A comparison of Sentence Production of Turkish Patıents wıth Early and Late-Onset Alzheimer's Disease

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Abstract
Alzheimer's disease (AD) is a degenerative brain disease and the most common cause of dementia, accounts for an estimated 60 percent to 80 percent of cases. AD has two subtypes: Early-onset and Late-onset Alzheimer's disease. Both types are characterized by a decline in memory, problem-solving and other cognitive skills that affect a person's ability to perform everyday activities. Language is the other problem that is observed in these patients. The aim of this study is to examine the sentences production of patients with early and late onset Alzheimer's disease by using four different language tests and to compare all the results within groups and language tests. Our aim is to reveal the differences in sentence processing and language performance of Turkish Alzheimer patients. In order to reveal the sentence production of Turkish Alzheimer patients, 23 patients with early-onset Alzheimer's disease, 39 patients with late-onset Alzheimer's disease from Dokuz Eylul University, Faculty of Medicine, Department of Neurology and an age/education-matched control group are included in this study. The data were analyzed using t test and Mann-Whitney U test. For comparison of content and tests, Chi-square test (χ^2) was performed. It was found that patients with early-onset AD used more basic sentences in Picnic Picture description test, Cookie Theft Picture description test and the Story Picture Sequencing test compared to late-onset AD patients. In Random Speech test, patients with late-onset AD used more basic sentences. The other finding was about the nominal and the verbal sentences. It was revealed that patients with early-onset AD used more nominal sentences in all tests compared to late-onset patients. In terms of verbal sentences, it was found that patients with late-onset AD used more verbal sentences than the early-onset patients. Comparison about sentence production of AD patients within tests shows that the highest percent of basic sentence use of AD patients is in Picnic Picture test and the lowest percent is in Random Speech test. In conclusion, early-onset AD patients perform worse due to their cognitive deficits compared to late-onset patients. They tend to use basic and nominal sentences more.

Keywords: Alzheimer, early-onset Alzheimer's Disease, late-onset Alzheimer's Disease, sentence production, nominal and verbal sentences

Introduction

The term "dementia" describes a group of symptoms that can be caused by many diseases. These symptoms are mental confusion, memory loss, disorientation, intellectual impairment or similar problems. Alzheimer Disease (AD) is the most frequent cause of irreversible dementia in adults (Mace and Rabins, 2017: 6). There are some criteria applied for the diagnosis of the AD. The criteria were specified as: a decline in intellectual abilities (sufficient to interfere with social or occupational functions); memory impairment; and at least one of either impaired abstract thinking, impaired judgement, personality change or other disturbance of higher cortical function (e.g. aphasia, apraxia, agnosia or constructional difficulty) (Smith, Chenery and Murdoch., 1987: 50).

A progressive language decline in language abilities is a widely known clinical indication of AD and it is said to be as one of the earliest symptom of it. At the beginning, language deficits are not severe; however, these problems become severe during the later stages of AD (Emery, 2000: 146). Various linguistic fields such as phonology, syntax and semantics are affected in AD. When phonological abilities are considered, it can be seen that these abilities are not affected severely during mild and moderate stages of AD. Like phonological abilities, syntactic features of AD patients are often preserved in the early

stages and become severely affected in the later stages (Bayles and Kazniak, 1987: 121; Glosser et al., 1998: 33; Kemper et al., 1993: 83). The spesific language problems observed in AD are word finding difficulties, decline in semantic and pragmatic levels, phonological and syntactic difficulties, writing disorders. These problems vary with the stages of the disease. In the early stages, language impairment involves lexical retrieval problems, loss of verbal fluency, and breakdown in comprehension of higher order written and spoken languages. In the moderate and severe stages of AD, the loss of verbal fluency is profound, with breakdown of comprehension and literal and semantic paraphrases prominent; in very severe AD, speech is often restricted to echolalia and verbal stereotypy (Ferris and Farlow, 2013: 1009).

