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Functional decline in Lewy body dementia compared to Alzheimer disease

Comparaison du déclin fonctionnel entre des patients atteints de démence à corps de Lewy et de la maladie d'Alzheimer

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Abstract. Introduction. *Lewy body dementia (LBD) is the second most frequent neurodegenerative disorder after Alzheimer disease (AD). In this study, we compared functional decline between LBD and AD patients, considering motor dysfunction, over an 18-month follow-up period.* Patients and methods. *We included all patients >70 years of age, with initial MMSE ≥ 20 and a diagnosis of possible or probable LBD or AD, who consulted at the memory centre of the Pitié-Salpêtrière hospital. Statistical analyses were performed using univariate tests and multivariate linear regression.* Results. *Thirty-seven AD and 36 LBD patients were included, with a median age of 81 and a median MMSE score of 24/30. Global ADL Katz score decreased significantly for LBD people, compared to AD patients: –0.40 ± 0.75* versus *0 ± 0.24; p=0.003. Global IADL score decreased in the two populations but without a significant difference between the two groups: –1.71 ± 2.19 in LBD* versus *–1.32 (± 1.55); p=0.38.* Conclusion. *This study shows a significant decrease in autonomy in LBD patients over time that was faster than that in AD patients, related, in particular, to bathing, dressing and personal care.*

Keywords: *functional decline, Lewy body dementia, Alzheimer disease, activities of daily living*

Résumé. *Introduction.* La perte d'autonomie est une problématique majeure chez les patients avec des troubles neurocognitifs. Nous avons comparé le déclin fonctionnel entre les patients atteints de démence à corps de Lewy (DCL) et de maladie d'Alzheimer (MA), en tenant compte de la dysfonction motrice. *Patients et méthodes.* Nous avons inclus tous les patients à partir de 70 ans, avec un score au MMSE initial ≥ 20, avec un diagnostic de DCL ou de MA possible ou probable, consultant au centre mémoire de la Pitié-Salpêtrière. *Résultats.* Trente-sept patients MA et 36 DCL ont été inclus (âge médian 81 ans et MMSE médian 24/30). Le score global à l'ADL de Katz diminue significativement : DCL : –0,40 ± 0,75 *versus* MA : –0 (± 0,24), p 0,003. Le score global IADL diminue dans les deux populations mais sans différence significative entre les deux groupes : DCL : –1,71(± 2,19) *versus* MA : –1,32 (± 1,55), p 0,38. *Conclusion.* Cette étude montre une diminution significative de l'autonomie chez les patients DCL plus rapide que chez les patients MA, notamment pour la toilette, l'habillage et les soins personnels.

Mots-clés : déclin fonctionnel, démence à corps de Lewy, maladie d'Alzheimer, activités de la vie quotidienne

Introduction

Dementia concerns about 50 million people worldwide and this figure will increase [1]. Lewy body dementia (LBD) is becoming more common with increasing age and accounts for about 5% of all dementia cases in older populations [2], being the second most frequent neurodegenerative disorder after Alzheimer disease (AD).

LBD patients suffer from motor, cognitive and psychiatric symptoms, as described in the consensus criteria, last revised in 2017 [3]. Core clinical features include fluctuating cognition, visual hallucinations, parkinsonism, and rapid eye movement (REM) sleep behaviour disorder. Impact on executive functions is at the forefront of the cognitive disorder with mostly attentional deficit and spatial and perceptual difficulties, which occur early. Memory and object naming tend to be less affected in LBD.

Functional decline in dementia is one of the main issues which decreases quality of life and increases the burden of carers [4] and care costs [5], imposing a heavy toll on health care services, leading to institutionalization and death [6]. Moreover, numerous studies have shown that cognitive decline and functional dependency clearly correlate with mortality, even when controlling for the effects of socio-demographic variables and health conditions [7].

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Some studies have compared functional decline between AD and LBD patients; however, the results differ. While patients with LBD are reported to be more functionally impaired [8] with an increased mortality rate [9], other studies have found the rate of functional decline to be similar between the two dementias [10, 11]. A more recent study showed that the functional course of LBD, compared to AD, may depend on the age of the patient [12], as patients with LBD, aged between 67 and 81 years, were shown to have varying levels of increased risk of functional decline, relative to AD patients of the same age.

The main aim of our study was to compare functional decline between LBD and AD patients, considering motor dysfunction, over an 18-month follow-up period. As a secondary goal, we performed sensitivity analysis to investigate potential confounding factors that may influence Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL) scores and determine explanatory variables.

Materials and methods

This was a retrospective monocentric study based on a clinical cohort. The cohort was composed of patients who were referred to our memory clinic as part of a tertiary hospital.

Our primary outcome was the evolution of the functional autonomy scales, Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL), over 18 months, independent of motor dysfunction.

Inclusion criteria

Patients aged >70 years with:

- one year of follow-up;
- MMSE (Mini-Mental State Examination) score ≥20 at the first evaluation from January 1st, 2007 to December 31st, 2020;
- a diagnosis of possible or probable LBD according to the fourth consensus report of the LBD consortium [3];
- a diagnosis of possible or probable AD according to the recommendations from the National Institute on Aging Alzheimer Association workgroups on diagnostic guidelines for AD [13];
- available data on ADL and IADL at baseline and after 18 months of follow-up.

Exclusion criteria

- No evaluation of baseline autonomy.
- No follow-up (death or data of autonomy scales not available).
- Evidence of stroke on MRI (multiple lesions from micro or macroangiopathy or cerebral amyloid angiopathy, *etc.*) or other disorders with sufficient impact to consider a diagnosis of mixed dementia (alcoholism, vitamin deficiency, *etc.*).

