

Demographic and Neuropsychologic Profiles of Patients with Neurodegenerative Dementia: Results from A Tertiary Referral University Hospital

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Abstract

Objective: Although the prevalence of dementia is increasing globally, the data related to dementia patients living in North Cyprus is very limited. The aim of this study was to evaluate the demographic and neuropsychological characteristics of patients diagnosed with neurodegenerative dementia.

Materials and Methods: The data of 105 patients with neurodegenerative dementia, who were followed up in the neurology departments of the Dr. Suat Günsel University of Kyrenia Hospital and Near East University Hospital between 2018 and 2021, were collected both retrospectively and prospectively. The patients underwent diagnostic procedures by neurologic examination, neuropsychologic evaluation based on the measures of attention and executive functions, memory, language, mood and visuospatial perception and neuroimaging. All the results were evaluated statistically according to the dementia subgroups.

Results: Out of 105 patients, 58 were female and 47 were male. The mean age was 74.34 ± 10.41 . The most common dementia type was Alzheimer's dementia (AD) (77/105), followed by Lewy body dementia (LBD) (15/105) and frontotemporal dementia (FTD) (13/105). The initial median mini mental state examination (MMSE) score was 20. There was a positive correlation between years in higher education and lower MMSE scores. Out of the 105 patients, 81 spoke Turkish and 13 spoke English as a native language. Depression occurred more frequent in earlier stages and milder cases. The visuospatial functions were affected more in LBD and FTD patients when compared to AD patients. Prosopagnosia was significant for the differential diagnosis of Parkinson's dementia from other forms of dementia. Also, a decrease in categorical fluency was observed in patients with higher depression scores.

Conclusion: These results are important as this is the first study determining the detailed dementia subgroups and neuropsychologic profiles of dementia patients living in North Cyprus.

Keywords: Dementia, neurodegeneration, prosopagnosia, aging, Alzheimer's disease

Introduction

There is a growing probability of chronic and age-associated diseases like dementia. The global prevalence of dementia in the general population older than 60 years of age is 5-7% (1). The majority of these patients live in low and middle income countries. The strongest known risk factor is age, but dementia

does not develop as a normal part of aging. The most common type of dementia is Alzheimer's disease (AD) accounting for 60-70% of all dementia patients (2,3).

Lewy body dementia (LBD) is an umbrella term covering two clinical entities, namely Parkinson's disease dementia (PD) and Dementia with Lewy bodies (DLB), making it the second most

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Received: 11.09.2022 **Accepted:** 14.11.2022



Cite this article as: Gelener P, Ertuğrul Mut S, Diker S, Çelik F. Demographic and Neuropsychologic Profiles of Patients with Neurodegenerative Dementia: Results from A Tertiary Referral University Hospital. Eur J Geriatr Gerontol 2023;5(1):59-65

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common type of neurodegenerative dementia after AD (4,5). DLB accounts for 24.7% of people with dementia (6). According to the DLB consortium, they are distinguished by the relative timing of motor Parkinsonism (7).

DLB should be diagnosed when dementia occurs before or concurrently with Parkinsonism, whereas PD is the dementia that occurs in the context of well-established Parkinson's disease (6).

Patients with Parkinson's disease (which is the second most common neurodegenerative disease) have a 2.5-6 times higher risk of developing dementia than people without disease (8). The cognitive involvement with executive and visuospatial impairments is typical in these patients (9).

Frontotemporal dementia (FTD) predominantly affects frontal and/or temporal lobes with three prototypes semantic dementia, progressive non-fluent aphasia and behavioral variants (10). Primary progressive aphasia (PPA) is in the frontotemporal spectrum group, where the prominent clinical feature is difficulty with language (11), whereas the behavioral variant of FTD requires three of six discriminating features consisting of disinhibition, apathy, loss of empathy, compulsive behaviors, hyperorality and dysexecutive neuropsychological profile (12).

After the consensus clinical diagnostic criteria were established in 2011, FTD was classified as a behavioral variant, whereas semantic and progressive non-fluent aphasia variants were classified under the umbrella of PPA (11,12).

FTD accounts for 20% of all cases of degenerative dementia. According to some sources, the prevalence of FTD is similar to that of AD with 15 cases per 100.000 in 45-64 age group (13,14).

The aim of this study is to determine the demographic findings and neuropsychological profiles of patients with neurodegenerative dementia living in North Cyprus.

