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Patterns of neuropsychological impairment in mild dementia: a comparison between Alzheimer's disease and multi-infarct dementia

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The objective was to investigate the clinical and psychometric differences between patients with dementia of Alzheimer type (DAT) and patients with multi-infarct dementia (MID), matched for age, sex, education, and severity. Sixteen patients with DAT, 16 patients with MID, and 30 healthy individuals, were drawn from a longitudinal study on aging and dementia. Subjects with medical or previous mental disorders were excluded. DAT and controls with focal brain abnormalities on magnetic resonance imaging (MRI) were excluded. Diagnosis of dementia was carried out according to DSM-III-R criteria. Dementia severity was staged using the Clinical Dementia Rating (CDR) scale, and only patients with a score of 0.5–1 on CDR were studied. The main outcome measures were quantitative clinical scales of the assessment of global mental status, depression and anxiety, as well as a wide battery of neuropsychological tests for the evaluation of executive/conceptual functions and memory, as well as attention verbal ability, and visuospatial skill functions. The performance of demented patients compared to normal controls was affected on all measurements except for depression and anxiety. DAT patients showed compared to MID patients a greater extent of impairment on tasks assessing verbal comprehension and memory while MID patients were more significantly impaired on measures of frontal lobe functioning. Clinically matched DAT and MID patients show a differential pattern of neuropsychological impairment when studied in an early stage of dementia and with a mild degree of severity. Such patterns might be of value for the development of clinical diagnostic criteria.

Key words: Alzheimer's disease; multi-infarct dementia; neuropsychology

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Dementia of Alzheimer's type (DAT) and multi-infarct dementia (MID) are the most common forms of dementia, accounting for up to 65–90% of demented patients in an older population (1–3). The essential features of DAT are an insidious onset with gradual progressive impairment of higher cortical functions including memory, language, visuospatial and constructive skills. MID is generally associated with a rather abrupt onset, a stepwise and fluctuating progression, and the presence of neurological signs and symptoms with heterogeneous behavioral and cognitive abnormalities (4). Differences in diagnosis, classification, and terminology, however, have characterized so far most studies on MID (5–6).

Despite widespread agreement on MID association with pervasive behavioral dysfunctions, the characterisation of these changes and their similarity to those observed in DAT remains unclear.

Several studies have attempted with rather negative results to distinguish the cognitive profiles between DAT and MID patients (7–12). Nevertheless, few studies have reported subtle differences between DAT and MID patients, matched for overall cognitive and functional impairment (13–19). Among these, though most have failed to defined specific patterns of cognitive impairment in the two groups, some studies have evidenced a greater sensibility for DAT patients to measures of memory and language-related tasks (13–17), while MID patients were reported to be particulary impaired on tasks measur-

ing motor or cognitive speed (18–19). Further, it has also been claimed that MID patients display such behavioral features as forgetfulness, disorientation, slowing of mental processing, and frontal systems' impairment, which are typically found in subcortical dementia (20–23).

Contributing factors to these inconsistent findings might include inaccurate diagnosis, different criteria for dementia, failure to equate groups for their overall levels of dementia, inclusion of moderate-severe demented patients with widespread behavioral impairments, and differences in methods related to cognitive assessment.

In an attempt to clarify possible differences between DAT and MID, we compared patients with mild dementia on a wide battery of neuropsychological tests, as recommended by the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA) (24). To insure comparable levels of overall cognitive impairment, both patient groups were matched for degree of dementia as well as age and education.

In particular, we predicted that mild DAT and MID patients (likely to show less pervasive mental disturbances) would show a differential pattern of cognitive impairments affecting executive/conceptual functions, memory and verbal ability due to their differential cortical/subcortical brain involvement.

Material and methods

Three groups consisting of a total of 62 subjects participated in the study: 16 DAT patients (10 women, 6 men), 16 patients with MID (7 women, 9 men) and 30 normal controls (18 women, 12 men). The normal control group consisted of healthy individuals, matched for age and education.

