Correlates of neuropsychiatric and motor tests with language assessment in patients with Lewy body dementia

Fernando Chiodini Machado[1]
https://orcid.org/000-0002-8116-4167

Fabricio Ferreira de Oliveira[1]
https://orcid.org/0000-0002-8311-0859

Sheilla de Medeiros Correia Marin[1]
https://orcid.org/0000-0002-0381-3221

Gustavo Sampaio[1]
https://orcid.org/0000-0002-4113-3606

Paulo Henrique Ferreira Bertolucci[1]
https://orcid.org/0000-0001-7902-7502

[1] *Department of Neurology and Neurosurgery, Paulista School of Medicine, Federal University of São Paulo (Unifesp), São Paulo, SP, Brazil.*

Received: 09/24/2019 – **Accepted:** 01/29/2020
DOI: 10.1590/0101-60830000000236

Abstract

Background: Lewy body dementia (LBD) impairs performance in daily activities and affects motor, language and visuospatial tasks. **Objective:** We aimed to correlate neuropsychiatric and motor assessments with language and visual organization tests in LBD. **Methods:** Twenty-two patients with dementia with Lewy bodies and ten patients with Parkinson's disease dementia participated on a cross-sectional study that assessed cognition, functionality, caregiver burden, verbal fluency, the primer-level dictation section of the Boston Diagnostic Aphasia Examination (PLD-BDAE), the Hooper Visual Organization Test, the Neuropsychiatric Inventory and the Movement Disorder Society – Unified Parkinson's Disease Rating Scale. **Results:** Language and visuospatial test results followed motor impairment and general cognitive performance. Whereas visual organization did not predict performance in the PLD-BDAE, visuospatial abilities and verbal fluency were concurrently associated, suggesting that linguistic impairment in LBD may be attributed to neuropsychological components of cognition and language. Only visual organization was associated with behaviour, suggesting that neuropsychiatric symptoms associate with differential impairment of visual organization in comparison with language in LBD. Schooling did not affect visual organization or language test performance, while the length of dementia was negatively associated with visual organization and verbal fluency. **Discussion:** Though visual organization tests follow behaviour and motor performance in LBD, there is differential impairment regarding language skills.

Machado FC et al. / Arch Clin Psychiatry. 2020;47(3):75-81

Keywords: Lewy body dementia, language, spatial processing, neuropsychiatry, neuropsychological tests.

Introduction

Deficits in visuospatial abilities, memory, executive functions and language are the most evident neuropsychological symptoms in patients with Lewy body dementia (LBD) syndromes, corresponding to frontal-striatal dopaminergic dysmodulation associated with diffuse cholinergic cortical dysfunction[1]. Essentially, the spectrum of these syndromes consists of dementia with Lewy bodies and Parkinson's disease dementia[2], comprising the second leading cause of degenerative dementia in older people after Alzheimer's dementia (AD)[3,4]. Nevertheless, sensitivity of clinical diagnosis of LBD is not always good, particularly in severe dementia, although specificity tends to be high[5].

The main etiological hypothesis for LBD entails the histopathological presence of Lewy bodies in the brainstem, subcortical nuclei, limbic cortex (cingulate cortex and amygdala), and in the neocortex[6,7]. In Parkinson's disease dementia, Lewy body formation and neuron loss usually start in brainstem nuclei and in the substantia nigra, whereas in dementia with Lewy bodies they occur in paralimbic and neocortical structures from disease onset[8]. In addition, amyloid pathology helps predict the onset of dementia in parkinsonian syndromes[9]. Nevertheless, cholinergic denervation is the main source of linguistic impairments in patients with LBD, particularly when involving cortical or subcortical language networks[10].

Approximately 80% of all patients with Parkinson's disease develop dementia, more frequently when they are male and have more severe motor signs at examination[11]. The burden of motor and neuropsychiatric manifestations of LBD considerably affects functional independence and social activities, impacting quality of life[2,8]. Visuospatial skills and behavioural symptoms are helpful for differential diagnosis between LBD and AD, whereas cerebrovascular risk might be more important for pathogenesis of AD[8,12], but cholinesterase inhibitors are usually valuable for treatment of neuropsychiatric symptoms of both AD and LBD[13,14].

Despite the fact that some associations are well established for dementia syndromes, such as functional decline following cognitive decline in severe dementia[15], impairment of language has not been deeply studied in LBD. We hypothesized that language domains could be primarily affected in LBD, whereas motor signs, behavioural symptoms, linguistic and cognitive features would be concurrently impaired; therefore, we aimed to analyse associations of neuropsychiatric and motor assessments with language and visual organization test results in patients with LBD.