Materials and Methods

Patient Selection and Diagnostic Evaluation

The data of 105 patients with neurodegenerative dementia who were followed up in the neurology departments of the Dr. Suat Günsel University of Kyrenia Hospital and Near East University Hospital between 2018 and 2021 were collected. The study was conducted both retrospectively (including the patients without any missing data in the system) and prospectively for newly diagnosed patients.

All the patients underwent neuropsychological assessment by a single certified neuropsychologist. All patients had dementia blood screen and structural imaging was performed preferentially with MRI.

The diagnostic procedure included movement disorder society PDD criteria, DLB consortium criteria, National Institute of

neurological disorders and stroke association criteria and FTD consortium new highly sensitive revised criteria (4,7,12,15-18). The final diagnosis was made by the neurologist.

Neuropsychological Assessment

The neuropsychologic tests were performed on all patients in Turkish or English according to the patient's native language. These assessments were focused on the main measures of attention and executive functions, memory, language, mood and visuospatial perception.

The neuropsychological test battery included 14 tests namely the mini-mental state test (19), digit span test (20,21), trails making test (22), verbal fluency (23), clock drawing test, stroop color word interference test (24), similarities (WAIS-R subtest) (25), Luria test, Benton line judgment orientation test (26), Benton facial recognition test (27), figure copying test, Boston naming test (28), Oktem verbal memory processes test (29) and geriatric depression scale (30).

According to the Turkish validated version of the mini mental state examination (MMSE), the cut-point for cognitive function was as follows: 24-30 points: Normal range, 23-18: Mild dementia, 17-0: Severe dementia (31).

The trail making test has been standardized in the Turkish alphabet in the B form, where the letters are in the range of A-I and the normal values of the test for participants aged 50 and over were determined by Cangoz et al. (32).

The standardized clock drawing test for the Turkish sample aged 50 and over was used for Turkish speaking patients (33).

Also, valid and reliable Turkish forms of the stroop color word interference test (34), Benton facial recognition test (35), and Boston naming test (36) were used.

For the Geriatric depression scale, the Turkish validity-reliability study was conducted by Ertan et al. (37) and the cut-off score was determined to be 14.

The inclusion criteria: The patients who were diagnosed with neurodegenerative dementia according to the above-mentioned criteria and underwent the neuropsychologic test battery that was performed by the same educated neuropsychologist.

The exclusion criteria: Patients were excluded if they had any psychiatric disorder, secondary causes of dementia like normal pressure hydrocephalus or Limbic encephalitis, mild cognitive impairment or neuroimaging evidence of another disorder that could explain their symptoms or had no neuroimaging available.

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures were approved by the University of Kyrenia Ethics Committee (date: 25.01.2022, no: GÜ/ETK-22-20).

Statistics

The normality of the data was evaluated using histograms, q-q plots and the Shapiro-Wilk test. Correlations between categorical variables were evaluated using the chi-square test and Monte-Carlo method. Age and group comparisons were made by using the Student's t-test. The level of statistical significance was set at $p < 0.05$. Analysis of the data was performed using SPSS 22 statistical software.

Results

The study included 105 patients with degenerative dementia. Out of these 105 patients, 58 (55.2%) were female and 47 (44.8%) were male. The mean age at diagnosis was 74.34 ± 10.41 . The causes of dementias were AD in 77 (73.3%), FTD in 13 (12.4%), DLB in 6 (5.7%) and PD in 9 (8.6%) patients.

The initial median MMSE score at diagnosis was 20 (ranging from 14 to 23). According to the MMSE scores, 43 (41.7%) of them had severe dementia, and 37 (35.9%) had mild dementia at the time of diagnosis. The MMSE score was normal in 23 (22.3%) patients.

The years of education were between 0-5 years in 26 (25.7%), 6-11 years in 45 (44.6%) and 12 years and above in 30 (29.7%) of the patients.

Depression was observed in 26 (36.1%) of the patients. There was also a statistically significant association between geriatric depression and MMSE scores ($p < 0.05$). Higher depressive scores were observed in milder dementia cases.

There was a statistically significant positive correlation between years in higher education and lower MMSE scores ($p < 0.05$).

Out of 105 patients, 81 (77.1%) of them spoke Turkish and 13 (12.4%) spoke English as a native language. Ethnic backgrounds included 61 (62.2%) Turkish Cypriots with permanent residency in North Cyprus, whereas the others comprised a mixture of citizens and residents from Turkey, England, Russia and Turkmenistan.