As shown in Table 1, patients with DAT had a mean age of 64.2 ± 7.4 years and a mean duration of formal education of 8.9 ± 3.7 years. Patients with MID had a mean age of 66.1 ± 6.1 years and a mean duration of formal education of 9.9 ± 4.7 years. Healthy controls had a mean age of 64.6 ± 7.1 years and a mean duration of formal education of 11.3 ± 3.9 years.

Table 1. Demographic and behavioral characteristics of controls, DAT and VD patients

Variable	Normal controls (n=30)	DAT cases (n=16)	VD cases (n=16)
Age (years)	64.6 (7.1)	64.2 (7.4)	66.1 (6.1)
Education (years)	11.3 (3.9)	8.9 (3.7)	9.9 (4.7)
Mini-Mental State Examination	28.3 (1.1)	22.9 (2.3)*	23.5 (2.4)
Blessed I.M.C.	32.5 (1.4)	25.6 (4.9)*	27.5 (2.5)*
Information WAIS	22.5 (3.9)	13.1 (6.4)*	16.1 (4.8)*
Vocabulary WAIS	60.1 (7.5)	37.8 (17.4)*	35.3 (18.3)*
Rome Depression Inventory	36.9 (9.7)	41.1 (15.1)	41.6 (13.7)
STAI x-1	42.3 (9.5)	40.2 (15.6)	37.8 (10.3)
STAI x-2	38.4 (10.5)	43 (15.4)	41.2 (16.6)

Data are expressed as mean (SD)
* Significant difference ($P<0.05$) between patient groups and controls

All subjects were recruited from a large sample of individuals enrolled in a longitudinal study on aging and dementia. Written informed consent was obtained from all subjects or the caregivers, where appropriate.

Each subject was examined according to the same comprehensive procedure which consisted of the followings: somatic examination, neurologic status, mental status, blood tests, urinanalyses, routine electro-cardiogram, and magnetic resonance imaging (MRI) of the brain.

Patients with metabolic disease, drug abuse, history of alcoholism, previous psychiatric disorders, or head injuries were excluded.

The clinical protocol included the Clinical Dementia Rating (CDR) (25) scale, the Mini-Mental State Examination (MMSE) (26), the Blessed Cognitive Scale I.M.C. (27), the "Rome Depression Inventory" (RDI) (a self-rating scale, validated on the Italian population, in which subjects evaluate 20 symptoms related to depression on a scale from 1 through 4) (28) and the State-Trait Anxiety Inventory (STAI-form X-1 and X-2) (29).

The diagnosis of dementia was made by two senior staff neurologists according to DSM-III-R criteria (30) and was determined separately from the neuropsychological battery we used.

In order to allow for inclusion of mildly impaired patients, admission criteria were set arbitrarily to a CDR score between 0.5 and 1 and a MMSE score equal or higher than 19/30.

The diagnosis of probable DAT was carried out according to the NINCDS-ADRDA criteria (24). All DAT patients presented with progressive cognitive impairments, had a history of mental decline of less than four years' duration, and achieved a score of 4 or less on the Hachinski Ischemic Scale (31). To further reduce the possibility of concurrent cerebrovascular disease, only DAT patients with no focal brain abnormalities on MRI were included.

The diagnosis of MID was carried out according to the DSM-III-R criteria (30) for this condition. All patients had a history of ischemic events occurred between 6 months and 4 years prior inclusion, and a score > 7 on the Hachinski Ischemic Scale.

Given the spectrum of neuropathologic aspects contributing to MID, only the patients with multiple cerebrovascular lesions on MRI study were included.

Thus, the MID group consisted of patients with either multi-lacunar state (more than 1 lesion with maximum diameter not exceeding 1.5 cm) or multi-

infarct state (more than 1 lesion with maximum diameter exceeding 1.5 cm) (32). In particular, 9 patients had multi-lacunar subcortical infarcts, 4 patients had multi-lacunar subcortical infarcts and a single cortical and/or subcortical infarct, and 3 patients had multiple cortical and/or subcortical infarcts.