Methods

Participants

In this cross-sectional study, consecutive outpatients with LBD in different levels of clinical evolution were recruited from the Department of Neurology and Neurosurgery at *Hospital São Paulo*, Federal University of São Paulo (Unifesp). All patients with LBD who were followed at the outpatient clinic were assessed from January 2014 to April 2015. Diagnosis of Parkinson's disease followed traditional

Address for correspondence: Fabricio Ferreira de Oliveira. Universidade Federal de São Paulo (Unifesp), Escola Paulista de Medicina, Departamento de Neurologia e Neurocirurgia. Rua Botucatu, 740, Vila Clementino – 04023-900 – São Paulo, SP, Brazil. Telephone: +55 (+11) 5576-4139. Fax: +55 (+11) 5575-5240. E-mail: fabricioferreiradeoliveira@hotmail.com

clinical criteria[16]. Patients had to be diagnosed with either probable or possible Parkinson's disease dementia according to Movement Disorder Society Task Force clinical diagnostic criteria[17], or either probable or possible dementia with Lewy bodies[18]. Basically, Parkinson's disease dementia developed within the context of established Parkinson's disease, requiring a combination of typical cognitive and behavioural features for diagnosis, while dementia with Lewy bodies preceded motor manifestations by at least one year, with a combination of core features (fluctuating cognition with varied attention or alertness, recurrent well-formed visual hallucinations, or spontaneous features of parkinsonism) and suggestive features (REM sleep behaviour disorder, severe neuroleptic sensitivity, low dopamine transporter uptake in basal nuclei). None of the patients had neuroimaging evidence of focal cerebrovascular diseases or any other structural brain diseases that could account for the cognitive or language deficits.

Clinical assessment

After diagnostic confirmation, patients and caregivers were assessed for: patient age, gender, schooling, estimated age at dementia onset, sleep satisfaction and estimated daily length of sleep[19], use of any medications, and scores on the Neuropsychiatric Inventory[20], the Mini-Mental State Examination[21], the Clinical Dementia Rating sum-of-boxes[22], a 15-item clock drawing test (free drawing)[23], the Schwab & England scale[24], Lawton's Scale for Instrumental Activities of Daily Living[25], the Brazilian Version of the Zarit Caregiver Burden Interview[26], forward digit span and reverse digit span, the Movement Disorder Society – Unified Parkinson's Disease Rating Scale[27], and the Hoehn & Yahr stages in the off state[28].

In a second evaluation, patients with LBD were also assessed with the Hooper Visual Organization Test (HVOT)[29], verbal fluency (VF)[30], and the primer-level dictation section of the Boston Diagnostic Aphasia Examination (PLD-BDAE)[31,32], including primer words, regular phonics, and common irregular words. All cognitive assessments were conducted on weekdays at morning time, by two examiners (FCM and FFO).

The Schwab & England scale[24] was employed for overall performance in activities of daily living. A trichotomous version (1 = unable; 2 = able with help; 3 = able without help) of Lawton's Scale for Instrumental Activities of Daily Living[25] was employed, with scores for using the telephone, getting to places beyond walking distance, grocery shopping, meal preparation, housekeeping, doing handyman work, doing laundry, taking own medications, and handling finances; caregivers provided all information, with a total score of 9 to 27.

For the HVOT, each participant was presented with 30 figures of fragmented objects in ascending order of difficulty[29]. For the VF tasks, the patient should generate the largest possible number of words in one minute for each category, including words beginning with F, A and S (F-A-S), as well as all animals, fruits and grocery items that might be known[33]. In the PLD-BDAE, the patient writes regular and irregular words to dictation[31].

Statistical analyses

Fisher's exact test and the Mann-Whitney test were used for comparisons of neurological features between dementia syndromes. Simple linear regressions were employed for comparisons between test results. A multiple linear regression model was employed for associations between each visual organization or language test (HVOT, VF, and the PLD-BDAE) and the following independent variables: schooling and length of the dementia syndrome; p-values were corrected with the Bonferroni test. The threshold of significance was set at $p < 0.05$.

Ethical aspects

This study is part of the research project 064990/2013 approved by the Ethics Committee of *Hospital São Paulo*, Unifesp, in October 2013. All invited patients and their legal representatives agreed to participate on the research and signed the Informed Consent Form before the evaluation.

Results

Overall, 39 participants were recruited; between the first and the second assessments, three patients passed away (7.7%), and four patients did not complete the second evaluation (10.3%), resulting in a final sample of 32 patients – 19 women (59.4%) and 13 men (40.6%). Twenty-one patients were diagnosed with probable dementia with Lewy bodies, one patient was diagnosed with possible dementia with Lewy bodies, nine patients were diagnosed with probable Parkinson's disease dementia, and one patient was diagnosed with possible Parkinson's disease dementia. Nineteen patients with dementia with Lewy bodies (86.4%) had visual hallucinations, versus six patients with Parkinson's disease dementia (60.0%), $p = 0.165$. Sixteen patients with dementia with Lewy bodies (72.7%) had parkinsonism, versus ten patients with Parkinson's disease dementia (100.0%), $p = 0.142$. Moreover, fifteen patients with dementia with Lewy bodies had fluctuations (68.2%). Demographic data and test results for all patients with LBD are summarized in Table 1.

There was no statistically significant difference between patients with dementia with Lewy bodies and patients with Parkinson's disease