Detailed descriptive statistic results of the Benton facial recognition, Benton line judgement orientation, clock drawing, Boston naming, similarities, verbal fluency, figure copying, Trails making, Stroop color Word interference, Oktem verbal memory processes, Attention and Fluency tests are shown in Table 1.

When the dementia subgroups and visuospatial, attention and executive functions were compared, a statistically significant association was observed. The visuospatial functions were affected more in LBD, FTD and PD compared to AD ($p < 0.05$) (Table 2).

The Benton facial recognition test was statistically significant for the differential diagnosis of PD from other types of dementia

Table 1. The neuropsychologic test results of the patients	
Variables (Neuropsychologic domains and tests)	Descriptive statistics n (%)
Benton facial recognition test	
Normal	23 (53.5)
Borderline	6 (14.0)
Impaired	7 (16.3)
Advanced impaired	7 (16.3)
Benton line judgement orientation test	
Normal	14 (35.9)
Impaired	25 (64.1)
Clock drawing test	
Normal	35 (38.9)
Impaired	55 (61.1)
Boston naming test	
Normal	26 (56.5)
Impaired	19 (41.3)
Similarities (WAIS-R subtest)	
Normal	23 (39.7)
Impaired	35 (60.3)
Lexical fluency	
Normal	16 (29.6)
Impaired	38 (70.4)
Figure copying	
Normal	49 (56.3)
Impaired	38 (43.7)
Luria's test	
Normal	14 (30.4)
Impaired	32 (69.6)
Trail making test	
Normal	5 (8.5)
Impaired	54 (91.5)
Stroop color word interference test	
Normal	2 (13.3)
Impaired	13 (86.7)
Oktem verbal memory processes test	
Normal	9 (10.1)
Impaired	80 (89.9)
Basic attention	
Normal	37 (40.7)
Impaired	54 (59.3)
Complex attention	
Normal	4 (4.7)
Impaired	82 (95.3)
Categorical fluency	
Normal	6 (40.0)
Impaired	9 (60.0)
Semantic fluency	
Normal	4 (26.7)
Impaired	11 (73.3)

($p < 0.05$) (Table 3). There was no other correlation between the other tests and dementia subgroups.

When the geriatric depression scales were compared with the diagnosis and different neuropsychologic domains; a decrease in categorical fluency was positively associated with higher depressive scores ($p < 0.05$). No other relation was observed among dementia subtypes, other neurodomains and depression.

Discussion

In the study group, the most common etiology of neurodegenerative dementia was AD (73.0%). The second most common type of dementia was LBD with 14.3% and 12.4% FTD respectively. There was a higher number of female patients (55.5%) and all these findings are parallel to the current literature.

Men have a higher risk of developing DLB (5) and the male predominance of FTD in the US, Greece and Turkey was reported in previous studies (38). However, there was a female predominance (17/28) in our LBD and FTD group.

The study population was relatively well educated as 74.6% had secondary or higher education. It is known that the sensitivity of MMSE is low in highly educated populations (39,40). In our patient group, we also observed a relation between higher education years and lower MMSE scores ($p < 0.05$). MMSE cannot distinguish dementia syndromes and some patients who meet

the criteria may score in the normal range (41). This is also in line with our findings as 22.3% of the patients were considered to be in the normal range according to the MMSE scores.

Late-life depression and dementia may share common neurobiology in older patients. Depression is considered as a prodrome and/or risk factor for dementia (42). Depression was observed in 26 (36.1%) of the patients.

In a recent published study, early stage Alzheimer’s patients had higher MMSE and more depressive symptoms (43). This finding is similar to ours as there was an association between geriatric depression and MMSE scores ($p < 0.05$). Higher depression scores were observed in cases of milder dementia and higher MMSE scores in our study group.