Neuropsychological assessment

A 3-h neuropsychological evaluation was administered on three separate sessions. The neuropsychological test battery was selected to extensively assess executive/conceptual functions and memory as well as a broad spectrum of cognitive functions such as attention, psychomotor speed, verbal ability, and visuospatial skills.

The tests consisted mostly of widely used and standardized verbal and non-verbal procedures (33, 34) (Appendix 1).

General ability was assessed by the Information and Vocabulary Subtests of the Wechsler Adult Intelligence Scale (WAIS) (35).

Executive and conceptual functions were assessed by the Stroop Color Interference Test (36), Raven's Coloured Progressive Matrices (RCPM) (37) and the Wisconsin Card Sorting Test (WCST) (38), computing number of categories achieved and perseverative errors.

Verbal memory was examined by the Paired-Associate Learning of the Wechsler Memory Scale (WMS) (39), the Babcock Story Recall Test (40), the California Verbal Learning Test (41). Nonverbal memory measures included the Corsi Test (42), the Visual Reproduction of the WMS (39), and the 7/24 Spatial Recall Test (43).

Assessment of attention and psychomotor speed consisted of the serial 7's task (26), the Digit Span subtest of the WAIS (forward and backward) (35), the Trail Making Test (TMT) part A (44), and the Digit Symbol subtest of the WAIS (35). A modified version of the Paced Auditory Serial Addition Test (PASAT) (45) was also administered.

With regard to verbal ability, auditory verbal comprehension was assessed by the VI part of the "Short Version" of the Token Test (13-items) (46); visual-confrontation naming was examined by a 30-item version of the Boston Naming Test (BNT) (47); phonemic and semantic verbal fluency was tested by the Controlled Oral Word Association Test (COWAT) (48) and by the Animal Naming test (33).

Visuospatial and constructive abilities were measured by the Block Design Subtest of the WAIS (35), the Rey-Osterrieth Complex Figure Copy (49), and a 15-items shortened version of the Hooper Visual Organization Test (50).

Statistical methods

To compare the results in the two patient groups and the normal controls one-way analyses of variance (ANOVAs) with post-hoc two-tailed unpaired t-tests were used. Statistical significance was defined as a P-value of 0.05 or less.

Results

In comparison with control subjects, patients with DAT and MID had significant deficits on the MMSE (DAT = 22.9 ± 2.3, MID = 23.5 ± 2.4) and on the Blessed-I.M.C. (DAT = 25.6 ± 4.9, MID = 27.5 ± 2.6) but they did not differ compared to each other (Table 1).

According to these as well as to the mean scores on measures of general ability such as the WAIS Information subtest (DAT = 13.1 ± 6.3, MID = 16.1 ± 4.8) and the WAIS Vocabulary subtest (DAT = 37.8 ± 17.4, MID = 35.3 ± 18.3), the extent of mental impairment was similar in the two groups of patients.

As evidenced by the mean scores on RDI and on both STAI X-1 and STAI X-2, there was no difference among the three groups relative to either depressive or anxiety symptoms (Table 1).

Table 2 presents the mean test scores of the two patients groups and controls. One-way ANOVAs revealed highly significant group effects for all tests ($P < 0.005$ to < 0.0001, see Table 2 for F values).

Post-hoc comparisons showed that both patient groups were significantly impaired relative to controls on all tests ($P < 0.04$ to < 0.0001), with the exception of the number of intrusions on the CVLT which did not differ between controls and MID.

No differences of performance between DAT and MID patients were found on measures of attention, executive functions, visuospatial and constructive skills.

With regard to language-related tasks, MID patients were significantly more impaired than DAT patients on the COWAT ($P < 0.02$), whereas the extent of the impairment on the Token Test ($P < 0.04$) was more severe for DAT patients than for MID patients.

The performance on tasks tapping conceptual functions was similar between the two patient groups with regard to total correct responses on the RCPM and to total categories achieved on the WCST, but MID showed a significant higher number of perseverative errors on WCST compared to DAT patients ($P < 0.05$).