Table 1. Demographic data and test results

Variables, *n* = 32	Mean or *n* (%)	SD	Range
Age at examination (years-old)	75.84	9.1	54-89
Age at dementia onset (years-old)	71.14	9.8	50-87
Length of the dementia syndrome (years)	4.81	3.4	1-12
Schooling (years)	3.59	3.4	0-12
Sleep Satisfaction	23 (71.9%)	-	
Hours of Sleep	8.25	2.3	-4-13
Daily amount of different medications	5.03	2.6	0-13
Daily amount of pills/injections	7.42	5.4	0-25.5
Clinical Dementia Rating sum-of-boxes (0.0-18.0 points)	10.63	4.1	4.0-18.0
Neuropsychiatric Inventory (0-144 points)	41.25	19.5	7-84
Mini-Mental State Examination (0-30 points)	17.72	5.7	7-27
Clock Drawing Test (0-15 points)	5.16	4.1	0-15
Schwab & England scale (0%-100%)	56.56%	25.6%	10%-90%
Lawton's Scale for Instrumental Activities of Daily Living (9-27 points)	13.41	4.4	9-22
Brazilian Version of the Zarit Caregiver Burden Interview (0-56 points)	20.00	8.4	3-35
Forward Digit Span	4.72	1.3	3-8
Reverse Digit Span	2.25	0.7	1-3
MDS-UPDRS – Part I	19.53	5.5	6-30
MDS-UPDRS – Part II	17.97	11.9	0-42
MDS-UPDRS – Part III	33.38	26.5	1-99
MDS-UPDRS – Part IV	3.47	5.0	0-17
Hoehn & Yahr stage – OFF state (0-5)	2.88	1.6	0-5
Hooper Visual Organization Test	6.97	3.4	0-15
Verbal Fluency (F-A-S)	6.44	5.7	0-24
Verbal Fluency (animals)	6.78	4.1	0-18
Verbal Fluency (fruits)	5.59	2.4	0-10
Verbal Fluency (grocery items)	6.31	3.7	0-15
PLD-BDAE	5.06	5.6	0-16

SD: standard deviation; MDS-UPDRS: Movement Disorder Society – Unified Parkinson's Disease Rating Scale; PLD-BDAE: primer-level dictation section of the Boston Diagnostic Aphasia Examination.

dementia regarding age (p = 0.291), gender (p = 0.999), schooling (p = 0.597), age at dementia onset (0.626), estimated length of sleep (p = 0.143), use of different medications (p = 0.067), or scores on the Neuropsychiatric Inventory (p = 0.655), the Mini-Mental State Examination (p = 0.382), the Clinical Dementia Rating sum-of-boxes (p = 0.291), the clock drawing test (p = 0.092), the Brazilian Version of the Zarit Caregiver Burden Interview (p = 0.871), forward digit span (p = 0.291), reverse digit span (p = 0.371), the HVOT (p = 0.855) or VF (p = 0.999), but patients with dementia with Lewy bodies were more satisfied with their sleep (p = 0.013).

Table 2 summarizes the results from simple linear regressions between visual organization and language test results for all patients with LBD. Visual organization was associated with category VF, whereas all language tests were correlated with each other, except for the association between VF (animals) and the PLD-BDAE.

Tables 3 and 4 list results from simple linear regressions regarding visual organization and language tests for predictions of associations with other neuropsychiatric features. Visual organization was associated with basic (but not instrumental) functionality, general cognitive tests, motor examination and the Neuropsychiatric Inventory total scores. All categories of VF were associated with general cognitive tests, and inversely associated with global dementia rating; however, only VF for F-A-S and for fruits was associated with the clock drawing test, only VF for F-A-S and for grocery items was associated with non-motor experiences of daily living, and only VF for fruits was associated with motor experiences of daily living and motor examination. All categories of VF were associated with forward digit span, except for fruits, the only category associated with reverse digit span. Sleep satisfaction was negatively associated with all categories of VF, except for fruits. The PLD-BDAE was associated with basic (but not instrumental) functionality, general cognitive tests, motor experiences of daily living and motor examination. Length of sleep, instrumental functionality, and caregiver distress regarding behavioural symptoms had no significant associations with visual organization or language tests.

Table 5 lists results from multiple linear regressions involving language and visual organization tests. Schooling did not affect performance in any test, while the length of the dementia syndrome was negatively associated with performance in the HVOT and VF (animals).

Table 2. Results from simple linear regressions for predictions between visual organization and language test results

Variable 1	Variable 2	Squared multiple R	*t*	F-ratio	p-value
HVOT	VF (F-A-S)	0.118	2.003	4.013	0.051
HVOT	VF (animals)	0.219	2.902	8.424	**0.007**
HVOT	VF (fruits)	0.366	4.160	17.307	**<0.001**
HVOT	VF (grocery items)	0.246	3.125	9.768	**0.004**
HVOT	PLD-BDAE	0.096	1.790	3.203	0.080
VF (F-A-S)	VF (animals)	0.453	4.983	24.826	**<0.001**
VF (F-A-S)	VF (fruits)	0.171	2.485	6.177	**0.018**
VF (F-A-S)	VF (grocery items)	0.445	4.909	24.096	**<0.001**
VF (F-A-S)	PLD-BDAE	0.213	2.851	8.126	**0.008**
VF (animals)	VF (fruits)	0.268	3.313	10.975	**0.003**
VF (animals)	VF (grocery items)	0.586	6.516	42.465	**<0.001**
VF (animals)	PLD-BDAE	0.045	1.185	1.404	0.244
VF (fruits)	VF (grocery items)	0.470	5.161	26.640	**<0.001**
VF (fruits)	PLD-BDAE	0.134	2.156	4.647	**0.037**
VF (grocery items)	PLD-BDAE	0.151	2.306	5.319	**0.027**

HVOT: Hooper Visual Organization Test; VF: verbal fluency; PLD-BDAE: primer-level dictation section of the Boston Diagnostic Aphasia Examination.

