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# MEMORY IMPAIRMENT IN DEMENTIA WITH LEWY BODIES RELATIVE TO ALZHEIMER'S DISEASE AND PARKINSON'S DISEASE WITH DEMENTIA

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## SUMMARY

### Background:

The cognitive profiles of patients with dementia with Lewy bodies (DLB) and Parkinson's disease with dementia (PD-D) are quite similar, though different from Alzheimer's disease. However, studies comparing the memory performance of patients with DLB, PD-D and AD are rare.

### Material/ Methods:

Patients with DLB, AD and PD-D – matched for general cognitive status – were compared on a range of memory measures. Semantic memory, verbal fluency and verbal learning were assessed.

### Results:

Delayed verbal recall was better preserved in DLB and PD-D than AD. Semantic memory was better preserved in PD-D than AD. Neither letter nor category fluency differentiated between the groups.

### Conclusions:

Our study shows the usefulness of the Auditory Verbal Learning Test (AVLT) as an easily administered verbal learning measure for further research assessing episodic memory in DLB in comparison to PD-D and AD.

**Key words:** episodic memory, semantic memory, learning

## INTRODUCTION

Dementia with Lewy bodies (DLB) is a relatively new clinical concept. The key features of DLB include:

- fluctuating cognition;
- visual hallucinations;
- parkinsonism.

Suggestive features include:

- low dopamine transporter uptake in basal ganglia in SPECT/PET scan;
- REM-sleep behavior disorders;
- hypersensitivity to neuroleptics.

Among the supportive features are:

- repeated falls and syncope;
- transient, unexplained loss of consciousness;
- severe autonomic dysfunction, such as orthostatic hypotension;
- urinary incontinence;
- hallucinations other than visual;
- systematized delusions;
- depression;
- relative preservation of medial temporal lobe structures on CT/MRI scan;
- generalized low uptake on SPECT/PET perfusion scan with reduced occipital activity;
- abnormal (low uptake) MIBG myocardial scintigraphy;
- prominent slow wave activity on EEG with transient sharp waves in the temporal lobes (McKeith 2005).

In clinical practice it is particularly important to achieve a differential diagnosis between DLB, Parkinson's disease with dementia (PD-D) and Alzheimer's disease (AD), as some medications may be harmful for DLB patients (e.g. neuroleptics); also, parkinsonism can be successfully treated with levodopa, while dopamine agonists should be avoided (they may trigger psychosis and hypotension).

The differential clinical diagnosis of DLB and PD-D can be difficult due to the overlap of the symptomatology. DLB and PD-D have many common motor, cognitive, and psychiatric features. The neuropathological evidence also suggests that both conditions are part of the same clinical spectrum (Jelinger 1996, Jelinger 2009, Tsuboi et al. 2007). DLB is differentiated from PD-D by time criterion. If the patient with Parkinson's disease (PD) develops dementia later than one year after the onset of motor symptoms, he/she is then diagnosed with PD-D. If parkinsonism and cognitive impairment appear simultaneously or if cognitive decline precedes the onset of motor symptoms, the patient is diagnosed with DLB.

The cognitive profile of DLB differs from amnesic Alzheimer's disease (AD). DLB patients present with earlier and more profound attentional, executive and visuoperceptual impairments than amnesic AD patients. The visuoperceptual deficits observed in DLB may be similar to those observed in a visual variant of AD (posterior cortical atrophy, PCA), although PCA patients present with more focal symptoms (e.g. visual agnosia, color agnosia, hemianopsia). In spite of quantitative differences between DLB and amnesic AD, these deficits and cognitive fluctuations in DLB pa-

tients may be reflected in different qualitative patterns of neuropsychological task performance in DLB compared with AD (Doubleday 2002). Memory deficit is regarded as specific for AD, while dysexecutive syndrome and visuospatial impairment are specific for DLB and PD-D (Shimomura et al. 1998, Simard et al. 2000, Collerton et al. 2003, Metzler-Baddeley 2007, Oda et al. 2009, Paçhalska & Łukaszewska 2011). Moreover, a study by Simard et al. (2002) showed that working memory was more impaired in DLB than in AD, while AD patients had more deficient verbal episodic memory.