With regard to memory and learning, impairment tended to be more generalized and of greater severity in patients with DAT on all tasks. Post-hoc comparisons showed that DAT patients were signifi-

Table 2. Neuropsychological performance of normal controls, DAT and MID patients

Variable	Normal controls (n=30)	DAT cases (n=16)	MID cases (n=16)	F value df 2,59	P
Attention and executive functions					
Serial Seven's	4.6 (0.6)	1.7 (1.5)*	2.8 (1.8)*	28.2	<0.0001
Stroop Word (n° word/45 sec)	38.7 (11.1)	14.5 (13.3)*	16.6 (9.2)*	28.7	<0.0001
Trail Making Test part A	45.1 (13.6)	173.4 (145.4)*	128.3 (82.4)*	13.4	<0.0001
Digit Symbol	45.6 (12.4)	15.8 (8.4)*	15.7 (5.3)*	59.6	<0.0001
PASAT (mdf)	53.9 (9.7)	15.1 (15.3)*	24.2 (11.6)*	45.9	<0.0001
Digit Span Forward	6.1 (1.0)	4.6 (1.1)*	4.6 (0.9)*	17.1	<0.0001
Digit Span Backward	4.3 (1.2)	3.1 (1.1)*	2.9 (0.9)*	11.6	<0.0001
Language					
Boston Naming Test (30-items)	29.7 (13.3)	19.5 (5.6)*	22.1 (4.2)*	5.9	<0.005
Token Test VI-Part	11.6 (1.2)	7.4 (2.6)*	9.3 (2.2)*#	24.9	<0.0001
COWAT	33.1 (9.7)	23.2 (9.9)*	15.6 (7.6)*#	19.6	<0.0001
Animal Naming	17.8 (4.9)	11.1 (4.1)*	10.6 (2.4)*	20.6	<0.0001
Visuo-spatial skills					
Rey Complex Figure Test	33.7 (2.7)	21.8 (24.8)*	20.7 (10.3)*	6.4	<0.005
Block Design WAIS	30.1 (15.7)	9.8 (8.8)*	14.9 (8.3)*	13.4	<0.0001
Hooper Test (15-items)	11.3 (2.6)	5.6 (5.6)*	5.4 (2.4)*	19.4	<0.0001
Cognition					
WCST (n° categories)	2.5 (0.9)	0.5 (0.9)*	0.9 (0.9)*	27.4	<0.0001
WCST (n° perseverative errors)	5.3 (5.2)	14.5 (7.4)*	22.2 (10.4)*#	21.1	<0.0001
Raven's CPM	31.8 (3.5)	17.1 (7.2)*	19.5 (5.3)*	50.5	<0.0001
Memory					
Corsi Cube Test	5 (1.1)	2.8 (1.3)*	4.1 (0.7)*#	18.2	<0.0001
WMS Visual Reproduction (Imm)	11.3 (3.0)	4.3 (2.2)*	5.8 (3.4)*	29.3	<0.0001
WMS Visual Reproduction (Del)	11.8 (4.1)	2.5 (2.9)*	4.4 (4.1)*	33.1	<0.0001
7/24 Spatial Recall Test	27.7 (4.4)	14.6 (4.2)*	19.3 (4.7)*#	41.1	<0.0001
WMS Paired-Associate Learning	14.1 (3.5)	7.9 (3.2)*	9.1 (3.6)*	19.1	<0.0001
Babcock Story Recall (Imm)	4.8 (1.3)	2.3 (1.9)*	3.4 (2.1)*	11.0	<0.0001
Babcock Story Recall (Del)	6.9 (1.2)	2.4 (2.5)*	4.5 (1.4)*#	33.9	<0.0001
CVLT (total recall)	53.2 (9.7)	23 (6.8)*	29.6 (6.8)*#	72.8	<0.0001
CVLT (delayed recall)	11.4 (3.2)	2.3 (2.6)*	4.2 (2.5)*#	55.6	<0.0001
CVLT (n° intrusions)	2.7 (3.8)	11.1 (8.1)*	5.7 (4.2)#	11.4	<0.005