Data collection

Demographic characteristics, medical history, and multimorbidity were evaluated using the Cumulative Illness Rating Scale (CIRS) and Rockwood scale [14, 15]. Symptoms during the first consultation in our memory clinic at the Pitié-Salpêtrière hospital were documented in a database. For the two scales of comorbidity, the higher the score, the more severe the comorbidity and frailty.

Cognitive function was measured at the first and second consultation using the Montreal Cognitive Assessment (MoCA) [16], FAB (Frontal Assessment Battery) [17] and MMSE [18]. For these three tests, a higher score reflects a higher level of cognition. Motor function was evaluated using the Hoen and Yahr scale [19] also during the two consultations, with a low score indicating less extrapyramidal signs. Data on medical imaging and investigation were documented at baseline (first consultation).

Our principal outcomes, ADL and IADL, were documented at baseline and the second consultation along with scores based on the Katz and Lawton scales [20, 21]. These scales were completed with a member of the family who lived with the patient or a personal caregiver. The total score was added to a computerized database, and details for each item were reviewed within a specific section. For these two latter scales, a higher score reflected better autonomy.

The ADL of the Katz scale is referred to as "Katz ADL". The IADL of the Lawton scale was divided into three subscores: a score for "Lawton ADL" composed of "Hygiene", "Eating", "Dressing", "Personal care", "Mobility", "Bathing"; a score for "Sexualized items" composed of "Food preparation", "Housework" and "Laundry"; and a score for "Other items" composed of "Telephoning", "Shopping", "Transport", "Management of treatment", and "Finance".

Statistical analysis

Qualitative variables were described as number (percentages), and quantitative variables were described as mean (± standard deviation) or median (1st quartile-3rd quartile) if the variable was discrete or without normal distribution (graphically assessed).

First, for quantitative variables, a comparison of baseline characteristics between the AD and LBD group was made using the univariate t-test or Wilcoxon-Man-Whitney test if data were not normally distributed or discrete, and the Chi-2 or Fisher's exact test was used for qualitative variables.

Second, we analysed ADL and IADL scores at baseline and at the second consultation, stratified by AD or LBD; scores were compared at baseline using a single Wilcoxon-Mann-Whitney test. IADL variation was analysed for the entire sample and statistically tested using a paired t-test for global mean-variation (total IADL) and McNemar test for

number variation (number of individuals with 1 point) for every IADL item.

Third, corresponding to our primary outcome, we compared IADL and ADL mean differences (from two consultations) between AD and LBD groups overall and for subscores. For every item, we defined a new variable, "1 point decrease between two consultations", which was described as a percentage. The T-test was used for mean differences and Fisher's exact test for percentages of "1 point decrease between two consultations".

Fourth, multivariate linear regressions were used to compare mean differences between AD and LBD groups adjusted for MMSE, CIRS and Hoehn and Yahr at baseline. Linearity, equality of variances, absence of autocorrelations and normality of linear regression residuals were verified.

Finally, as our secondary aim, we performed sensitivity analyses to investigate the role of potential confounding factors on IADL and ADL. Correlation of functional decline was studied using subscales of cognitive impairment (executive functions, visuo-spatial disorders, *etc*.), with the hypothesis that functional decline may be more important in LBD than AD due to a more severe impact on executive and visuo-spatial functions in LBD, independent of motor decline. Thus, subgroup analyses (forest plots) were performed for univariate IADL and ADL differences between AD and LBD groups, stratified by FAB level, MMSE level and gender. Univariate mean difference was also analysed by forest plot for ADL, IADL and all IADL subclasses. We finally built three new multivariate linear regression models without sexualized items, with adjustment for gender and FAB score in order to investigate potential effects on IADL between the AD and LBG groups.

Alpha risk was bilaterally fixed at a level of 5% and analyses were performed using R Studio v1.4.1103.

Results

Patient selection

Screening of the database revealed 71 patients diagnosed with LBD and 252 with AD. In total, 73 patients were included; 37 met the criteria for AD and 36 for LBD. Details are shown in the flow chart in *figure 1*. The final diagnosis was confirmed after reviewing clinical files.

Patient characteristics

Baseline characteristics, shown in *table 1*, were similar for age, sex and global cognition. Median age of our population was 81 and the median MMSE score was 24/30, which corresponds to a level of mild cognitive impairment among patients with major neurocognitive disorders.