AD has been divided into two categories with respect to age of first clinical symptoms: early-onset and late-onset. Early-onset, or symptoms beginning before the age of 60-65 years, represents 6-7 % of all cases. The vast majority of AD cases present as late-onset, at ages older than 60-65 years (Golden and Josephs, 2015: 8). Early-onset Alzheimer disease (EOAD), with onset in individuals younger than 65 years, although overshadowed by the more common late-onset AD (LOAD), differs significantly from LOAD. EOAD comprises approximately 5% of AD and is associated with delays in diagnosis, aggressive course, and age-related psychosocial need (Mendez, 2017: 264). The consequences of being diagnosed early with a disease that implies progressive decline of cognitive abilities and activities of daily living performance, as well as changes in personality and behavioral disturbances, are enormous (Bakker et al., 2013: 38). Early onset differs in the areas of the brain which are targeted, rather than only in the rate of progression. The early onset patients appear to be hit harder in attention-related areas of memory, while the late onset patients appear to have more damage in areas related to recall and recognition (Kensinger, 1996: 27).

A crucial difference between early and late onset patients was language dysfunction. Early onset was associated with more language deficits. Early onset patients had more cases of aphasia (the loss or impairment of ability to use or understand speech) than the late onset patients (Kensinger, 1996: 26). The language impairment of early and late-onset AD has been examined in various research studies. Several kinds of language functions were described as more severely deteriorated in early rather than late-onset patients. However; other studies reported more profound language dysfunctions in late-onset patients. Due to the result of one or more methodological factors including lack of statistical power caused by small sample size, inappropriate measures and the presence of uncontrolled variables, differences about language impairment between early and late-onset Alzheimer's Disease could not be described well (Immamura et al., 1998: 946).

The aim of this study is to investigate the sentence production of patients with early-onset and late-onset Alzheimer's disease by using four different language tests and to compare all the results with a control group and within tests. In this investigation, basic sentences which were produced by all groups were examined in order to reveal how many of them are nominal and verbal sentences.

Methods

Participants

In order to decide the sample size of the study, a power analysis was used. Considering the results of the analysis, 62 patients (23 EOAD / 39 LOAD) from Dokuz Eylul

University, Faculty of Medicine, Department of Neurology and an age/education-matched control group consisting of 26 normal people were included in the study. The ages of all the groups were similar (EOAD: 59.86/ EOAD: 78.5/ CG: 62.88). Education levels of all participants are similar (at least secondary level).

Procedures

Before applying the language tests, a neurologist and a psychologist did a clinical interview, made a physical and neurological examination by using Mini-Mental State Examination (MMSE; Folstein et al., 1975), Auditory Verbal Learning Test (AVLT; Rey, 1964) Verbal Fluency Test (VFT) and Clinical Dementia Rating (CDR). In order to describe the linguistic performance of patients with EOAD and LOAD, four different language tests were used (Picnic Picture description test, Cookie Theft Picture description test, the Story Picture Sequencing test and Random Speech test). A pilot study was conducted to reveal the validity of these tests. The description abilities of the patients were evaluated with two Picture description tests: Picnic Picture (Western Aphasia Battery, Revised: Kertesz, 2007) and Cookie Theft (Boston Diagnostic Examination of Aphasia, Goodglass and Kaplan, 1983). These tests are chosen because it is stated that these tests are the most sensitive materials to assess the language performance of AD patients (Bayles et al., 1987). By using all these language tests the description and sequencing abilities as well as the spontanous speech of EOAD and LOAD patients were aimed to be examined. Patients were interviewed for approximately 10 minutes each with four tests and all interviews were recorded with a tape recorder and transcribed based on the DuBois' Discourse Transcription Symbols (1993). After analyzing the sentence production of all the groups, just grammatically acceptable sentences were considered as the data (Grammatically Unacceptable Sentences; Subject Group: 9.56 % / Control Group: 8.11 %). In this study, only basic sentences were analyzed as nominal and verbal basic sentences and all the data were compared within the groups and the tests.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) version 16.0 for Windows was used for the statistical analysis. Non-parametric analyses were performed as there was no equivalence in number, normal distribution, or homogeneity of variances (Qui-square and U-Mann–Whitney). There was a symmetrical distribution for the basic sentence structures related with the group comparisons, t test was performed.