Table 3. Results from simple linear regressions for predictions between test results (with reference to visual organization and language functions)

Variable 1	Variable 2	Squared multiple R	*t*	F-ratio	p-value
HVOT	Clinical Dementia Rating sum-of-boxes	0.272	-3.352	11.234	**0.002**
HVOT	15-item Clock Drawing Test	0.217	2.880	8.293	**0.007**
HVOT	Forward Digit Span	0.046	1.208	1.459	0.235
HVOT	Reverse Digit Span	0.025	0.870	0.758	0.605
HVOT	Lawton's Scale for Instrumental Activities of Daily Living	0.079	1.604	2.573	0.116
HVOT	Schwab & England scale	0.212	2.839	8.058	**0.008**
HVOT	Mini-Mental State Examination	0.239	3.071	9.433	**0.005**
HVOT	MDS-UPDRS – Part I	0.015	-0.679	0.461	0.509
HVOT	MDS-UPDRS – Part II	0.092	-1.745	3.046	0.088
HVOT	MDS-UPDRS – Part III	0.136	-2.169	4.707	**0.036**
HVOT	Hoehn & Yahr stage – OFF	0.139	-2.198	4.833	**0.034**
VF (F-A-S)	Clinical Dementia Rating sum-of-boxes	0.239	-3.072	9.437	**0.005**
VF (F-A-S)	15-item Clock Drawing Test	0.164	2.429	5.900	**0.020**
VF (F-A-S)	Forward Digit Span	0.314	3.703	13.715	**0.001**
VF (F-A-S)	Reverse Digit Span	<0.001	0.116	0.013	0.904
VF (F-A-S)	Lawton's Scale for Instrumental Activities of Daily Living	0.057	1.351	1.826	0.184
VF (F-A-S)	Schwab & England scale	0.043	1.156	1.336	0.256
VF (F-A-S)	Mini-Mental State Examination	0.313	3.889	15.128	**<0.001**

Variable 1	Variable 2	Squared multiple R	*t*	F-ratio	p-value
VF (F-A-S)	MDS-UPDRS – Part I	0.235	-3.039	9.236	**0.005**
VF (F-A-S)	MDS-UPDRS – Part II	0.030	-0.961	0.923	0.654
VF (F-A-S)	MDS-UPDRS – Part III	0.056	-1.332	1.775	0.190
VF (F-A-S)	Hoehn & Yahr stage – OFF	0.003	0.325	0.106	0.746
VF (ANIMALS)	Clinical Dementia Rating sum-of-boxes	0.208	-2.811	7.901	**0.008**
VF (ANIMALS)	15-item Clock Drawing Test	0.019	0.773	0.598	0.549
VF (ANIMALS)	Forward Digit Span	0.274	3.366	11.329	**0.002**
VF (ANIMALS)	Reverse Digit Span	0.005	-0.398	0.158	0.696
VF (ANIMALS)	Lawton's Scale for Instrumental Activities of Daily Living	0.054	1.310	1.715	0.198
VF (ANIMALS)	Schwab & England scale	0.081	1.627	2.648	0.110
VF (ANIMALS)	Mini-Mental State Examination	0.192	2.670	7.127	**0.012**
VF (ANIMALS)	MDS-UPDRS – Part I	0.077	-1.587	2.517	0.119
VF (ANIMALS)	MDS-UPDRS – Part II	0.017	-0.723	0.523	0.518
VF (ANIMALS)	MDS-UPDRS – Part III	0.056	-1.334	1.780	0.189
VF (ANIMALS)	Hoehn & Yahr stage – OFF	<0.001	-0.081	0.007	0.934
VF (FRUITS)	Clinical Dementia Rating sum-of-boxes	0.222	-2.929	8.580	**0.006**
VF (FRUITS)	15-item Clock Drawing Test	0.154	2.338	5.468	**0.025**
VF (FRUITS)	Forward Digit Span	0.070	1.498	2.244	0.141
VF (FRUITS)	Reverse Digit Span	0.184	2.597	6.745	**0.014**
VF (FRUITS)	Lawton's Scale for Instrumental Activities of Daily Living	0.108	1.905	3.629	0.063
VF (FRUITS)	Schwab & England scale	0.205	2.780	7.729	**0.009**
VF (FRUITS)	Mini-Mental State Examination	0.231	3.006	9.037	**0.005**
VF (FRUITS)	MDS-UPDRS – Part I	0.038	-1.083	1.173	0.287
VF (FRUITS)	MDS-UPDRS – Part II	0.128	-2.096	4.392	**0.042**
VF (FRUITS)	MDS-UPDRS – Part III	0.187	-2.626	6.899	**0.013**
VF (FRUITS)	Hoehn & Yahr stage – OFF	0.075	-1.562	2.439	0.125
VF (GROCERY ITEMS)	Clinical Dementia Rating sum-of-boxes	0.311	-3.680	13.546	**0.001**
VF (GROCERY ITEMS)	15-item Clock Drawing Test	0.095	1.780	3.168	0.082
VF (GROCERY ITEMS)	Forward Digit Span	0.452	4.976	24.761	**<0.001**
VF (GROCERY ITEMS)	Reverse Digit Span	0.065	1.442	2.080	0.156
VF (GROCERY ITEMS)	Lawton's Scale for Instrumental Activities of Daily Living	0.078	1.598	2.555	0.117
VF (GROCERY ITEMS)	Schwab & England scale	0.111	1.941	3.766	0.059
VF (GROCERY ITEMS)	Mini-Mental State Examination	0.330	3.843	14.773	**<0.001**
VF (GROCERY ITEMS)	MDS-UPDRS – Part I	0.134	-2.153	4.637	**0.037**
VF (GROCERY ITEMS)	MDS-UPDRS – Part II	0.046	-1.209	1.461	0.235
VF (GROCERY ITEMS)	MDS-UPDRS – Part III	0.075	-1.558	2.428	0.126
VF (GROCERY ITEMS)	Hoehn & Yahr stage – OFF	0.011	-0.567	0.321	0.582
PLD-BDAE	Clinical Dementia Rating sum-of-boxes	0.159	-2.380	5.665	**0.022**
PLD-BDAE	15-item Clock Drawing Test	0.420	4.663	21.745	**<0.001**
PLD-BDAE	Forward Digit Span	0.114	1.966	3.867	0.056
PLD-BDAE	Reverse Digit Span	0.092	1.744	3.042	0.088
PLD-BDAE	Lawton's Scale for Instrumental Activities of Daily Living	0.025	0.881	0.776	0.611
PLD-BDAE	Schwab & England scale	0.114	1.967	3.870	0.056
PLD-BDAE	Mini-Mental State Examination	0.300	3.590	12.890	**0.001**
PLD-BDAE	MDS-UPDRS – Part I	0.052	-1.287	1.657	0.205
PLD-BDAE	MDS-UPDRS – Part II	0.154	-2.338	5.468	**0.025**
PLD-BDAE	MDS-UPDRS – Part III	0.274	-3.364	11.316	**0.002**
PLD-BDAE	Hoehn & Yahr stage – OFF	0.128	-2.098	4.401	**0.042**