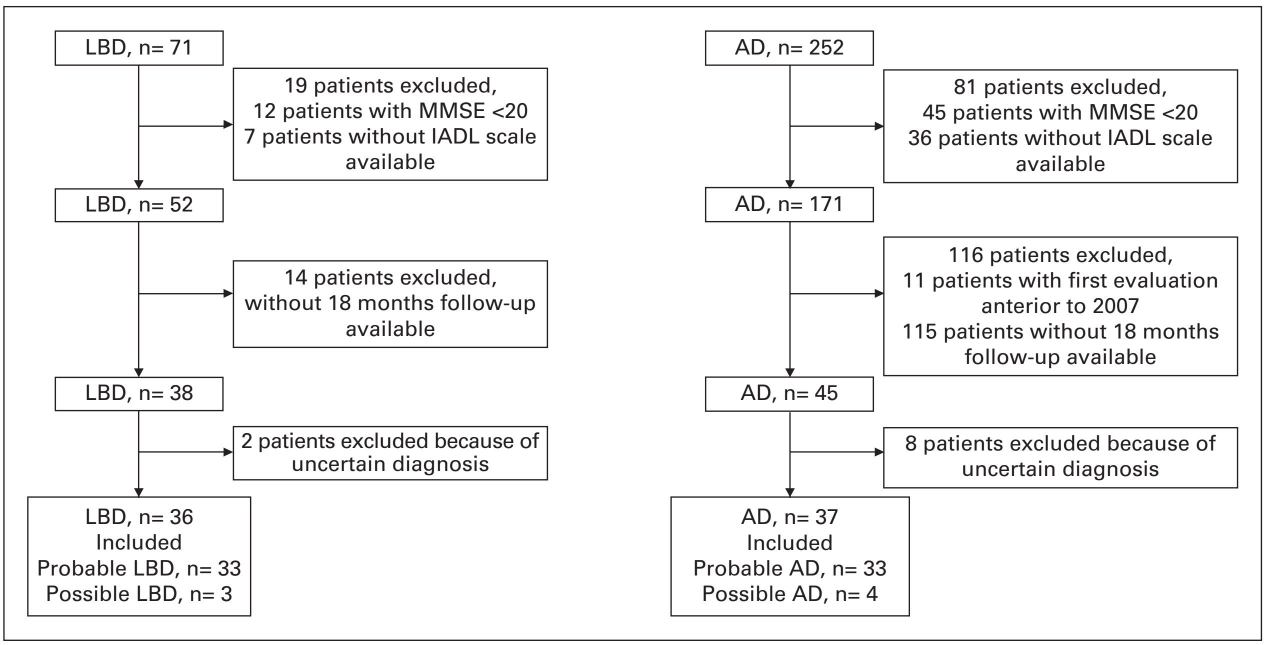

***Figure 1.** Flow chart.*

Figure 1. Diagramme de flux.

However, LBD patients had significantly more comorbidities and physical dysfunction than AD patients. Also, executive functions were more impaired. Other symptoms related to the pattern of the disease were more frequent (parkinsonism, hallucinations, REM sleep behavioural disorders, and fluctuating cognition).

At the second consultation (*table 2*), the median MMSE score of all patients remained at 24 (20-26), but was lower in each category, consistent with the evolution of the cognitive disorder.

The Hoehn and Yahr score increased (from 0 to 2 [1-2] for LBD; $p<0.001$), also consistent with the evolution of LBD.

Overall autonomy scales

Comparing the two groups at baseline (*table 3*), LBD patients appeared less independent than AD patients for body care (81% *versus* 97%; $p=0.99$), dressing (78% *versus* 97%; $p=0.72$), going to the toilet (81% *versus* 97%; $p=0.70$) and transferring (81% *versus* 100%; $p=0.45$), but without significance.

Total IADL score decreased significantly between the two consultations: from 11 (9-12) to 10 (7-11); $p<0,001$ (*table 4*). When we compared each item, most were significantly decreased: shopping, cooking, housekeeping, doing the laundry, management of treatment and finance, personal care and bathing.

Table 1. *Baseline characteristics according to AD or LBD.*

Tableau 1. Caractéristiques de base selon qu'il s'agit de la MA ou de la MCL.

	All patients N = 73	**AD N= 37**	**LBD N= 36**	***p* value**
Age (years)	81 (±5)	80 (±5)	81 (±4)	0.22
>85	12 (16)	6 (16)	6 (17)	0.99
Gender				0.13
Female	35 (48)	21 (57)	14 (39)	
Male	38 (52)	16 (43)	22 (61)	
Medical history				
CIRS	**6 [4-8]**	**4 [3-6]**	**7 [5.75-11]**	**<0.001**
Rockwood	**4 [4-5]**	**4 [3-5]**	**5 [4-5]**	**0.01**
Hypertension	18 (25)	10 (27)	8 (22)	0.79
Diabetes	6 (8)	3 (8)	3 (8)	0.99
eGFR	55 (±17)	54 (±14)	56 (±20)	0.61
Missing values	*15 (21)*	*5 (14)*	*10 (28)*	-
Cardiological disease	3 (4)	3 (8)	0 (0)	0.24
Atrial fibrillation	17 (23)	5 (14)	12 (33)	0.06
Lacuna	3 (4)	0 (0)	3 (8)	0.11
Hypothyroidism	3 (4)	1 (3)	2 (6)	0.61
Apnoea sleeping syndrome	7 (10)	1 (3)	6 (17)	0.06
Treated	**5 (7)**	**0 (0)**	**5 (14)**	**0.03**
Dyslipidaemia	19 (26)	10 (27)	9 (25)	0.99
Smoker	22 (30)	12 (32)	10 (28)	0.80
Current smoker	4 (5)	3 (8)	1 (3)	0.61
Yearly number of packets	4 [2.75-6]	5 [4-6]	2 [2-4.5]	0.06
Alcohol consumption (<3 glass per day)	15 (21)	9 (24)	6 (17)	0.56
Cognitive scores				
MMSE	24 [22-27]	25 [23-27]	24 [22-27]	0.21
FAB	**12 [11-14]**	**13 [12-15]**	**11 [10-13]**	**<0.001**