Comparative studies analyzing memory function in PD-D, DLB and AD are rare. Only two studies - in which patients were matched in terms of cognitive status - have compared episodic memory in AD, DLB and PD-D patients. Patients with DLB and PD-D had memory scores superior to those of AD patients on the Dementia Rating Scale (DRS) (Aarsland et al. 2003). A similar pattern of results was noted by Noe et al. (2004) for verbal material in the Buschke Selective Reminding Test (BSRT). However, DLB patients performed worse on the visual memory measure in the same study. There is evidence that patients with DLB perform better than patients with AD in verbal recall tests (Noe et al. 2004, Simard et al. 2002). It has been suggested that memory impairment in DLB results from defective encoding as a consequence of a slowed learning process, rather than a consolidation deficit (Hamilton et al. 2004). In DLB and PD-D patients have problems with spontaneous retrieval of information without significant loss after a delay, as evidenced by improvement in the delayed recognition trials (Tröster 2008). Problems with delayed free recall but not recognition tasks are consistent with the type of fronto-striatal dysfunction connected with DLB, compared to the hippocampal atrophy associated with AD (Crowell et al. 2007). Poor learning results may sometimes stem from working memory impairment (see Metzler-Baddeley 2007) and / or defective encoding (Goldmann et al. 2008).

In this study we compare the verbal learning profile in DLB to PD-D and AD patients. To our knowledge this is the first attempt to analyze verbal learning of unstructured material with a straightforward procedure, unlike the one from BSRT. It was assumed that AD patients would have major difficulty in delayed recall, while DLB patients would present with the greatest number of intrusions. Ours is also the first study comparing semantic memory in DLB, PD-D and AD. We hypothesized that semantic memory scores would not differentiate between the groups. The identification of different memory pattern in the results of neuropsychological tests would be valuable in the differential diagnosis of AD, DLB and PD-D.

## **MATERIAL AND METHODS**

### **Patients**

We studied 13 DLB patients, 13 patients with probable AD, and 18 patients with PD-D, who volunteered for the study. Dementia with Lewy bodies was diagnosed according to the improved diagnostic criteria of the third report of the DLB Consortium, published in 2005 (McKeith et al. 2005). All the DLB patients met the criteria for probable DLB. Alzheimer's disease was diagnosed based on the diagnostic criteria of the DSM-IV (Wciórka 2008). PD was diagnosed according to the Parkinson's

Disease United Kingdom Brain Bank criteria (Gelb 1999, Hughes 1993). As current diagnostic criteria for PD-D were published in 2007 (Emre 2007) and the study was conducted in 2004-2005, PD-D was diagnosed according to DSM-IV (Wciórka 2008). All groups were matched for age, years of education, and global cognitive performance (Mini-Mental State Examination) (see: Table 1).

### Clinical Diagnostic Criteria

In all patients, a neurological examination was accompanied by a structured interview with the caregivers. All these patients received magnetic resonance imaging to exclude focal brain lesions. PD-D patients were tested in the “on” phase. DLB patients were not examined during a period of marked confusion.

Our neuropsychological assessment included the Mini-Mental State Examination (Folstein et al. 1975) to match the patients for general cognitive impairment. Semantic memory was assessed by Information and Vocabulary subscales from Wechsler Adult Intelligence Scale-Revised (Brzeziński et al. 2004). Verbal fluency was tested by means of letter (“K”) and semantic (“animal”) 60-second fluency trials (Lezak 2004). Verbal learning was assessed with the 15-word Auditory Verbal Learning Test (AVLT) (Choynowski & Kostro 1980, Lezak 2004). AVLT is the most popular verbal learning measure, but it has never been used to assess this parameter in DLB, AD and PD-D. In contrast to the BSRT (used by Noe et al. 2004), the test procedure in the AVLT is easy, and test performance relies less on cognitive control and working memory, and more on the episodic memory that it is supposed to test. Additionally, Ferman et al. (2006) indicated that the AVLT percentage retention, in conjunction with the results of the TMT A, the BNT, and the “copy” test of the Rey-Osterrieth Com-