Data are expressed as mean (SD);
* Significant difference ($P<0.05$) between patient groups and controls.
# Significant difference ($P<0.05$) between DAT and VD patient groups.
PASAT = Paced Auditory Serial Addition Test, COWAT = Controlled Oral Word Association Test, WCST = Wisconsin Card Sorting Test, CVLT = California Verbal Learning Test.

cantly more impaired than MID patients on both verbal and non-verbal memory tasks such as Corsi Cube Test ($P<0.004$), 7/24 Spatial Recall Test ($P<0.01$), Babcock Story Recall Test-Delayed ($P<0.01$), CVLT-Total Recall and CVLT-Delayed Recall ($P<0.01$).

Discussion

The primary finding of this investigation indicates that clinically matched DAT and MID patients show a differential pattern of cognitive impairment, when studied in an early phase of the disease and with a mild degree of severity.

Although both groups were significantly impaired on all tasks compared to controls, and equally impaired on tasks measuring attention, executive functions and visuospatial skills, DAT patients showed relatively greater impairment on tasks assessing verbal comprehension as well as verbal and nonverbal memory, compared with MID patients.

On the other hand, patients with MID showed significantly greater impairment compared with DAT patients on the COWAT, and displayed a higher number of perseverative errors on the Wisconsin Card Sorting Test, indicating a greater vulnerability to tasks assessing frontal lobe functioning (51, 52).

Previous studies have attempted with contradictory results to characterize the neuropsychological

deficits in MID and/or to distinguish MID from DAT.

Several investigators failed to find any significant difference in the pattern of neuropsychological impairments between MID and DAT patients (7–12, 53), but a lower performance of MID patients on measures of motor function and manual dexterity (18, 19).

In contrast to these studies, Gainotti et al. (16) reported distinctive patterns of impairment in different etiological forms of dementia such as DAT, Huntington disease (HD), Parkinson disease (PD), and MID. In particular, DAT patients performed significantly worse on most verbal and non-verbal tasks compared to the other groups.

In a more recent study, Gainotti et al. (54) reported a higher frequency in DAT patients compared with MID patients of additional selective qualitative features such as "closing-in" on drawing copy tasks and "globalistic" responses in Raven's Coloured Progressive Matrices.

Other investigators have tried to study systematically the neuropsychological profiles of DAT and MID, by using well-defined criteria for dementia, and equating groups for severity. Parlato et al. (17) reported a difference in verbal recall between DAT and MID patients with repeated administrations of verbal material: DAT patients showed a poorer secondary memory. These findings have been replicated by Barr et al. (15) who found DAT patients to be significantly more impaired on measures of learning and naming.

Our results are partially consistent with previous reports showing that DAT and MID patients are not clearly distinguishable on a wide array of measures of cognitive functions. At variance with some studies (18, 19), we did not observe a greater impairment for MID patients on tasks measuring sensory-motor speed. These negative findings might be due to the selection of less sensitive and/or multi-factorial procedures (Trail-Making Test and the Digit Symbol Test).

In agreement with previous reports (14–17, 20), we found that DAT patients showed a greater impairment on most measures of memory. In fact, except for the Paired-Associate Learning Test and the Visual Reproduction Tests of the WMS on which the differences in performance between DAT and MID patients did not reach significance because of floor effect, DAT patients performed significantly lower than MID patients on verbal and non-verbal memory tasks such as the Corsi Test, the 7/24 Spatial Recall Test, the Babcock Story Recall Test, and the California Verbal Learning Test.

On the other hand, we found that MID patients were more severely affected than DAT patients on tests sensitive to frontal lobe impairment as they showed a lower performance on the phonemic generation task (COWAT) and a higher number of perseverative errors on the WCST.

These data extend the recent study of Villardita (20), which showed some similarities and differences between DAT and MID patients matched for age, sex, education and degree of functional disability over various stages of severity from mild to severe. That is, although visual memory, constructional praxis, problem-solving abilities were equally affected in both groups, verbal memory and naming were more severely impaired in DAT patients, while patients with MID had significantly greater impairment in attentional processes, self-regulation and executive behavioral programming.