MoCA	22 [21-24]	22 [20-23]	23 [22-25]	0.29
Missing values	*54 (74)*	*25 (68)*	*29 (81)*	-
Physical scores (Parkinson score)				
UPDRS	**3 [0-10.5]**	**0 [0-1]**	**10.5 [4.5-12.75]**	**<0.001**
Missing values	*34 (47)*	*16 (43)*	*18 (50)*	-
Hoen and Yahr	**0 [0-1]**	**0 [0-0]**	**1 [0-2]**	**<0.001**
Missing values	*3 (4)*	*0 (0)*	*3 (8)*	-
Symptoms				
Parkinsonism	**40**	**0 (0)**	**27 (75)**	**<0.001**
Hallucinations	**18 (25)**	**2 (5)**	**16 (44)**	**<0.001**
REM sleep behavioural disorder	**11 (15)**	**0 (0)**	**11 (31)**	**<0.001**
Cognitive fluctuations	**25 (34)**	**0 (0)**	**25 (69)**	**<0.001**
Medical imaging and investigation				
[123I] FP-CIT SPECT	15 (21)	0 (0)	15 (42)	
Fazekas score	1 |1-2]	1 [1-2]	2 [1-2]	0.10
Missing values	*23 (32)*	*6 (16)*	*17 (47)*	-
Scheltens score	2 [1-3]	2 [1-2]	2 [2-3]	0.30
Missing values	*19 (26)*	*5 (14)*	*14 (39)*	-
Lumbar puncture performed[1]	**19 (26)**	**14 (38)**	**5 (14)**	
Lower Aβ and increased phosphotau protein		**14 (100)**	**1 (20)**	**<0.001**
Lower Aβ and normal tau and phosphotau proteins		**0(0)**	**2 (40)**	
Normal Aβ, tau and phosphotau proteins		**0**	**2(40)**	

Data are expressed as mean ± SD, median (25–75 interquartile range), or number (percentage). Comparison between the two groups was performed by t-test or Mann-Whitney U test for quantitative variables and chi-square test or Fisher's exact test for qualitative variables.

CIRS: Cumulative Illness Rating Scale; eGFR: extra-glomerular Filtration Rate (mL/min, Cockcroft); MMSE: Mini-Mental State Examination; FAB: Frontal Assessment Battery; MoCA: Montreal Cognitive Assessment; UPDRS: Unified Parkinson Disease Rating Scale.

[1]Specific biomarkers in favour of AD.

All missing values are specified in the table.

Autonomy scales according to disease

There was a significant difference in total IADL score between AD and LBD patients at baseline (*table 5*); LBD patients were more dependent than AD patients (10 [8-12] *versus* 11 [10-13]; *p*=0.02).

Analysis of each item of IADL by group showed that the LBD group was significantly more impaired regarding the use of the telephone (86% *versus* 97%; *p*=0.004), transport (69% *versus* 95%; *p*=0.02) and mobility (53% *versus* 84%; *p*=0.02).

Mean difference in autonomy scale between the two groups

The total Katz ADL score decreased significantly for LBD patients compared to AD patients: –0.40 (± 0.75) *versus* 0 (±0.24); *p*=0.003 (*table 6*). Total IADL score decreased in the two populations but without significant difference between the two groups: –1.32 (±1.55) for AD *versus* –1.71 (±2.19) for LBD; *p*=0.38. For Lawton ADL, as a subdivision of global IADL, the decrease was significantly higher for LBD compared to AD: –0.16 (±0.50) for AD *versus* –0.73 (±1.40) for LBD; *p*=0.02. This difference in Katz ADL remained significant after adjustment for MMSE, CIRS and Hoehn and Yahr scores: –0.36 (–0.67; –0.04); *p*=0.03 (*table 7*). However, the difference in IADL total score remained non-significant, even after adjustment for these significant prognostic factors: –0.54 (–1.68; 1.6); *p*=0.35 (*table 8*).

Sensitivity analysis

Finally, for sensitivity analysis, using univariate analysis (*supplementary figure 1*), there was a significant decrease in

Table 2. *Cognitive and physical score at second consultation.*

Tableau 2. Score cognitif et physique à la deuxième consultation.

	All patients N = 73	**AD N= 37**	**LBD N= 36**	***p* value**
Cognitive scores				
MMSE	24 [20-26]	24 [21-26]	23 [19-27]	0.97
Missing values	*3 (4)*	*2 (5)*	*1 (3)*	-
FAB	12 [11-15]	12 [11-15]	14 [12-15]	0.65
Missing values	*50 (68)*	*20 (54)*	*30 (83)*	-
MoCA	19 [16-21]	19 [18-21]	19 [16-24]	0.29
Missing values	*37 (51)*	*14 (38)*	*23 (64)*	-
Physical scores (Parkinson score)				
UPDRS	**2 [0-7.5]**	**0 [0-0.5]**	**8 [4-12]**	**0.006**
Missing values	*58 (79)*	*29 (78)*	*29 (81)*	-
Hoen and Yahr	**0 [0-2]**	**0 [0-0]**	**2 [1-2]**	**<0.001**
Missing values	*3 (4)*	*0 (0)*	*3 (8)*	-

Data are presented as median (25–75 interquartile range). Comparison between the two groups was performed using the Mann-Whitney U test for quantitative variables.
MMSE: Mini-Mental State Examination; FAB: Frontal Assessment Battery; MoCA: Montreal Cognitive Assessment; UPDRS: Unified Parkinson Disease Rating Scale.

ADL between the LBD and AD groups when global cognitive function was more impaired at baseline (MMSE score <22): –1.1 (–1.88; –0.31).