Table 1 Demographic data

	1 DLB (n=13)	2 AD (n=13)	3 PDD (n=18)	F	p
age at the time of the assessment (yr)	73.77 (4.46)	75.00 (8.24)	71.67 (3.27)	1.69	0.20
gender (male), n(%)	5(38%)	7 (54%)	12 (67%)	-	-
education (yr)	10.54 (3.23)	10.00 (4.74)	9.28 (4.07)	0.39	0.69
number of years since the subjective onset of symptoms	2.15 (1.91) [1-3]	1.25 (1.66) [2-3]	9.00 (4.19) [3-1,3-2]	30.10	<0.001
MMSE	16.92(6.56)	15.31(6.18)	19.06 (4.49)	1.69	0.20
age at onset	71.62 (4.86) [1-3]	73.92 (8.20) [2-3]	62.67 (4.41) [3-1,3-2]	16.14	<0.001

Values are expressed as mean (SD), unless otherwise indicated  
The significant intergroup differences are indicated in brackets

plex Figure, is a highly sensitive and specific instrument for the differential diagnosis of DLB and AD. Three AVLT scores were computed: the number of words repeated in all trials, the number of intrusions, and the percentage of information lost over a 10-minute delay. Motor function was assessed by the Finger Tapping Test from the Halstead-Reitan Neuropsychological Assessment Test Battery (Kądziaława 1990).

### Statistical procedure

For group comparisons, parametric data were analyzed by Student's t test and one-way analysis of variance (ANOVA) with Scheffe's or Tamhane's TS post hoc tests. A significance level of  $P < 0.05$  was used in all comparisons.

## RESULTS

### Demographic characteristics and dementia severity

All groups were matched in terms of age, education and general cognitive impairment (MMSE), as shown in Table 1. The disease duration was much longer in PD-D patients than in DLB and AD, which is consistent with the late onset of dementia in the course of the disease.

### Neuropsychological findings

AD group had lower Information Scores than the PD-D group (see Table 2), but the difference between AD and DLB was not statistically significant. Neither the Vocabulary score, nor category fluency, nor letter fluency differentiated among the groups. Delayed recall in AVLT was more deficient in AD patients than in the DLB and PD-D groups. The difference in immediate recall scores did not reach statistical significance. DLB patients generated the highest number of intrusions in AVLT, but the difference was statistically nonsignificant, as proved by Tamhane's TS post hoc test. Motor speed was higher in AD than in DLB and PD-D patients.

Table 2 Cognitive assessment results

Test (range)	DLB (1)	AD (2)	PDD (3)	F	p
Information (1-19)	<b>6.67 (2.02)</b>	<b>4.54 (2.93)</b> [2-3]	<b>7.78 (2.84)</b> [3-2]	<b>5.60</b>	<b>0.01</b>
Vocabulary (1-19)	7.50 (3.96)	4.67 (3.92)	7.71 (2.91)	2.95	0.07
category fluency	7.69 (3.99)	7.54 (4.05)	9.89 (4.23)	1.63	0.21
letter fluency	4.46 (2.63)	6.00 (3.03)	4.17 (1.33)	1.50	0.24
AVLT sum of 5 trials (0-75)	21.50 (11.97)	14.15 (8.14)	22.17 (8.08)	3.14	0.05
AVLT sum of intrusions	16.50 (16.78)	5.92 (4.77)	6.89 (7.63)	4.01	0.03
AVLT loss of information following a delay	<b>39.51 (23.95)</b> [1-2]	<b>84.34 (26.54)</b> [2-1,2-3]	<b>55.84 (26.64)</b> [3-2]	<b>9.73</b>	<b>0.0004</b>
Finger tapping test (T)	<b>18.75 (11.79)</b> [1-2]	<b>33.04 (17.38)</b> [2-1,2-3]	<b>18.58 (10.08)</b> [3-2]	<b>5.29</b>	<b>0.01</b>

AVLT- Auditory Verbal Learning Test

Values are expressed as mean (SD), unless otherwise indicated

The significant intergroup differences are indicated in brackets

## DISCUSSION

Impairment of working and episodic memory is quite common in DLB (Metzler-Baddeley 2007, Simard et al. 2000). However, as explained by Metzler-Baddeley (2007), the interpretation of memory impairment in DLB is difficult, since perceptual, attentional and executive deficits may be interfering with the encoding or retrieval of information and, as a consequence, contribute to lower memory scores. Thus abnormal memory scores may not reflect true memory deficits, but other cognitive problems. Moreover, the assessment of memory in DLB may be significantly obscured by cognitive fluctuations.

