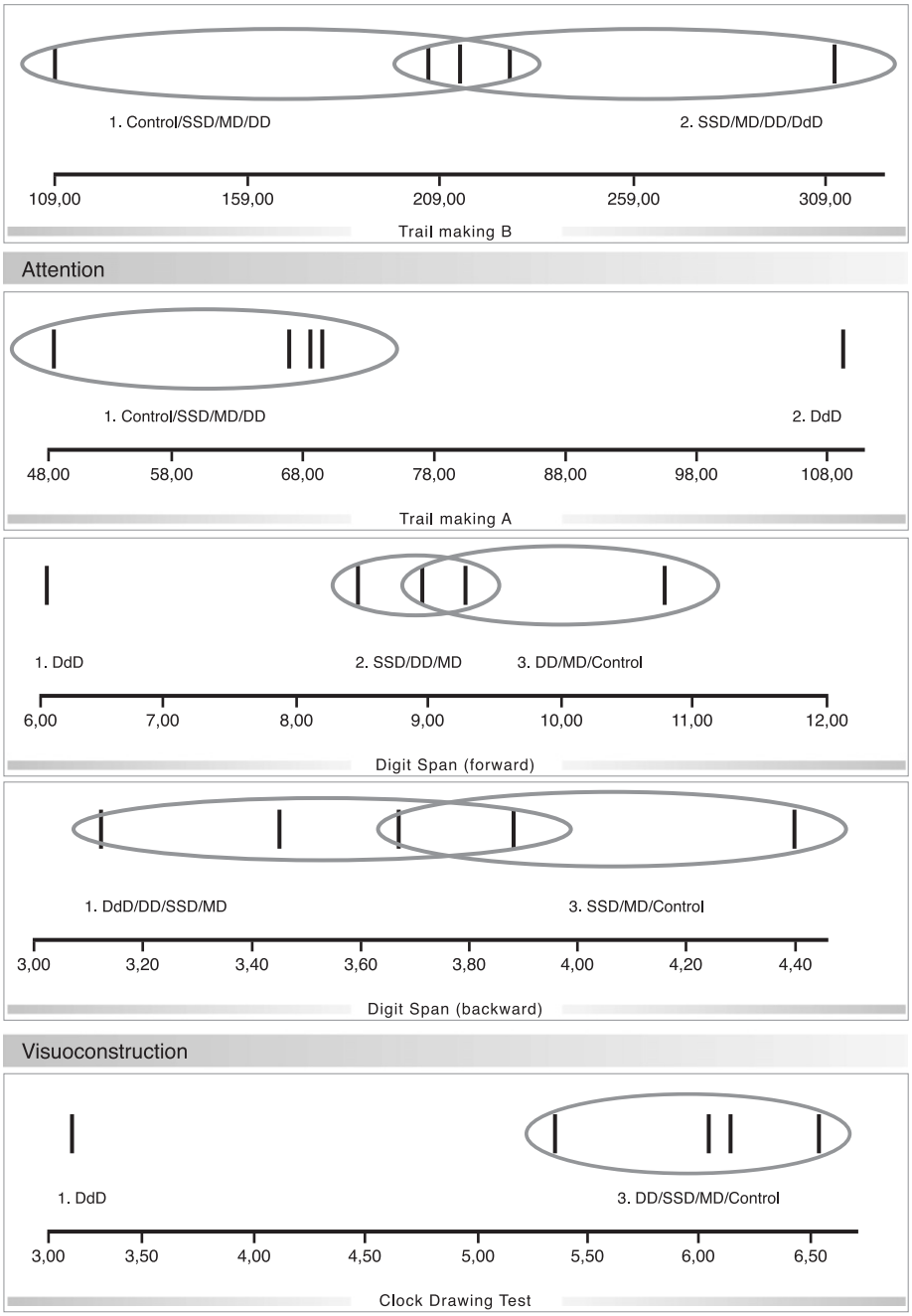
Table 4 shows significant differences between normal controls and all depressive groups in Zarit's caregivers' burden scale.

5.4.2. Activities of Daily Living (ADL)

MDD and DdD presented impairment in activities of daily living in comparison with controls. Moreover, the DdD group had the worst performance (Table 4).

5.4.3. Comparisons among all groups

Caregivers of patients with SSD or DD were also assigned to a group with controls, but the same caregivers were



Note:
Homogeneous subgroups are defined by those groups showing statistically significant differences when considering simultaneous 95% confidence intervals involving all comparisons between groups. Test multiplicity was corrected with Scheffe´s test and the overall type I error was 5% for all comparisons involving one variable. Homogeneous groups involving more than one patient group are shown with circles. When a group belongs to more than one homogeneous groups, there was not enough evidence to conclusively classify that patient group into alternative subgroup.

Fig. 1 (*continued*).

associated with a group with all other caregivers of depressive patients (Fig. 2).