The present study demonstrates that subtle cognitive difference due to different ethiologies such as DAT and MID are identifiable at least in the early stages when the degree of dementia is mild and mental impairments are not pervasive yet.

The neuropsychological features of our patients with MID appears strongly related with signs of frontal lobe dysfunction resembling the so-called "subcortical" dementia syndromes (55–57). In fact, there is evidence that patients with "subcortical dementia" tend to be mildly impaired on memory tasks, particularly if episodic, while showing a profound disruption on tasks assessing conceptual functions, reasoning, and executive functions (58–60).

As far as our data are concerned, the pattern of neuropsychological abnormalities found in mild DAT and MID patients extends previous studies on cerebrovascular patients suffering Binswanger's disease as well as on patients with dementia due to either multi-lacunar state or white matter changes (21–23, 61–64) and supports a differential extent of impairment in the domains of memory, language, and frontal lobe functioning, as expected according to the cortical-subcortical model (55, 57, 65).

Further, this study confirms the assumption that a "subcortical" syndrome is likely in the presence of "multifocal partial lesions" which collectively disrupt the integration by the frontal lobes of networks for complex behavior (66).

These data are also in accord with recent metabolic findings on DAT and MID patients. Differences between DAT and MID patients exist in the extent of metabolic impairment in subcortical structures. DAT is associated with a greater cortical hypometabolism particularly at the level of the temporoparietal cortical regions whereas subcortical areas and sensory-motor cortices are more affected in patients with MID (67).

A different involvement of the frontal lobes in DAT and MID has also been evidenced by PET studies. In particular, it has been showed that while MID patients show a multifocal pattern of cortical

hypometabolism which usually includes the frontal lobes also in an early phase, DAT patients show a quite typical pattern of metabolic decrease in the temporo-parietal regions that extends to the frontal areas only in a late phase (68, 69). Finally, severely MID and DAT patients display similar widespread metabolic changes involving frontal and temporoparietal association cortices (69).

These observations are consistent with our clinical data and suggest that DAT and MID can be distinguished from each other when investigated in the early phase whereas in more advanced stages of the diseases differences might be minimal leading to less clear-cut distinction due to widespread neuropathological involvement.

Besides the theoretical implications, the evidence of a differential pattern of cognitive impairment in DAT and MID has major practical importance as it might encourage to develop more rationale screening tools based on the assessment of conceptual and memory abilities, and to define more precise clinical criteria for both differentiating DAT and MID, and evaluating the efficacy of pharmacological interventions.

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Appendix

The neuropsychological test battery consisted mostly of widely used and standardized verbal and nonverbal procedures. In order to assess a wide range of cognitive functions within a 3-h evaluation (administered on three separate sessions of one hour each), some of the tests have been shortened. A full description of these tests is presented below.

General ability

WAIS-information subtest (35) – This test measures general ability and verbal skills. It consists of 29

questions arranged in order of difficulty which test general knowledge normally available to people. Performance is measured according to provided scoring criteria and presented as raw scores ranging from 0 through 29.

WAIS-Vocabulary Subtest (35) – This test measures both verbal and general mental ability. It consists of forty words arranged in order of difficulty to which subjects are required to give a definition or to describe the meaning. Performance is measured according to provided scoring criteria and presented as raw scores ranging from 0 through 80.

Attention and executive functions

Stroop Interference Test (36) – This test examines reading fluency, executive functions, and mental shifting skills. The material for this test consists of three white cards, each containing ten rows of ten items. Randomized color names (blue, green, red) are in black print on card A; card B is identical except each color name is printed in some color other than the color it names; card C displays colored dots in the same array of three colors. There are four trials, each consisting of a different task; on trial 1, the subject reads card A; on trial 2 he reads card B ignoring the color of the print; for trail 3 he names the colors on card C; on trial 4 he names the colors of the print on card B. For this study, only performance data on trial 4 have been presented. Scoring is expressed in terms of total words correctly read within 45 seconds on trial 4.