In our study, immediate recall was not significantly poorer in AD than in the DLB and PD-D group. This suggests quite similar immediate recall deficits in AD and DLB. However, the observed trend towards statistical significance – lower scores in DLB – was in accordance with Noe et al.'s results (2004). In DLB, initial encoding is compromised by the attentional problems, which is observed in immediate recall results. However, a small part of the information is usually successfully encoded, and can be recalled in a delayed recall task (Lambon-Ralph et al. 2001; Bidzan et al. 2012).

As expected, delayed recall was most deficient in the AD group, which is consistent with previous observations (Noe 2004, Aarsland 2003, Calderon 2001) and the specificity of the amnesic AD variant, which is characterized by profound episodic memory impairment with significant loss of information over delay (Stopford 2008).

Semantic memory impairment, present in both AD and DLB, is not a key feature of any of these disorders. No semantic memory differences between DLB and AD patients were identified in our study, which is in accordance with previous findings (Calderon 2001, Lambon-Ralph et al. 2001; cf. Metzler-Baddeley 2007). It is worth noting that in Lambon-Ralph et al.'s study (2001), DLB patients were characterized by more severe semantic deficits for pictures than words, which may stem from the overlap of semantic and visuo-perceptual impairment.

Neither letter nor category fluency differentiated between the groups in our study, which is in accordance with the results obtained by Noe et al. (2004). Other studies have shown that DLB patients' performance is lower than AD patients' performance on letter fluency (Calderon et al. 2001, Lambon-Ralph et al. 2001, Won Park et al. 2011), which may be due to executive impairment. Patients with various neurodegenerative diseases may achieve similar results on verbal fluency trials because of different deficits. Category dysfluency in AD is mainly the effect of semantic impairment (see Levy et al. 2002), as evidenced by problems with clustering (Tröster et al. 1998, Tröster 2008, Troyer et al. 1998), while PD patients have problems with semantic retrieval (cf. Levy et al. 2002) and difficulties with switching from one subcategory to another (Tröster et al. 1998, Tröster 2008).

In our study, the patients with DLB had the largest number of intrusions in the memory test, although the difference was not statistically significant. It was demonstrated that DLB patients present with an overall tendency to intrusions during the testing and interview, which is a differentiating qualitative feature between AD and DLB (Doubleday et al. 2002). The difference in our study may not have reached statistical significance because we analysed only the intrusions occurring during the verbal learning task.

It is worth mentioning that no significant differences between the patients with DLB and PD-D were identified in our study, which is consistent with previous studies (cf. Metzler-Baddeley 2007). The clinical and neuropsychological characteristics can be similar in PD-D and DLB. This confirms that the PD-D and DLB syndromes constitute a continuum of Lewy body disease, rather than distinct disease entities (Janvin et al. 2006).

Additionally, differences were identified in our study between DLB, PD-D and AD patients in the finger tapping test, which is in accordance with previous findings (Gnanalingham 1997). The differences result from the bradykinesia characteristic for PD-D and DLB patients.

Our study has several limitations. To begin with, the sample sizes were small. Semantic memory was tested only in the verbal domain, which may have influenced the results. Only verbal memory was tested, and the testing procedure did not include a recognition trial to differentiate between retrieval and encoding/storage deficits. What is more, our study focused only on the quantitative measures, and did not take into account the qualitative features of the patients' performance, which may be of utmost importance (Doubleday 2002).

## CONCLUSIONS

Our study shows the utility of AVLT as an easily administered verbal learning measure for further research to assess episodic memory in DLB in comparison to PD-D and AD. It is likely that analysis of intrusions, in combination with cognitive control assessment, could shed light on memory impairment in DLB.

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