Two ADL groups emerged. One consisted of patients with DdD, the other of all other depressive groups and the control group (Fig. 2).

6. Discussion

Different subtypes of geriatric depression exist. Four subtypes of depression were evaluated in the following investigation: major depression disorder, dysthymia

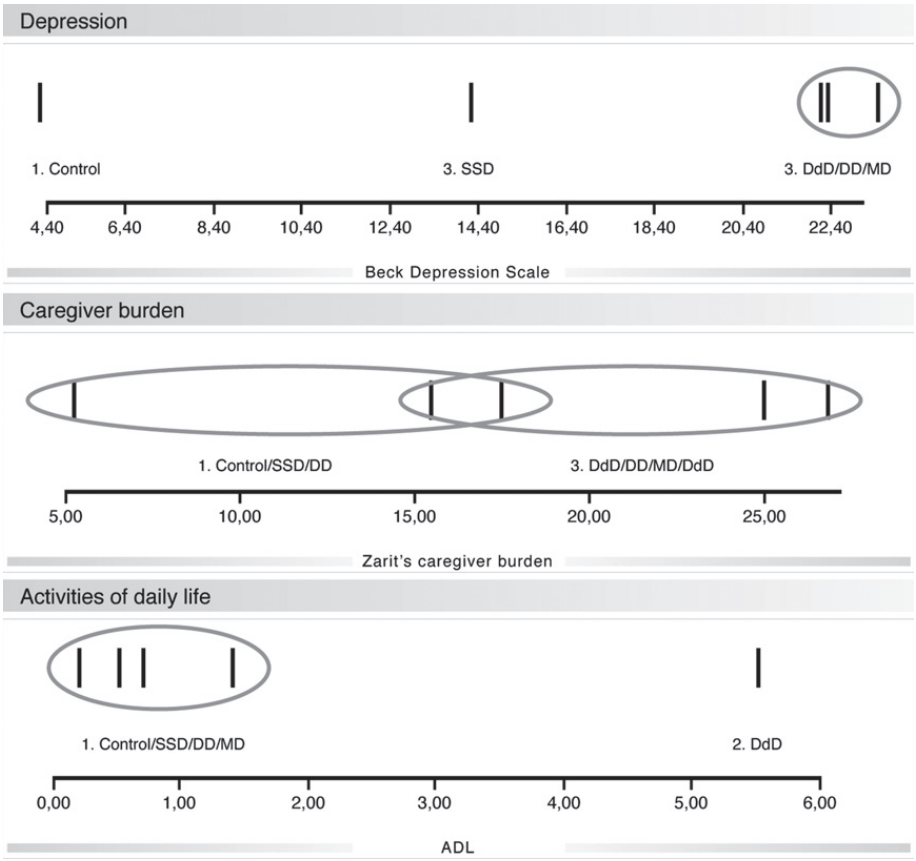


Fig. 2. Patient and caregiver reported outcomes: homogeneous groups emerging from multiple comparisons (95% simultaneous confidence intervals).

disorder, subsyndromal depression, and depression due to dementia of Alzheimer's type. These groups were investigated and different variable associations and clinical manifestations were observed.

6.1. Risk factors

Vascular risk factors and co-morbidities such as high blood pressure, high blood cholesterol level, cigarette smoking,

Table 4
Neuropsychiatric assessment and quality of life: caregivers' burden and daily life activities.

	MDD	DD	SSD	DdD	Controls
	N:34	N:29	N:28	N:18	N:30
Hamilton Anxiety Scale	**17.0 ± 6.9**	**16.2 ± 7.0**	**15.9 ± 7.8**	**14.3 ± 6.7**	2.2 ± 2.8
Hamilton Depression Scale	**18.6 ± 6.0**	**17.8 ± 7.1**	**15.1 ± 4.8**	**16.8 ± 5.7**	1.9 ± 1.7
Beck Depression Inventory	**23.4 ± 9.0**	**22.2 ± 9.5**	**14.2 ± 7.5**	**22.1 ± 10.4**	4.4 ± 3.1
Caregivers' burden	**25 ± 18**	**17.5 ± 13.7**	**15.5 ± 13.3**	**26.8 ± 6.7**	5.2 ± 7.7
Daily life activities	**1.4 ± 2**	0.7 ± 1.4	0.5 ± 0.9	**5.5 ± 2.2**	0.21 ± 0.8

Note: Groups with statistically significant differences versus controls are shown in bold. The overall type I error for all comparison involving a variable was set at 5%. Dunnet's test was used to adjust for multiplicity.
MDD: major depression disorder.
DD: dysthymia disorder.
SSD: subsyndromal depression.
DdD: depression due to dementia.

stroke, diabetes, and heart disease were assessed. Also evaluated were sociological risk factors of depression, such as marital status and level of activity.