Results

The study sample consisted of 23 patients with EOAD, 39 patients with LOAD and 26 normal people. The characterization of the study sample and details of both subgroups can be seen in Table 1. Age, gender, education level and MMSE mean scores were considered as the variables for the study.

Table 1. *Comparisons of demographic and clinical variables in both groups: EOAD, LOAD and CG*

	EOAD (n=23)	LOAD(n=39)	CG (n=26)	p
Age	59.86	78.5	62.88	0.292

Education	5	8	15	0.309
Gender♀	10	23	14	0.469
MMSE	19	29	30	<0.005

*EOAD: Early-onset Alzheimer's Disease/CG: Control Group

The comparisons of basic sentence structures obtained in four language tests are presented in table 2, 3 and 4. According to the results shown in table 2, patients with EOAD performed significantly poorly than the control group in Picnic Picture, Cookie Theft and Story Picture Sequencing tests. However, there is a statistically significant difference between patients with EOAD and the control group in Random Speech test (p=0.001).

Table 2. *Comparisons of basic sentence structures on four language tests of EOAD and CG*

Language Tests	N	Group	Mean	Standart Deviation	p
Picnic Picture	26	CG	9.615	4.833	0.872
	23	EOAD	9.391	4.812	
Cookie Theft	26	CG	5.846	3.662	0.748
	23	EOAD	5.521	3.328	
Story Picture Sequencing	26	CG	5.615	4.233	0.314
	23	EOAD	6.956	4.986	
Random Speech	26	CG	2.653	1.547	0.001
	23	EOAD	5.304	3.036	

Results in table 3 suggest that patients with LOAD performed significantly poorly than the control group in Picnic Picture, Cookie Theft and Story Picture Sequencing tests. Although not reaching statistical significance, a high mean of the basic sentence structures was noticed. On the other hand, there is a statistically significant difference between patients with EOAD and control group in Random Speech test (p=0.003).

Table 3. *Comparisons of basic sentence structures on four language tests of LOAD and CG*

Language Tests	N	Group	Mean	Standart Deviation	p
Picnic Picture	26	CG	9.615	4.833	0.514
	39	LOAD	10.871	8.915	
Cookie Theft	26	CG	5.846	3.662	0.192
	39	LOAD	6.666	4.618	
Story Picture Sequencing	26	CG	5.615	4.233	0.192
	39	LOAD	7.512	6.462	
Random Speech	26	CG	2.653	1.547	0.003
	39	LOAD	5.179	3.992	

As seen in table 4, there is no statistically significant difference between patients with EOAD and LOAD. However, when the mean of the sentences are considered, it is revealed that the patients with LOAD performed much better compared to the patients with EOAD in Picnic Picture, Cookie Theft and Story Picture Sequencing tests.

Table 4. *Comparisons of basic sentence structures on four language tests of EOAD and LOAD*

Language Tests	N	Group	Mean	Standart Deviation	p
Picnic Picture	23	EOAD	9.391	4.812	0.476
	39	LOAD	10.871	8.915	
Cookie Theft	23	EOAD	5.521	3.328	0.303
	39	LOAD	6.666	4.618	
Story Picture Sequencing	23	EOAD	6.956	4.986	0.724
	39	LOAD	7.512	6.462	
Random Speech	23	EOAD	5.304	1.547	0.897
	39	LOAD	5.179	3.036	

The comparisons of nominal sentence structures obtained in four language tests are presented in table 5, 6 and 7. It was found that there was a statistically significant difference about the nominal sentence structures between the EOAD and control groups in Picnic Picture, Cookie Theft and Story Picture Sequencing tests (p=0.001, p=0.020, p=0.003). However, there was no difference in Random Speech test within the groups.

Table 5. *Comparisons of nominal sentence structures on four language tests of EOAD and CG*

Language Tests	N	Group	p
Picnic Picture	26	CG	0.001
	23	EOAD	
Cookie Theft	26	CG	0.020
	23	EOAD	
Story Picture Sequencing	26	CG	0.003
	23	EOAD	
Random Speech	26	CG	0.142
	23	EOAD	

The results in table 6 revealed that there was a statistically significant difference about the nominal sentence structures between the LOAD and control groups in Picnic Picture, Cookie Theft and Story Picture Sequencing tests (p=0.001, p=0.015, p=0.000). There was no difference in Random Speech test within the groups.