Patients with neurodegenerative dementia have different neuropsychological profiles, which can only be distinguished in the early phases of dementia. For example, in typical AD, episodic memory is impaired whereas executive functions and behavior are relatively spared. On the other hand, in FTD, episodic memory is typically spared, whereas executive functions (working memory, planning, generation, abstraction, problem solving and mental flexibility) and behavior are impaired (12,44). In DLB, executive, visuospatial and attention deficits are more prominent compared to other types of dementia (5,45,46). This finding is similar to our finding in that the visuospatial functions were affected

Table 2. The relation between dementia subgroups and attention, executive and visuospatial functions

Variables	Diagnosis				p
	AD (n=77)	LBD (n=6)	FTD (n=13)	PD (n=9)	
Visuospatial functions					
Normal	28 (45.9)	0 (0.0)	2 (16.7)	2 (25.0)	0.039
Impaired	33 (54.1)	6 (100.0)	10 (83.3)	6 (75.0)	
Attention and executive functions					
Normal	2 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	0.999
Impaired	68 (97.1)	6 (100.0)	13 (100.0)	9 (100.0)	

AD: Alzheimer’s dementia, LBD: Lewy body dementia, FTD: Frontotemporal dementia, PD: Parkinson disease dementia

Table 3. The relation between dementia subgroups and prosopagnosia

Variables	Diagnosis				p
	AD (n=77)	LBD (n=6)	FTD (n=13)	PD (n=9)	
Benton facial recognition					
Normal	18 (60.0)	2 (100.0)	3 (50.0)	0 (0.0)	0.020
Borderline	5 (16.7)	0 (0.0)	1 (16.7)	0 (0.0)	
Impaired	4 (13.3)	0 (0.0)	2 (33.3)	1 (20.0)	
Advanced impairment	3 (10.0)	0 (0.0)	0 (0.0)	4 (80.0)	

AD: Alzheimer’s dementia, LBD: Lewy body dementia, FTD: Frontotemporal dementia, PD: Parkinson disease dementia

more dominantly at the time of diagnosis in patients with LBD, FTD and PD compared to the patients with AD ($p < 0.05$) (Table 2).

Prosopagnosia is widely reported in patients with posterior cortical atrophy (pathologically considered as AD) and FTD, but is less expected in PD (47,48). A very interesting case of index patient was reported with a novel PSEN mutation causing early onset AD with prosopagnosia and Parkinsonism together (49). According to a recent study, prosopagnosia was the most unique symptom of right temporal variant of FTD. This finding was not seen in AD and less in FTD group (50). According to our findings, prosopagnosia was a statistically significant finding for the differential diagnosis of Parkinson's dementia from other types of dementia ($p < 0.05$). Similarly, it has previously been reported in different studies that unfamiliar face recognition memory and facial expression recognition may be impaired in the course of Parkinson's disease (47,51). The mechanism proposed here, is the addition of the posterior-cortical defect over frontal executive impairment (52). Also, cases who developed paroxysmal prosopagnosia episodes before progressing from Parkinson's disease to PD were reported in the literature (48).

In our study group, when depression was compared with the dementia subgroup and neuropsychologic domains; no association was found between depression and dementia subgroups. Some studies suggest that action naming is more affected in FTD, whereas object naming is more disturbed in AD (53).

According to our findings, a decrease in categorical fluency was positively associated with higher depressive scores ($p < 0.05$).

It is also important to emphasize that neuropsychological profiles are not always definite rules. Foreexample approximately 10% of patients with FTD may show episodic memory deficits at initial presentation (54,55).

Another point is that the large FTD consortium study was carried out mainly on Western European and North American behavioral FTD patients whose native language is English and it may not effectively diagnose those speaking other languages (56).

Study Limitations

In our patient group, only 13.3% of the patients spoke English as their native language and 37.8% of them had migration backgrounds. It is known the patients with migration backgrounds may also cause different challenges, including language skills and cultural characteristics, leading to difficulties in evaluating cultural and language sensitive cognitive tests causing under diagnosis (57,58). This may be one of the limitation of our study. Another limitation is that our battery did not include specific tests such as the social recognition test (which is highly recommended in recent studies) in FTD patients. Our sample size is also limited to the patients at two different tertiary referral centers.

Conclusion

Our study revealed the first data of patients with neurodegenerative dementia in North Cyprus. The most common type was AD, followed by LBD and FTD. Depression occurred more in patients in the earlier stages. The visuospatial functions were affected more in LBD and FTD patients and prosopagnosia was significant for the differential diagnosis of PD from other forms of dementias.

Ethics

Ethics Committee Approval: This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures were approved by the University of Kyrenia Ethics Committee (date: 25.01.2022, no: GÜ/ETK-22-20).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: P.G., S.E.M., S.D., F.Ç., Design: P.G., S.E.M., S.D., F.Ç., Data Collection or Processing: P.G., S.E.M., S.D., F.Ç., Analysis or Interpretation: P.G., S.E.M., Literature Search: P.G., S.E.M., Writing: P.G., F.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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