HVOT: Hooper Visual Organization Test; VF: verbal fluency; PLD-BDAE: primer-level dictation section of the Boston Diagnostic Aphasia Examination; MDS-UPDRS: Movement Disorder Society – Unified Parkinson's Disease Rating Scale.

Discussion

In this study, associations among neuropsychiatric features of patients with LBD could be more accurately evaluated by specific tests. Knowledge of less studied clinical features, such as language disorders in LBD, can be useful to promote deinstitutionalized care and caregiver education.

Visual organization and PLD-BDAE test results were not significantly correlated, suggesting that the HVOT does not predict performance in the PLD-BDAE; in other words, this finding confirms that impairment of language may be a primary feature of LBD, and not necessarily secondary to cognitive deficits[34]. Nonetheless, VF and visuospatial abilities were concurrently associated in LBD. Visual organization is related to the frontal-subcortical circuitry that is

affected early in the course of LBD[35]. Moreover, poor VF is associated with incident dementia in Parkinson's disease, and could be due to impaired self-generated search[13]. Nevertheless, other studies have found that naming tests can be the best predictor of performance in the HVOT[35]. Patients with dementia with Lewy bodies have disproportionate deficits in visuospatial skills, attention and letter fluency[36]. Visuospatial processing, attention and executive functions in Parkinson's disease dementia have also been described to be similar to dementia with Lewy bodies[37].

Impaired connectivity with the frontal cortex leads to severely impaired grammatical expression in patients with LBD: failing to complete sentences, omitting the verb phrase, perseveration,

Table 4. Results from simple linear regressions for predictions between visual organization and language tests, features of sleep and neuropsychiatric inventory test results

Variable 1	Variable 2	Squared multiple R	t	F-ratio	p-value
HVOT	12-item Neuropsychiatric Inventory total scores	0.152	2.323	5.396	**0.026**
HVOT	12-item Neuropsychiatric Inventory – caregiver distress total scores	0.084	1.663	2.765	0.103
HVOT	Sleep satisfaction	0.017	-0.712	0.507	0.511
HVOT	Hours of sleep	0.051	-1.270	1.613	0.211
VF (F-A-S)	12-item Neuropsychiatric Inventory total scores	0.097	-1.791	3.208	0.080
VF (F-A-S)	12-item Neuropsychiatric Inventory – caregiver distress total scores	0.011	-0.589	0.347	0.567
VF (F-A-S)	Sleep satisfaction	0.170	-2.479	6.146	**0.018**
VF (F-A-S)	Hours of sleep	0.019	-0.769	0.592	0.546
VF (ANIMALS)	12-item Neuropsychiatric Inventory total scores	0.008	-0.505	0.255	0.623
VF (ANIMALS)	12-item Neuropsychiatric Inventory – caregiver distress total scores	<0.001	-0.097	0.009	0.920
VF (ANIMALS)	Sleep satisfaction	0.140	-2.213	4.899	**0.033**
VF (ANIMALS)	Hours of sleep	0.051	-1.273	1.621	0.210
VF (FRUITS)	12-item Neuropsychiatric Inventory total scores	0.005	0.383	0.147	0.706
VF (FRUITS)	12-item Neuropsychiatric Inventory – caregiver distress total scores	0.005	0.383	0.146	0.706
VF (FRUITS)	Sleep satisfaction	0.100	-1.825	3.330	0.075
VF (FRUITS)	Hours of sleep	0.060	-1.381	1.907	0.174
VF (GROCERY ITEMS)	12-item Neuropsychiatric Inventory total scores	<0.001	-0.080	0.006	0.934
VF (GROCERY ITEMS)	12-item Neuropsychiatric Inventory – caregiver distress total scores	0.025	0.873	0.763	0.607
VF (GROCERY ITEMS)	Sleep satisfaction	0.166	-2.441	5.957	**0.020**
VF (GROCERY ITEMS)	Hours of sleep	0.025	-0.873	0.762	0.606
PLD-BDAE	12-item Neuropsychiatric Inventory total scores	0.002	-0.269	0.073	0.785
PLD-BDAE	12-item Neuropsychiatric Inventory – caregiver distress total scores	0.011	-0.567	0.322	0.581
PLD-BDAE	Sleep satisfaction	<0.001	0.039	0.001	0.968
PLD-BDAE	Hours of sleep	0.010	0.540	0.291	0.600

HVOT: Hooper Visual Organization Test; VF: verbal fluency; PLD-BDAE: primer-level dictation section of the Boston Diagnostic Aphasia Examination.