Trail Making Test (part A) (44) – This test assesses speed for visual search, attention, and motor function. It requires the connection, by making pencil lines, between 25 encircled numbers randomly arranged on a page in proper order. Scoring is expressed in terms of the time required for completion.

WAIS-Digit Symbol Subtest (35) – This is a test of psychomotor performance, sustained attention, response speed, and visuo-motor coordination. It consists of four rows containing in all 100 small blank squares, each paired with a randomly assigned number from 1 to 9. The subject's task is to fill in the blank spaces with a symbol that is paired to the number above the blank spaces as quickly as he can. Scoring is expressed in terms of the total number of squares filled in correctly within 90 s.

Modified Paced Auditory Serial Addition Test (PASAT) (45) – This is a mental tracking task developed to assess sustained attention. Subjects are instructed to listen to a series of 61 consecutive randomized digits (from 1 through 9), auditorily presented every 1.2 s by a tape-recorder. The task requires subjects to sequentially recall, while listening each single digit, the item immediately preceding the last auditorily presented number (for example, given the series 2-5-7-6-3..., the subject would recall the number 2 immediately after the presentation of digit 5, which will be recalled after the presentation of digit 7, and so on). Scoring is expressed in terms of correct responses (range 0–60).

WAIS-Digit Span Subtest (35) – This subtest comprises two different tasks such as the digit forward and the digit backward and assesses attention and working memory. Both tests consist of seven pairs of random number sequences that the examiner reads aloud; in the digit forward condition the subject's task is to repeat each sequence exactly as it is given, while in the digit backward condition the task is to repeated each sequence in an exactly reversed order. Scoring is expressed as raw scores and reflects the longest correctly reported sequence of digits.

Language

Boston Naming Test (shortened version) (47) – This is a test for the assessment of the ability to name pictured objects. In its original form, it consists of 60 line drawings, ranging from simple, high frequency to rare words presented one at a time on cards. In this study, a shortened version has been developed, consisting of 30 items, randomly selected throughout the original series. Scoring is expressed in terms of total correct responses (range 0–30).

Token Test (shortened version) (46) – This is a test for the assessment of verbal comprehension and symbolic processing. The sixth section of the original "Short Version" has been utilized which consists of thirteen items. Ten tokens differing in form (circle and square) and in colour (black, white, yellow, red, and green) laid out horizontally in two parallel rows make up the test material.

The test consists of a series of oral commands to execute according to the token names and the verbs and the propositions in the instruction. Scoring is expressed in terms of correct responses (range 0–13).

Controlled Oral Word Association (COWAT) (48) – This is a phonemic word generation task and measures naming ability, speed of verbal production, mental organization, strategy, and short-term memory. It consists of three one-minute word-naming trials. The task requires the subject to say as many words as he or she can think of that begin with a given letter of the alphabet. The score is the sum of all acceptable words produced in the 3 one-min trials.

Animal Naming Test (33) – This is a category word generation task and measures naming ability, speed of verbal production, and semantic organization. The task requires the subject to say as many animal exemplars as he or she can think of within a 1-min interval. The score is the sum of all acceptable words produced.

Visuospatial skills

Rey-Osterrieth Complex Figure Test (49) – This test assesses visuo-spatial constructional ability. The materials consist of blank piece of paper, colored pencils, and the Rey-Osterrieth Figure, the procedure having the subject to copy the figure. Performance is measured according to provided scoring criteria ranging from 0 through 36.

WAIS-Block Design Subtest (35) – This test measures visuo-spatial skills, perceptual organization, and problem-solving ability. It is a construction timed test in which the subject is presented with red and white blocks. The task is to use the blocks to construct replicas of two block constructions made by the examiner and eight designs printed in smaller scale. Performance is measured according to provided scoring criteria and presented as raw scores.

Hooper Visual Organization Test (shortened version) (50) – This test examines visuo-perceptual functions, mental imagery, and conceptual reorganization. In its original form, it consists of 30 pictures of more or less readily recognizable cut-up objects, requiring the subject to name each object verbally. In this study, we used a shortened version made up with 15 original pictures (randomly selected throughout the original series). Scoring is expressed in terms of total correct responses.