Concerning executive dysfunction at baseline (*supplementary figure 2*) for Katz ADL, however, there was no significant difference in FAB score at baseline between the two groups, with a tendency for lower FAB scores: –0.3 (–1; 0.4). For the IADL, there was significant loss of autonomy associated with lower FAB scores: 1.7 (–1.33; 4.73).

Data related to gender were heterogenous for the two types of ADL (*supplementary figure 3*); for Lawton ADL, a difference was more apparent in males: –0.79 (–1.43; –0.16), but for Katz ADL, a difference was more apparent in females: –0.68 (–1.11; –0.25). There was no significative difference in IADL.

Based on univariate analysis, a significative difference was observed only for Katz ADL (–0.4 [–0.67; -0.14]) and Lawton ADL (–0.57 [–1.06; –0.07]) (*supplementary figure 4*), as for the multivariate analysis.

Lastly, sensitivity analysis showed a significant difference in the model without sexualized items (–1.06 [–1.93; -0.19]) (*supplementary table 1*).

Discussion

In this study of functional decline in LBD and AD patients, we observed a faster decline in LBD patients compared to AD patients regarding ADL, independent of motor dysfunction, comorbidities and MMSE score.

Global cognitive decline did not appear to explain this faster decrease in autonomy in LBD patients, apart from when initial cognitive impairment was more severe (MMSE < 22) (*supplementary figure 1*), suggesting that cognitive impairment may lead to reduced autonomy.

Concerning executive dysfunction, this may play a role in the decline of autonomy in LBD patients as described in AD patients [22]. However, this was not apparent in our study, probably due to the extent of missing data used for the FAB score at the second evaluation. Furthermore, the FAB score was higher at the second assessment, although data were available only for six patients, all under anticholinesterase therapy. Nevertheless, based on univariate analysis, when adjusting IADL for FAB at baseline, a significant difference was observed for patients with severe executive dysfunction (*supplementary figure 2*), suggesting that lower executive functions at baseline increase the risk of reduced IADL autonomy. This means that the level of executive dysfunction is likely to influence autonomy.

Our initial study hypothesis also concerned visuo-spatial complications. Hallucinations, more frequent in LBD patients than AD patients, are a marker of occipitoparietal damage, and are therefore associated with visuo-spatial disorders. Moreover, an early visuo-spatial deficit is known to manifest in LBD patients, however, this was not measured in our study.

Regarding the characteristics of the population, our study population appears to be similar to those of other studies, based on the following:

Table 3. *ADL at baseline and second consultation.*

Tableau 3. ADL à l'inclusion et à la deuxième consultation.

	All patients N = 73		**AD N= 37**		**LBD N= 36**		***p*[1]**
	Baseline	2nd C	Baseline	2nd C	Baseline	2nd C	
Total							
ADL[1]	6 [5.5-6]	6 [5-6]	6 [6-6]	6 [6-6]	6 [5.5-6]	5.5 [5-6]	0.36
Body care							
0.5 point	2 (3)	3 (4)	1 (3)	2 (5)	1 (3)	1 (3)	0.99
1 point	65 (89)	54 (74)	36 (97)	34 (92)	29 (81)	20 (56)	
Missing value	*6 (8)*	*15 (21)*	*0 (0)*	*1 (3)*	*6 (17)*	*14 (39)*	
Dressing							
0.5 point	2 (3)	3 (4)	1 (3)	1 (3)	1 (3)	2 (6)	0.72
1 point	64 (88)	54 (74)	36 (97)	35 (95)	28 (78)	19 (53)	
Missing value	*6 (8)*	*15 (21)*	*0 (0)*	*1 (3)*	*6 (17)*	*14 (39)*	
Going to the toilet							
0.5 point	1 (1)	1 (1)	1 (3)	1 (3)	0 (0)	0 (0)	0.70
1 point	65 (89)	56 (77)	36 (97)	35 (95)	29 (81)	21 (58)	
Missing value	*6 (8)*	*15 (21)*	*0 (0)*	*1 (3)*	*6 (17)*	*14 (39)*	
Transferring							
0.5 point	1 (1)	3 (4)	0 (0)	3 (8)	1 (3)	0 (0)	0.45
1 point	66 (90)	55 (75)	37 (100)	33 (89)	29 (81)	22 (61)	
Missing value	*6 (8)*	*15 (21)*	*0 (0)*	*1 (3)*	*6 (17)*	*14 (39)*	
Continence							
0.5 point	6 (8)	5 (7)	5 (14)	4 (11)	1 (3)	1 (3)	0.43
1 point	59 (81)	51 (70)	31 (84)	31 (84)	28 (78)	20 (56)	
Missing value	*6 (8)*	*15 (21)*	*0 (0)*	*1 (3)*	*6 (17)*	*14 (39)*	
Eating							
0.5 point	1 (1)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0.99
1 point	66 (90)	57 (78)	36 (97)	35 (95)	30 (83)	22 (61)	
Missing value	*6 (8)*	*16 (22)*	*0 (0)*	*2 (5)*	*6 (17)*	*14 (39)*	

[1]*p* value based on Wilcoxon-Mann-Whitney or Fisher's exact test between AD and LBD at baseline.

Data are presented as median (25–75 interquartile range) for quantitative variables and number (percentages) for qualitative variables.

2nd C: second consultation; ADL: Activities of Daily Living.

– there were more women in the AD group and more men in LBD group, reflecting the typical epidemiology of the disease [23, 24];
– there was less autonomy in ADL in the LBD group, concordant with motor dysfunction, especially for mobility, but also IADL [8, 23];
– there was more impairment in executive functions in the LBD group, related to the pattern of the disease.