Table 5. Multiple linear regressions for visual organization and language test results*

Variable (units)	Coefficient**	Coefficient** for schooling	Coefficient** for the length of dementia	Adjusted squared multiple R	*t*	F-ratio	p-value** for the regression
HVOT	8.259 (p < 0.001)	0.210 (p = 0.242)	-0.425 (p = 0.025)	0.113	7.591	2.980	0.067
VF (F-A-S)	6.783 (p = 0.001)	0.3 (p = 0.341)	-0.296 (p = 0.358)	0.000	3.534	0.716	0.497
VF (animals)	8.508 (p < 0.001)	0.146 (p = 0.504)	-0.468 (p = 0.042)	0.075	6.363	2.259	0.123
VF (fruits)	6.615 (p < 0.001)	-0.096 (p = 0.463)	-0.141 (p = 0.292)	0.009	8.312	1.143	0.333
VF (grocery items)	7.295 (p < 0.001)	0.093 (p = 0.643)	-0.273 (p = 0.191)	0.000	5.891	0.903	0.416
PLD-BDAE	3.889 (p = 0.048)	0.443 (p = 0.155)	-0.087 (p = 0.781)	0.004	2.067	1.069	0.356

*Multiple linear regressions for each of the listed dependent variables in relation to the following factors (2 degrees of freedom): schooling (years) and estimated length of the dementia syndrome (years).

**All p-values have been corrected with the Bonferroni test.

SD: standard deviation; HVOT: Hooper Visual Organization Test; VF: verbal fluency; PLD-BDAE: primer-level dictation section of the Boston Diagnostic Aphasia Examination.

requiring additional time to plan sentences[34]. We observed similar errors in the narrative discourse of our patients, but it should be noted that cortical involvement may occur earlier in dementia with Lewy bodies compared to Parkinson's disease dementia[38].

Cognitive and functional tests are usually correlated with one another in all stages of AD[23]. In our study with patients with LBD, we found that the higher the Clinical Dementia Rating sum-of-boxes scores, the lower were language and visuospatial test results. Likewise, language and visuospatial test results followed Mini-Mental State Examination scores. This could be helpful for differential diagnoses, since visuospatial abilities are more impaired in LBD than in other dementia syndromes[39]. In comparison with AD, patients with LBD have better contextual verbal delayed recall and recognition, and less short-term memory deficits, but worse letter fluency deficits and qualitative measures of executive functioning, and worsening visuoperception following overall cognitive decline[37,40].

The Hoehn and Yahr stages grade severity of parkinsonism[28], while the clock drawing test is a measure of visuospatial dysfunction also useful for screening cognitive impairment[23]. When performances in the HVOT and in the PLD-BDAE were worse, patients also had more severe parkinsonism and lower scores in the clock drawing test. It has been shown that patients with LBD who lose more motor function also have the greatest visuospatial impairment[13].

Only VF had a negative association with sleep satisfaction, but not with length of sleep, suggesting that sleep satisfaction may be inversely correlated with the stage of LBD. Sleep disorders occur in three quarters of autopsy-confirmed cases of dementia with Lewy bodies, but may not necessarily correlate with sleep satisfaction; in addition to attentional, executive functioning, and visuospatial impairments, the presence of impaired verbal learning helps identify prodromal dementia with Lewy bodies in patients with sleep disorders[41]. Moreover, it has been shown that the severity of psychotic symptoms in patients with Parkinson's disease is directly associated with the severity of cognitive impairment and sleep disturbances[42].

In our analyses, only the HVOT was associated with total scores of the Neuropsychiatric Inventory. Behavioural symptoms may affect sustained attention and, therefore, cognitive functioning[43]. Despite the increased frequency of visual hallucinations in LBD when compared to other dementia syndromes, they also lead to worse prognosis[8]. Still regarding neuropsychiatric symptoms, caregiver distress had no significant associations with visual organization or language tests, possibly representing low sensitivity to score variations in these tests.

All categories of VF were associated with forward digit span, except for fruits, the only category associated with reverse digit span. These findings suggest that attention and executive functions are important for most forms of category VF, but working memory might not decline concurrently.

Visual organization and language performance were not affected by education. This could be due to the cross-sectional nature of our study, but also to the fact that mechanisms of neurodegeneration supersede protective factors in these patients.

The length of the dementia syndrome was negatively associated with visual organization and VF for animals, an important finding to be correlated with the rapid cognitive decline usually found in patients with LBD[12]. On the other hand, instrumental functionality had no significant associations with visual organization or language tests, possibly due to the fact that instrumental functional decline occurs earlier, while visuospatial and language decline happen throughout the course of LBD.