Cognition

Wisconsin Card Sorting Test (Shortened Version) (38) – This test assesses the ability to form abstract concepts, and shift and maintain the set. The subject is given a pack of 64 different cards (varying in color, form, and number) and is then instructed to place each response card in a pile below one of the four stimulus cards (differing for color, form, and number) trying to get as many right as possible without time limit. The subject is told each time whether the response is right or wrong according to an implicit sorting principal (colore, form, or number) which shifts after 10 consecutive correct responses. Scores adopted in the study included: number of categories (number of correct sorts) and number of perseverative errors (number of uncorrect responses defined as one that would have been correct on the immediately preceding stage of the tests, or, as a continued response in terms of the patient's initial preferences).

Raven's Coloured Progressive Matrices (37) – This is a test for the assessment of perceptual functions, visuo-spatial reasoning and abstraction skills. It consists of 36 visual pattern matching and analogy problems pictured in nonrepresentational designs. In particular, each item contains a pattern problem with one part removed and six pictured inserts of which one contains the correct pattern. The subject is required to point to the correct pattern piece. Scoring is expressed as total correct responses (range 0–36).

Memory

Corsi Cube Test (42) – This test assesses immediate nonverbal recall span. It consists of nine cubes fastened in a random order to a board. Each time the examiner taps the blocks in a prearranged sequence of increasing length and complexity; the subject is required to attempt to copy his tapping pattern. By adding one tap to each succeeding successful sequence, the examiner's ascertains the subject's span for immediate span recall, which is expressed by the longest sequence correctly imitated.

WMS-Visual Reproduction Subtest (39) – This is a recall test for designs. It consists of the presentation of three cards with printed designs which are shown for five seconds (the third card has a double design). Following each exposure (immediate recall) the subject is required to draw what he remembers of the design. After a 20-min interval (delayed recall) the subject is asked again to reproduce the designs. Performance is measured according to provided scoring criteria ranging from 0 through 14.

7/24 Spatial Recall Test (43) – This is a completely nonverbal memory task. It consists in the presentation through five learning trails, each with a 10-second exposure, of an array of seven poker chips randomly placed on a 6X4 checkerboard, and require, immediately after each exposure, the subject to reproduce the original seven chip pattern with nine chips and an empty board. Scoring is expressed in terms of total correctly placed chips from trials 1 through trial 5 (range 0–35).

WMS-Paired Associates Learning Subtest (39) – This is a verbal learning test. It consists of ten word pairs, six forming "easy" association and the other four "hard" word pairs. The list is read 3 times, with a memory trial following each presentation. Performance is measured according to provided scoring criteria ranging from 0 through 21.

Babcock Story Recall Test (40) – This test examines both immediate and delayed verbal recall. It consists of a short 21-unit story which is orally presented to the subject. Following the first presentation, the subject is required to recall the story. Immediately after the recall, there is a second presentation which is followed by a 20 minutes of delayed recall. Scoring is expressed, separately for the immediate and the delayed recall, according to a hyerarchical score system based on the relative saliency of meaningful units correctly recalled (40), ranging from 0 through 8.

California Verbal Learning Test (Italian version) (41) – This is a test that evaluate immediate memory span, new learning, vulnerability to interference, and recognition memory. It consists of 16 randomly distributed items (list A) belonging to 4 categories (tools, fruits, vegetables, clothes) read aloud (with a one-second interval between each word) for five consecutive trials, each trial followed by a free-recall test. The order of presentation remains fixed across trials. Upon completion of trail 5, an interference list of 16 new items (list B) belonging to 4 categories (clothes, fruits, foods, beverages) is presented followed by a free-recall test of that list. Immediately following this, an immediate delayed recall and a 15-minutes delayed recall of list A is tested without further presentation of those words. Finally, a cued recall and a recognition trial is required. Scoring in this study is expressed in terms of total recall from trial 1 through trial 5 (range 0–80), 15-min delayed recall (range 0–16), and total number of intrusions (recall of extra-list words).