Vascular factors are increasingly considered to be involved in the pathogenesis of two of the most common problems found in patients presenting to geriatric psychiatrists, namely, dementia and depression (Flicker, 2008, Hoptman et al., 2009). Unfortunately, there is a paucity of evidence that the treatment of vascular factors can either prevent or ameliorate the symptoms of these common conditions. There is mounting evidence, however, that a minimum of these patients should at least have a good quality of standard medical care for these vascular risk factors (Flicker, 2008).

There is also some recent evidence on the direct effect of vascular factors on brain disorder. The previously described cognitive effects of coronary heart disease on cognitive function have been supported by evidence of loss of gray matter volume in multiple parts of the gray matter of the brain, including some that play a major role in cognitive function and behavior (Almeida et al., 2008). The evidence for such relationships is reinforced by the observation that one third of stroke survivors will experience depressive symptoms.

Depression has been correlated with an increased number of white matter lesions, which represent cumulative vascular damage to the brain. Coupled with this, depression has also been demonstrated to be an independent risk factor for cardiovascular and cerebrovascular events (Flicker, 2008, Hoptman et al., 2009).

Prospective studies reveal more depression in females than in males. Other risk factors are being widowed, concomitant diseases (Harlow, 1991), low education (Gallo and Lebowitz, 1999), impaired functional level (Bruce et al., 1990), lack of satisfaction, feelings of loneliness, smoking (Green et al., 1992), and alcohol abuse. On the other hand, depressive symptoms in the elderly are a risk factor for cognitive impairment and functional deficit (Bassuk et al., 1998).

Although physical alterations and cognitive impairment were not included among the diagnostic criteria, late-life major depression is often associated with these factors. Physical alterations include hypercortisolemia, increased abdominal fat, decreased bone density, and increased risk for type 2 diabetes and hypertension (Alexopoulos, 2005).

In the present study we observed that inactivity (OR 5.3, CI: 2–14.2), marital status (OR 3.39, CI: 1.19–9.6), heart diseases (OR 12.5, CI: 1.6–96.3), and high cholesterol level (p:.032; OR:0) were variables associated with depression. DdD and MDD were the most inactive groups.

6.2. Cognitive functions

Non-demented elderly people with major depression often have difficulties with concentration, speed of mental processing, and executive function (Dillon et al., 2009a; Lockwood et al., 2002). These deficits improve, but do not completely resolve, after remission of late-life depression. Symptoms or syndromes of depression often precede cognitive decline and dementia (Devanand et al., 1996; Dillon et al., 2009a).

Butters et al. propose that depression alters an individual's risk of cognitive dysfunction, shortening the latent period between the development of Alzheimer's disease (AD) neuropathology and the onset of clinical dementia, thus increasing the incidence and prevalence of AD among older adults with depression.

Many individuals with later-onset depression may be in the prodromal stage of AD, their hippocampus having already sustained substantial neuronal injury due to cumulative AD neuropathology (Butters et al., 2008).

6.3. Cognitive profiles

In Alzheimer's disease senile plaques and neurofibrillary tangles populate the cortex and there is generalized cortical atrophy, especially of the frontal and temporal lobes, with neuronal degeneration affecting particularly the outer three layers. The typical clinical findings include dysphasias, anomia and aphasia (Cummings and Benson, 1984), dyscalculia, dyspraxias and agnosias, and are said to be indicative of cortical dysfunction (Turner et al., 2002).

In the subcortical dementias, on the other hand, the lesions occur predominantly in the basal ganglia, the brainstem nuclei, and the cerebellum, and the clinical picture is correspondingly different. In subcortical dementia (e.g., in Parkinson's disease and Huntington's dementia), there is a learning impairment that can be partially corrected by providing richer (more salient) cues to encourage learning and promote recognition (Pillon et al., 1993). In contrast, it was claimed that cortical dementias (such as Alzheimer's dementia) are characterized by accelerated forgetting (Cummings, 1986).

Our findings show that geriatric depressive patients had significant differences with controls in almost all cognitive domains. However, each depressive group had a certain particular neuropsychological profile.

Patients with depression due to dementia of Alzheimer's type presented severe impairment in memory and language typical of a cortical cognitive profile. Moreover, the poor performance in visuospatial abilities differentiates them from the other depressive groups. Executive and attentional problems were also observed.

Patients with major depression and dysthymic disorder showed a subcortical profile with moderate impairment in memory and mild impairment in language. Executive and attentional abilities were also severely compromised.

Subsyndromal depressive patients had a subcortical profile similar to MDD and DD patients. This subtype of depression, however, had a low level of depressive symptoms that do not justify the magnitude of cognitive impairment.

6.4. Quality of life

According to WHO (1990), depression reduces a person's active life by four years. As the population ages, dementia, depression, and other mental conditions of the aged will demand more attention from clinicians and investigators to minimize the impact of such conditions on disability, the use of health care services, and the quality of life for older adults and caregivers (Tannock and Katona, 1995).