Table 6. *Comparisons of nominal sentence structures on four language tests of LOAD and CG*

Language Tests	N	Group	p
Picnic Picture	26	CG	0.002
	39	LOAD	
Cookie Theft	26	CG	0.015
	39	LOAD	
Story Picture Sequencing	26	CG	0.000
	39	LOAD	
Random Speech	26	CG	0.432
	39	LOAD	

Results in table 7 suggest that there is no statistically significant difference between patients with EOAD and LOAD related with the nominal sentence production. The number of the nominal sentences produced by the EOAD patients is more than the LOAD patients. However, this difference is not statistically significant.

Table 7. Comparisons of nominal sentence structures on four language tests of EOAD and LOAD

Language Tests	N	Group	p
Picnic Picture	23	EOAD	0.596
	39	LOAD	
Cookie Theft	23	EOAD	0.837
	39	LOAD	
Story Picture Sequencing	23	EOAD	0.717
	39	LOAD	
Random Speech	23	EOAD	0.421
	39	LOAD	

The comparisons of verbal sentence structures obtained in four language tests are presented in table 8, 9 and 10. It was revealed that there was a statistically significant difference about the verbal sentence structures between the EOAD and control groups in all tests. In all tests, patients with EOAD produced less verbal sentences compared to the control group.

Table 8. *Comparisons of verbal sentence structures on four language tests of EOAD and CG*

Language Tests	N	Group	p-değeri
Picnic Picture	26	CG	0.037
	23	EOAD	
Cookie Theft	26	CG	0.019
	23	EOAD	
Story Picture Sequencing	26	CG	0.009
	23	EOAD	
Random Speech	26	CG	0.002
	23	EOAD	

Results in table 9 suggest that there was a statistically significant difference about the verbal sentence structures between the LOAD and control groups in all tests and it is also revealed that the LOAD group produced less verbal sentences compared to the control group.

Table 9. *Comparisons of verbal sentence structures on four language tests of LOAD and CG*

Language Tests	N	Group	p-değeri
Picnic Picture	26	CG	0.003
	39	LOAD	
Cookie Theft	26	CG	0.004
	39	LOAD	
Story Picture Sequencing	26	CG	0.040
	39	LOAD	
Random Speech	26	CG	0.009
	39	LOAD	

According to the results in table 10, there is no statistically significant difference between patients with EOAD and LOAD related with the verbal sentence production. However, the mean of the verbal sentence production is higher in LOAD group compared to the EOAD group.

Table 10. *Comparisons of verbal sentence structures on four language tests of EOAD and LOAD*

Language Tests	N	Group	p-değeri
Picnic Picture	23	EOAD	0.517
	39	LOAD	
Cookie Theft	23	EOAD	0.971
	39	LOAD	
Story Picture Sequencing	23	EOAD	0.744
	39	LOAD	
Random Speech	23	EOAD	0.820
	39	LOAD	

Table 11 shows the comparison of language tests based on basic sentence structures within groups. According to the table, there was a significant positive correlation between language tests and basic sentence structures (p=0.000). It means that the use of basic sentence structures of EOAD patients, LOAD patients and the control group were changed within tests. The highest percent of basic sentence use of EOAD patients and the control group is in Picnic Picture test and the lowest percent is in Random Speech test.

Table 11. *Comparison of language tests based on basic sentence structures within groups*

Groups	Picnic Picture f (%)	Cookie Theft f (%)	Story Picture Sequencing f (%)	Random Speech f (%)	p
CG	40.5	24.6	23.7	11.2	0.000
EOAD	34.6	20.3	25.6	19.5	0.001
LOAD	36	22.1	24.9	17.1	0.000

Discussion

The sentence production of AD patients shows that these patients use more basic sentence structures than the control group. Although not reaching statistical significance, it is clear that patients with EOAD and LOAD tend to use basic sentences in their speeches. Another finding is that EOAD patients use more basic sentences compared to LOAD patients. These findings are parallel to the studies in the literature. In these studies the sentence structures of AD patients were examined and it was revealed that they used less complex sentence structures compared to the control group (Hier et al., 1985, Croisile et al. 1996, Waters and Caplan, 1997, 1999, 2001).