The most important limitations of our study comprise its small sample size, its cross-sectional nature, and the fact that all patients were recruited from a single centre, thus limiting generalizability. Also, the size of our sample did not allow stratification into patient groups according to diagnoses (dementia with Lewy bodies or Parkinson's disease dementia), but pathophysiology is similar for these two diseases[16,37], and our results were mostly unaffected by this choice. Furthermore, the wide age range of the patients (spanning 45 years) could have affected our results due to the fact that young and older adults use different strategies to accommodate to impairments in executive function[44] but, considering that all patients were over 50 years-old and had at least one year of dementia diagnosis, we believe this to be unlikely.

We conclude that language and visual organization tend to follow motor skills and general cognitive performance in patients with LBD. Whereas visual organization did not predict performance in the PLD-BDAE, visuospatial abilities and VF were concurrently associated, suggesting that features of linguistic impairment in LBD may be attributed to components of cognition and language. Moreover, only visual organization was associated with behavioural performance, suggesting that neuropsychiatric symptoms are differentially associated with visual organization in comparison with linguistic features in LBD. Future studies should address neuropsychiatric correlations in prospective assessments.

Conflicts of interest

The authors report no conflicts of interest related to this paper.

References

1. Kehagia AA, Barker RA, Robbins TW. Neuropsychological and clinical heterogeneity of cognitive impairment and dementia in patients with Parkinson's disease. Lancet Neurol. 2010;9(12):1200-13.
2. Aarsland D, Ballard CG, Halliday G. Are Parkinson's Disease With Dementia and Dementia With Lewy Bodies the Same Entity? J Geriatr Psychiatry Neurol. 2004;17(3):137-45.
3. Papka M, Rubio A, Schiffer RB. A review of Lewy body disease, an emerging concept of cortical dementia. J Neuropsychiatry Clin Neurosci. 1998;10(3):267-79.
4. Tomlinson BE, Blessed G, Roth M. Observations on the brains of demented old people. J Neurol Sci. 1970;11(3):205-42.
5. Nelson PT, Jicha GA, Kryscio RJ, Abner EL, Schmitt FA, Cooper G, et al. Low sensitivity in clinical diagnoses of dementia with Lewy bodies. J Neurol. 2010;257(3):359-66.
6. Sung JY, Kim J, Paik SR, Park JH, Ahn YS, Chung KC. Induction of neuronal cell death by Rab5A-dependent endocytosis of alpha-synuclein. J Biol Chem. 2001;276(29):27441-8.
7. Trojanowski JQ, Lee VMY. Aggregation of neurofilament and alpha-synuclein proteins in Lewy bodies: implications for the pathogenesis of Parkinson disease and Lewy body dementia. Arch Neurol. 1998;55(2):151-2.
8. Oliveira FF, Machado FC, Sampaio G, Marin SMC, Chen ES, Smith MC, et al. Contrasts Between Patients With Lewy Body Dementia Syndromes and APOE-ε3/ε3 Patients With Late-onset Alzheimer Disease Dementia. Neurologist. 2015;20(2):35-41.
9. Alves G, Lange J, Blennow K, Zetterberg H, Andreasson U, Førland MG, et al. CSF Aβ42 predicts early-onset dementia in Parkinson disease. Neurology. 2014;82():1784-1790.
10. De Oliveira, FF, Marin SMC, Bertolucci PHF. Neurological impressions on the organization of language networks in the human brain. Brain Inj. 2017;31(2):140-50.
11. Pigott K, Rick J, Xie SX, Hurtig H, Chen-Plotkin A, Duda JE, et al. Longitudinal study of normal cognition in Parkinson disease. Neurology. 2015;85(15):1276-82.
12. Magierski R, Kloszewska I, Sobów TM. The influence of vascular risk factors on the survival rate of patients with dementia with Lewy bodies and Alzheimer disease. Neurol Neurochirur Pol. 2010;44(2):139-47.
13. Emre M. Dementia associated with Parkinson's disease. Lancet Neurol. 2003;2(4):229-37.
14. McKeith I, Del Ser T, Spano PF, Emre M, Wesnes K, Anand R, Cicin-Sain A, Ferrara R, Spiegel R. Efficacy of rivastigmine in dementia with Lewy bodies: a randomised, double-blind, placebo-controlled international study. Lancet. 2000;356(9247):2031-6.
15. Wajman JR, Oliveira FF, Marin SMC, Schultz RR, Bertolucci PHF. Is there correlation between cognition and functionality in severe dementia? The value of a performance-based ecological assessment for Alzheimer's disease. Arq Neuropsiquiatr. 2014;72(11):845-50.
16. Tolosa E, Wenning G, Poewe W. The diagnosis of Parkinson's disease. Lancet Neurol. 2006;5(1):75-86.