Being a caregiver to a patient with Alzheimer's disease (Machnicki et al., 2009a) or to a patient with depression

(Dillon et al., 2009b) is associated with impaired health status and declines in health-related quality of life. Caregiving to elderly relatives by family members increased almost three fold in the last century due to the growing incidence and prevalence of chronic and degenerative disorders (Machnicki et al., 2009a).

Caregiving is a multidimensional concept (Pearlin et al., 1990), with impacts on both physical and mental health, as well as on family finances and the family's structure of time. The clinical community has recognized caregiver burden as an important and multidimensional problem. As such, caregiver burden can be examined from different perspectives, including health-related quality of life (HRQoL) (Machnicki et al.,2009a).

Behavioral symptoms are an important factor associated with caregiver burden in patients with cognitive impairment, dementia, or depression, while functional (daily life activities) and cognitive factors seem to also have an influence on patients with cognitive impairment (Machnicki et al., 2009b). The present research showed that depression produced impairment in the daily life activities of patients and affected the quality of life of both patients and caregivers.

6.5. Limitations

The cohort referred to a memory clinic with memory complaints is a biased sample, and the results cannot be generalized to other non-memory symptomatic cohorts. Given the cross-sectional nature of this study, it was not possible to ascertain the temporal sequence of events. As usual in observational research, confounding bias may exist because observed differences could be accounted by other variables that were not considered in the matching and the statistical analyses. Therefore, risk could not be inferred from this study as only associations may exist. Many variables were examined in this work. It is known that this can inflate the probability of erroneously finding statistically significant differences. Correction for multiplicity was done for all tests of a given variable to preserve the overall type I error at 5%. This is a standard and widely used method. A more advanced alternative would have been correction for multiple tests taking into account that several outcome variables were analyzed. This was not done because it is difficult to treat those variables in a common multivariate distribution that relates all outcomes that were analyzed. In a sensitivity analysis, the overall type I error for all tests for a given variable was reduced to 0.2% before applying the Dunnet or Scheffé method (0.2% equals 5% divided by 21, the number of neuropsychological and patient reported outcomes variables in Tables 3 and 4). The majority of the statistically significant results versus controls were retained in this alternative analysis; differences among the depressive were more difficult to detect, but this sensitivity analysis applied an additional correction for type I error that is known to be overly conservative. Another alternative to this approach would have been to perform sequential tests, where the total number of comparisons could have been reduced depending on the results of some initial tests. Given the exploratory nature of this research, it was preferred to perform an unrestricted number of tests and to try to correct for multiplicity with known methods. Finally, measurement bias in the data used remains a possibility (as typical in epidemiological research), however it is unclear to which degree this was present (for example, in patient reported variables) and how it could have influenced the reported results.

7. Conclusion

All the data collected in this research demonstrate the following clinical characteristics of each depressive group.

Major depression disorder (MDD) patients presented a moderate level of depressive symptoms with moderate anxiety. A subcortical cognitive profile with greater impairment in executive functions and memory was found. This group had significant affection in daily life activities and in caregivers' burden in comparison with normal controls.

Dysthymia disorder (DD) patients showed moderate depressive symptoms in association with anxiety. A subcortical profile was found, with attention and memory being the most affected domains. These patients did not show significant impairment in daily life activities; however, they scored significantly higher in the caregivers' burden scale in comparison with controls.

The subsyndromal depressive disorder (DSS) group demonstrated mild depressive symptoms with moderate anxiety. Subcortical cognitive impairment was observed, language and memory being the domains most implicated. This group had important cognitive manifestations in spite of the fact that it was the group that showed the lowest level of depressive symptoms. DSS patients did not present great impairment in daily life activities, but had significant differences in the caregivers' burden scale in comparison with controls. This group could be considered at risk of degenerative disease.

The depression due to dementia of Alzheimer type (DdD) group presented moderate depressive symptoms associated with anxiety. These patients had the greatest cognitive impairment with a cortical profile, with memory, visuospatiality, and language being the predominant domains. This group showed the highest score in daily life activities and in the caregivers' burden scale. In summary, despite its limitations, this study offered valuable information that could be used to design additional studies in the area

Depression is a mental disease that affects not only the psychological well-being of a patient (by causing mood disorders), but also the patient's neuropsychological profile (through cognitive impairment).

Geriatric depression is associated with heart disease, high cholesterol levels, marital status, and inactivity. Subtypes of geriatric depression exist and have clinical features, such as cognitive profiles, daily life activities, and caregivers' burden, that can help differentiate among them. Patients with subsyndromal depression associated with cognitive impairment could be considered at risk of degenerative disease.

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Conflict of interest

All authors declare that they have no conflicts of interest.

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