Concerning comorbidities, the CIRS score was more elevated in the LBD group than the AD group (7 *versus* 4). This is consistent with studies showing that mortality is increased in LBD patients [9]. However, the clinical pertinence of 3 points on this scale of a maximum of 56 (0/05) is unclear [6].

For the Rockwood scale, the difference was also significant between LBD and AD, by only one point [15]. This score measures the frailty of elderly people, taking into account

Table 4. *iADL at baseline and second consultation in the overall sample.*

Tableau 4. iADL à l'inclusion et à la deuxième consultation.

	Baseline	2nd C	Difference	*p*
Total				
iADL	11 [9-12]	10 [7-11]	**-1.51 (±1.88)**[1]	**<0.001**
Using the telephone				
1 point	67 (92)	66 (90)	-1 (-1)	0.62
Missing value	*2 (3)*	*1 (1)*	-	-
Shopping				
1 point	45 (62)	32 (44)	**-13 (-18)**	**<0.001**
Missing value	*5 (7)*	*5 (7)*	-	-
Food preparation				
1 point	34 (47)	19 (26)	**-15 (-21)**	**<0.001**
Missing value	*22 (30)*	*24 (33)*	-	-
Housework				
1 point	37 (51)	26 (36)	**-11 (-15)**	**0.003**
Missing value	*25 (34)*	*23 (32)*	-	-
Laundry				
1 point	35 (48)	28 (38)	**-7 (-10)**	**0.01**
Missing value	*26 (36)*	*25 (34)*	-	-
Transport				
1 point	60 (82)	61 (84)	1 (1)	0.99
Missing value	*2 (3)*	*1 (1)*	-	-
Management of treatment				
1 point	41 (56)	25 (34)	**-16 (-22)**	**<0.001**
Missing value	*2 (3)*	*1 (1)*	-	-
Finance				
1 point	51 (70)	34 (47)	**-17 (-23)**	**<0.001**
Missing value	*2 (3)*	*2 (3)*	-	-
Hygiene				
1 point	64 (88)	58 (79)	-6 (-8)	0.08
Missing value	*2 (3)*	*1 (1)*	-	-
Eating				
1 point	68 (93)	70 (96)	2 (3)	0.99
Missing value	*1 (1)*	*1 (1)*	-	-
Dressing				
1 point	65 (89)	61 (84)	-4 (-5)	0.27
Missing value	*2 (3)*	*1 (1)*	-	-
Personal care				
1 point	67 (92)	61 (84)	**-6 (-8)**	**0.04**
Missing value	*2 (3)*	*1 (1)*	-	-
Mobility				
1 point	50 (68)	46 (63)	-4 (-5)	0.21
Missing value	*2 (3)*	*1 (1)*	-	-
Bathing				
1 point	64 (88)	59 (81)	**-5 (-7)**	**0.02**
Missing value	*2 (3)*	*1 (1)*	-	-

[1]Mean difference between the first and second consultation.

Data are presented as median (25–75 interquartile range) for quantitative variables and number (percentages) for qualitative variables. Comparison between the two groups was performed using the paired t-test for quantitative variables and Mcnemar test for qualitative variables.

2nd C: second consultation; iADL: instrumental Activities of Daily Living.

Table 5. *iADL at baseline and second consultation stratified by AD or LBD.*

Tableau 5. iADL à l'inclusion et à la deuxième consultation stratifiés en fonction de la maladie d'Alzheimer ou de la démence à corps de Lewy.

	AD N= 37		**LBD N= 36**		***p*[1]**
	Baseline	2nd C	Baseline	2nd C	
Total					
iADL[1]	11 [10-13]	10 [8-12]	10 [8-12]	9 [5-11]	**0.02**
Using the telephone					
1 point	36 (97)	35 (95)	31 (86)	31 (86)	**0.004**
Missing value	*2 (5)*	*0 (0)*	*0 (0)*	*0 (0)*	
Shopping					
1 point	29 (78)	21 (57)	16 (44)	11 (31)	0.99
Missing value	*2 (5)*	*1 (3)*	*3 (8)*	*4 (11)*	
Food preparation					
1 point	18 (49)	10 (27)	16 (44)	9 (25)	0.99
Missing value	*10 (27)*	*11 (30)*	*12 (33)*	*13 (36)*	
Housework					
1 point	17 (46)	14 (38)	20 (56)	12 (33)	0.73
Missing value	*10 (27)*	*9 (24)*	*15 (42)*	*14 (39)*	
Laundry					
1 point	20 (54)	17 (46)	15 (42)	11 (31)	0.50
Missing value	*12 (32)*	*11 (30)*	*14 (39)*	*14 (39)*	
Transport					
1 point	35 (95)	34 (92)	25 (69)	27 (75)	**0.02**
Missing value	*0 (0)*	*0 (0)*	*2 (6)*	*1 (3)*	
Management of treatment					
1 point	22 (59)	13 (35)	19 (53)	12 (33)	0.81
Missing value	*0 (0)*	*0 (0)*	*2 (6)*	*1 (3)*	
Finance					
1 point	26 (70)	17 (46)	25 (69)	17 (47)	0.80
Missing value	*0 (0)*	*0 (0)*	*2 (6)*	*2 (6)*	
Hygiene					
1 point	34 (92)	33 (89)	30 (83)	25 (69)	0.70
Missing value	*0 (0)*	*0 (0)*	*2 (6)*	*1 (3)*	
Eating					
1 point	37 (100)	37 (100)	31 (86)	33 (92)	0.10
Missing value	*0 (0)*	*0 (0)*	*1 (3)*	*1 (3)*	
Dressing					
1 point	36 (97)	35 (95)	25 (69)	26 (72)	0.10
Missing value	*0 (0)*	*0 (0)*	*2 (6)*	*1 (3)*	
Personal care					
1 point	34 (92)	34 (92)	33 (92)	27 (75)	0.62
Missing value	*0 (0)*	*0 (0)*	*2 (6)*	*1 (3)*	
Mobility					
1 point	31 (84)	27 (73)	19 (53)	19 (53)	**0.02**
Missing value	*0 (0)*	*0 (0)*	*2 (6)*	*1 (3)*	
Bathing					
1 point	34 (92)	34 (92)	30 (83)	25 (69)	0.70
Missing value	*0 (0)*	*0 (0)*	*2 (6)*	*1 (3)*	