The syntactic abilities of AD patients are observed in many studies and in these studies it is mainly accepted that the syntactic abilities of AD patients are preserved. However, the stages of AD are determinant of the language impairment and the impairment is just observed in the complex sentence structures (Caramelli et al., 1998; Emery, 2000; Boschi, 2017: 13). The performance of AD patients becomes worse when the complex sentence structures occur more frequently (Caplan and Waters, 1999). Related with the stages of AD, Kertesz (2004) found out that in the early stages of AD, these properties were preserved; however; in the severe stages language impairment became worse and the patients had lots of problems about sentence production. A similar finding was seen in the

study of Ehrlich et al., (1997). According to this study, the syntactic ability about the complex sentence structures are not preserved in moderate and severe AD patients.

The studies that compare patients with early and late-onset Alzheimer's disease indicate that the linguistic difference between the EOAD and LOAD patients are not clear and it is mainly about the small sample sizes and nonstandardized testing (Seines et al., 1988; Swearer et al., 1992). Except for these studies, there are also some other studies that show the difference between the linguistic performance of the patients with early and late-onset AD. Some of these studies claim that patients with LOAD perform worse compared to the patients with EOAD (Sevush et al., 1993; Bayles, 1991, 1992, 1993). On the contrary, the other studies prove that language impairment of the patients with early-late onset AD is faster and worse compared to the late-onset AD patients (Romero and Kurz, 1996; Seltzer and Sherwin, 1983; Sevush et al., 1993: 6; Binetti et al., 1993; Goldblum et al., 1994; Becker et al., 1988; Chui et al., 1985; Filley et al., 1986). In addition to these studies, some studies reveal not only similarities but also differences between early and late-onset AD considering their linguistic performance. For example, Koss (1996) found out that naming, repetition and some other linguistic performance of the early and late-onset AD patients were similar. However, in some aspects there were also some differences within the groups.

Except for the basic sentences, nominal and verbal sentence structures were also analysed within tests and groups in our study. According to the results, the number of nominal and verbal sentences used by the EOAD and LOAD patients differs from the control group. EOAD patients prefer nominal sentences more compared to the control group whereas LOAD patients prefer verbal sentences more. In literature, nominal and verbal sentence structures are not investigated a lot. In some studies, it is revealed that EOAD patients tend to use nominal sentences more compared to the verbal ones (Can et al., 2016); however patients with LOAD use verbal sentences more compared to the normal people (Can et al., 2017) . In other studies, only verb and noun production is analysed and it is indicated that verb production deficits in AD seemed to be driven more by semantic than by executive impairment. They suggest that picture naming is a task predominantly dependent on temporal or posterior brain areas, whereas verbal fluency is more dependent on frontal or frontal subcortical brain areas. Even though patients with AD have no frontal brain atrophy, they do experience difficulty in naming and fluency tasks involving verbs (Beber et al., 2015).

Considering the sentence production of EOAD and LOAD patients in our study, it was found out that EOAD patients used more basic sentences; LOAD patients used more verbal sentences in their speech. It is believed that this difference is related to working memory problems due to the deficits in neural interconnections between the posterior and frontal brain areas. These problems can also cause difficulties in sentence comprehension and sentence production (Altmann and McClung, 2008). Some studies related to sentence processing indicate a left-temporal network for syntactic processing and bilateral tempro-frontal networks for semantic processing (Lukic et al., 2013).

To conclude, in this study the sentence production of EOAD and LOAD patients were examined through four different language tests and it was revealed that EOAD patients tended to use basic sentences and nominal sentences more frequently compared to LOAD patients. It is believed that the difference about the sentence processing of the two subtypes of AD is related with the working memory problems.

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