17. Emre M, Aarsland D, Brown R, Burn DJ, Duyckaerts C, Mizuno Y, et al. Clinical Diagnostic Criteria for Dementia Associated with Parkinson's Disease. Mov Disord. 2007;22(12):1689-707.
18. McKeith IG, Dickson DW, Lowe J, Emre M, O'Brien JT, Feldman H, et al. Diagnosis and management of dementia with Lewy bodies: Third report of the DLB consortium. Neurology. 2005;65(12):1863-72.
19. De Oliveira FF, Bertolucci PHF, Chen ES, Smith MAC. Assessment of sleep satisfaction in patients with dementia due to Alzheimer's disease. J Clin Neurosci. 2014;21(12):2112-7.
20. Camozzato AL, Kochhann R, Simeoni C, Konrath CA, Franz AP, Carvalho A, et al. Reliability of the Brazilian Portuguese version of the Neuropsychiatric Inventory (NPI) for patients with Alzheimer's disease and their caregivers. Int Psychogeriatr. 2007;20(2):383-93.
21. Bertolucci PHF, Brucki SMD, Campacci SR, Juliano Y. The Mini-Mental State Examination in an outpatient population: influence of literacy. Arq Neuropsiquiatr. 1994;52(1):1-7.
22. Lima APV, Castilhos R, Chaves MLF. The Use of the Clinical Dementia Rating Scale Sum of Boxes Scores in Detecting and Staging Cognitive Impairment/Dementia in Brazilian Patients with Low Educational Attainment. Alzheimer Dis Assoc Disord. 2017;31(4):322-7.
23. de Oliveira FF, Wajman JR, Bertolucci PHF, Chen ES, Smith MC. Correlations among cognitive and behavioural assessments in patients with dementia due to Alzheimer's disease. Clin Neurol Neurosurg. 2015;135:27-33.
24. Schwab RS, England AC. Projection technique for evaluating surgery in Parkinson's disease. In: Gillingham FJ, Donaldson MC, editors. Third Symposium on Parkinson's disease. Edinburgh: Livingstone; 1969.
25. Lawton MP. Instrumental Activities of Daily Living (IADL) Scale: Self--reported version. Psychopharmacol Bull. 1988;24:789-91.
26. Taub A, Andreoli SB, Bertolucci PHF. Dementia caregiver burden: reliability of the Brazilian version of the Zarit caregiver burden interview. Cad Saude Publica. 2004;20(2):372-6.
27. Goetz CG, Tilley BC, Shaftman SR, Stebbins GT, Fahn S, Martinez-Martin P, et al. Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale Presentation and Clinimetric Testing Results. Mov Disord. 2008;23(15):2129-70.
28. Hoehn MM, Yahr MD. Parkinsonism: onset, progression and mortality. Neurology. 1967;17(5):427-42.
29. Hooper EH, editor. Hooper Visual Organization Test (VOT). Los Angeles: Western Psychological Services; 1983.
30. Radanovic M, Diniz BS, Mirandez RM, Novaretti TMS, Flacks MK, Yassuda MS, et al. Verbal fluency in the detection of mild cognitive impairment and Alzheimer's disease among Brazilian Portuguese speakers: the influence of education. Int Psychogeriatr. 2009;21(6):1081-7.
31. Goodglass H, Kaplan E, Barresi B, editors. The assessment of aphasia and related disorders. Philadelphia: Lippincott Williams & Wilkins; 2001.
32. Radanovic M, Mansur LL, Scaff M. Normative data for the Brazilian population in the Boston Diagnostic Aphasia Examination: influence of schooling. Braz J Med Biol Res. 2004;37(11):1731-8.
33. Rodrigues AB, Yamashita ET, Chiappetta ALML. Teste de fluência verbal no adulto e no idoso: verificação da aprendizagem verbal. Rev CEFAC. 2008;10(4):443-51.
34. Ash S, McMillan C, Gross RG, Cook P, Gunawardena D, Morgan B, et al. Impairments of speech fluency in Lewy body spectrum disorder. Brain Lang. 2012;120(3):290-302.
35. Higginson CI, Wheelock VL, Levine D, Pappas CTE, Sigvardt KA. Predictors of HVOT performance in Parkinson's disease. Appl Neuropsychol. 2011;18(3):210-5.
36. Ferman TJ, Smith GE, Boeve BF, Graff-Radford NR, Lucas JA, Knopman DS, et al. Neuropsychological differentiation of dementia with Lewy bodies from normal aging and Alzheimer's disease. Clin Neuropsychol. 2006;20(4):623-36.
37. Levy JA, Chelune GJ. Cognitive-Behavioral Profiles of Neurodegenerative Dementias: Beyond Alzheimer's Disease. J Geriat Psychiatry Neurol. 2007;20(4):227-38.
38. Donaghy PC, McKeith IG. The clinical characteristics of dementia with Lewy bodies and a consideration of prodromal diagnosis. Alzheimers Res Ther. 2014;6(4):46.
39. De Oliveira FF, Machado FC, Sampaio G, Marin SMC, Naffah-Mazzacoratti MG, Bertolucci PHF. Neuropsychiatric feature profiles of patients with Lewy body dementia. Clin Neurol Neurosurg. 2020;194:105832.
40. McKeith IG. Dementia with Lewy bodies. Br J Psychiatry. 2002;180:144-7.
41. Génier Marchand D, Postuma RB, Escudier F, De Roy J, Pelletier A, Montplaisir J, et al. How does dementia with Lewy bodies start? Prodromal cognitive changes in REM sleep behavior disorder. Ann Neurol. 2018;83(5):1016-26.
42. Moustafa AA, Krishna R, Frank MJ, Eissa AM, Hewedi DH. Cognitive correlates of psychosis in patients with Parkinson's disease. Cogn Neuropsychiatry. 2014;19(5):381-98.
43. Pagonabarraga J, Kulisevsky J. Cognitive impairment and dementia in Parkinson's disease. Neurobiol Dis. 2012;46(3):590-6.
44. Kemper S, Schmalzried R, Herman R, Leedahl S, Mohankumar D. The effects of aging and dual task demands on language production. Neuropsychol Dev Cogn B Aging Neuropsychol Cogn. 2009;16(3):241-59.