[1]*p* value based on the Wilcoxon-Mann-Whitney or Fisher's exact test between AD and LBD at baseline.

Data are presented as median (25–75 interquartile range) for quantitative variables and number (percentages) for qualitative variables.

2nd C: second consultation; iADL: instrumental Activities of Daily Living.

Table 6. *Difference[1] in ADL and iADL between AD and LBD.*

Tableau 6. Différence entre les échelles ADL et iADL entre maladie d'Alzheimer et démence à corps de Lewy.

	All patients N = 73	**AD N= 37**	**LBD N= 36**	***p* value**
Delay between the two consultations	13 [12-15]	14 [11-15]	13 [12-15.25]	0.88
ADL				
Total	**- 0.20 (±0.59)**	**0 (±0.24)**	**-0.40 (±0.75)**	**0.003**
iADL				
Total	**-1.51 (±1.88)**	**-1.32 (±1.55)**	**-1.71 (±2.19)**	**0.38**
Lawton ADL				
Total	**-0.43 (±1.06)**	**-0.16 (±0.50)**	**-0.73 (±1.40)**	**0.02**
Reduced ability regarding:				
Hygiene (= continence)	7 (10)	2 (5)	5 (14)	0.25
Eating	1 (1)	0 (0)	1 (3)	0.49
Dressing	9 (12)	2 (5)	7 (19)	***0.08***
Personal care	8 (11)	1 (3)	7 (19)	**0.03**
Mobility	11 (15)	6 (16)	5 (14)	0.99
Bathing	7 (10)	0 (0)	7 (19)	**0.005**
Sexualized items				
Total	**-0.55 (±0.88)**	**-0.48 (±0.68)**	**-0.63 (±1.07)**	**0.58**
Reduced ability regarding:				
Food preparation	12 (16)	6 (16)	6 (17)	0.99
Housework	13 (18)	7 (19)	6 (17)	0.99
Laundry	8 (11)	3 (8)	5 (14)	0.45
Other items				
Total	**-0.80 (±0.91)**	**-0.80 (±0.83)**	**-0.79 (±1.01)**	**0.98**
Reduced ability regarding:				
Use of the telephone	3 (4)	1 (3)	2 (6)	0.61
Shopping	14 (19)	9 (24)	5 (14)	0.38
Transport	3 (4)	1 (3)	2 (6)	0.61
Management of treatment	17 (23)	9 (24)	8 (22)	0.99
Finance	18 (25)	9 (24)	9 (25)	0.99

Data are presented as mean (±SD) for quantitative variables or proportion (percentages) for qualitative variables. Comparison between the two groups was performed using the t-test for quantitative variables and Fisher's exact test for qualitative variables.

ADL: Activities of Daily Living; iADL: instrumental Activities of Daily Living.

[1]For total value: mean difference between score at second consultation and baseline; for subcategories: proportion of 1-point loss between baseline and second consultation.

mobility and dependence. This is concordant with impairment of autonomy in the LBD population at baseline.

For the principal analysis of this study, we chose to use the IADL scale of Lawton in its complete form, including the ADL, dividing it into three parts: (1) Lawton ADL comprising six ADL items, (2) three items of sexualized IADL, and (3) five items of global IADL. The six Lawton ADL items are not totally concordant with the Katz scale; however, over time, the two scales may be used to globally examine the same activities. The sexualized IADL items are more complicated, because gender can influence the data [25], however, this did not appear to be the case here (*supplementary figure 3*). In this study, the lack of sensitivity for these three items appears to be related to the large amount of associated missing data in our statistical analysis. Indeed, based on the previous sensitivity analysis (*supplementary table 1*), there was a significant

Table 7. *Association between difference in ADL (between the two consultations) and significant prognostic factors (71 patients) based on linear regression.*

Tableau 7. Association entre la différence ADL (entre les deux consultations) et les facteurs pronostiques significatifs (71 patients) basée sur la régression linéaire.

	Adjusted difference	95% CI	*p* value
Cognitive disorder			
Alzheimer disease	Ref	Ref	Ref
Lewy body dementia	**-0.36**	**(-0.67;-0.04)**	**0.03**
Cognitive score			
MMSE at baseline (for 1 point)	0.04	(-0.01;0.09)	0.09
Comorbidity score			
CIRS at baseline (for 1 point)	0.02	(-0.02;0.07)	0.25
Functional score			
Hoen and Yahr at baseline (for 1 point)	-0.11	(-0.22;0.01)	0.06

Table 8. *Association between difference in iADL (between the two consultations) and significant prognostic factors (71 patients) based on linear regression.*

Tableau 8. Association entre la différence iADL (entre les deux consultations) et les facteurs pronostiques significatifs (71 patients) basée sur la régression linéaire.

	Adjusted difference	95% CI	*p* value
Cognitive disorder			
Alzheimer disease	Ref	Ref	Ref
Lewy body dementia	-0.54	(-1.68;1.60)	0.35
Cognitive score			
MMSE at baseline (for 1 point)	0.01	(-0.17;0.18)	0.96
Comorbidity score			
CIRS at baseline (for 1 point)	0.02	(-0.13;0.17)	0.78
Functional score			
Hoen and Yahr at baseline (for 1 point)	0.08	(-0.31;0.49)	0.66

difference in the model without the sexualized items, indicating that without taking these three items into account (Food preparation, Housework and Laundry), there was a significant difference in the evolution of total IADL score.

In our overall sample, we noticed that there was a significant decrease in autonomy in shopping, cooking, housekeeping, and management of treatment and finance. IADL is known to be affected early due to cognitive decline [26]. However, it should be noted that this study was based on self-reporting.

Loss of autonomy in LBD patients appears to be faster than in AD patients with regards to ADL for bathing, dressing and personal care. Mobility could be the first to be lost, as expected based on motor dysfunction, but this was not the case in our study because half of the LBD patients were already non-autonomous at baseline, and the results of the multivariate analysis adjusted for the Hoehn and Yahr score remained similar. In several studies, these three ADL items, particularly bathing, are reported to be lost before other instrumental activities, and several authors have attempted to elaborate a hierarchy of combined ADL and IADL.

Katz and colleagues predicted that the order of loss of function would be as follows: (1) bathing, (2) dressing, (3) going to the toilet, (4) transferring, (5) continence, and (6) feeding [20]. Lawton expanded our understanding of functional status by defining more complex functions as IADL (cooking, shopping, banking, cleaning and use of the telephone) [21]. Other studies have subsequently attempted to combine ADL and IADL, placing items within a hierarchy. Spector *et al.* and Kempen *et al.* have advocated the combination of ADL and IADL items when constructing scales [27, 28].

In a Canadian elderly sample, Thomas *et al.* found that bathing was more difficult than a number of IADL items such as management of treatment and use of the telephone [29]. Njegovan *et al.* [30] showed that bathing is lost before use of the telephone or finance management. Spector *et al.* found that bathing is the fourth activity for which patients need help [27].

Among the characteristic neuropsychological deficits in LBD, visuospatial and executive impairments exist. Kamiya *et al.* [31] showed that decreased visuospatial cognition in AD patients influences ADL which is apparent in activities such as bathing and dressing.

Artero *et al.* [32] showed that elderly people with a deficit in attention show greater difficulties in dressing, using the toilet and bathing, and visuospatial complications are related to greater difficulty in performing these latter tasks. A decline in visuospatial tasks is seen to constitute a significant risk factor for a parallel decline in the ability to dress (OR: 19,28), more so than using the telephone for example (OR: 5,59). A decline in attentional ability was observed to increase the risk of loss of independence using the toilet (OR: 4,94).

Our investigation has several limitations including the fact that it was retrospective, monocentric, and a small sample size was used. Nevertheless, based on the use of several models combining autonomy scales, with sensitivity analysis reinforcing the validity of the results to explore a possible bias, we may elaborate on some investigative leads for prospective studies. First, it should be noted that use of the IADL with the sexualized items led to an excessive amount of missing values and a loss of

power (*supplementary table 1*). Second, with more detailed data on the type of cognitive disorder (executive function, visuospatial cognition), we may attempt to elucidate the mechanisms. Additionally, it may be interesting to take into account neuropsychological complications and behavioural disorders as these appear to be involved in cognitive impairment and quality of life [33, 34]. Behavioural disorders can interfere with autonomy and might be another interesting variable, which was, unfortunately not considered here.

Finally, the most important possible bias is related to the inability to fully differentiate between AD and LBD in our cohort, even though we attempted to do this as rigorously as possible. Only a small percentage of LBD patients had undergone a lumbar puncture and one of these patients had CSF biomarkers in favour of AD, however, we concluded that this patient had LBD based on the clinical pattern and scintigraphy results. One patient consumed a significant amount of wine, which was taken into account regarding his cognitive disorder, however, this did not correspond to alcoholic dementia.

On the other hand, this original study has several strengths. By investigating each type of activity individually, we were able to more precisely examine the extent of change among the different activities. Moreover, the multivariate statistical analysis shows that loss of autonomy is independent of important cofactors, such as motor dysfunction and comorbidities. This study complements and confirms previous data in the literature.

Keywords

- Functional decline is a major problem in patients with major neurocognitive disorders associated with Alzheimer's disease or Lewy Body Dementia.
- Our work shows that patients with LBD have a more rapid loss of autonomy, particularly for toileting, dressing and personal care, than those with Alzheimer's disease,
- This difference is independent of the MMSE score, comorbidities and motor dysfunctions associated with parkinsonism.

Conclusion

This study shows a decrease in autonomy in LBD patients with mild cognitive decline over a median follow-up of 13 months, which occurs faster than in AD patients, related, in particular, to bathing, dressing and personal care [12-15]. These results are in accordance with studies in which the ADL and IADL scales are combined, which may be related to visuospatial or/and executive function impairment. Further investigation on specific cognitive activities and their consequences are needed to confirm our findings and elucidate the mechanisms involved.

Conflicts of interest : None of the authors have any conflict of interests to disclose.

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