Original Article

Clustering and Switching Strategies in Verbal Fluency Tasks: Comparison between Amyotrophic Lateral Sclerosis (ALS) and Healthy Controls

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ABSTRACT

Background: Recent studies have demonstrated that Amyotrophic Lateral Sclerosis (ALS) patients suffer from cognitive and language impairments. One of the most striking and consistent cognitive dysfunctions in these patients is verbal fluency deficits. The aim of this study is the determination of verbal fluency performance of Persian speakers with ALS.

Methods: It was a cross-sectional, analytical-descriptive study. In this study, 30 individuals (15 patients with ALS, and 15 healthy people) were examined by verbal fluency test. Verbal fluency test is a cognitive-linguistic test that has two subtests: phonemic fluency and semantic fluency; in each of them, words normally fall in clusters. Finally, the total number of words, mean cluster sizes and number of switches between clusters are counted and the results are compared between patients with ALS and healthy control groups.

Results: There was a significant difference between the patient group and the control group in the mean naming total scores ($P \leq 0.05$) and in the mean switching scores ($P \leq 0.05$), but not in the mean clusters scores ($P \geq 0.05$).

Conclusion: Result of this study shows that ALS patients have a deficit in total naming and switching parts of verbal fluency test, but they have no impairment in clustering part. Based on these results, it seems that these patients may have problems in searching in the lexicon, but no problem in accessing words in clusters.

Introduction

Amyotrophic Lateral Sclerosis (ALS), or Lou Gehrig's disease, is the most common motor neuron disease. ALS is a progressive neurodegenerative disease that involves motor neurons of the brain and spinal cord.

In this disease, there are signs and symptoms of upper motor neuron and lower motor neuron involvement [1]. Although the traditional perspectives identified ALS as an exclusively motor neuron disease, recent studies suggest that there is also cognitive alteration in these patients. In other words, new researches demonstrate that in these patients, cortical involvement exceeds beyond the primary motor cortex [2, 3]. There is some evidence for memory deficit, language impairment and predominantly disturbances on executive function [1]. Numerous studies have documented the presence

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of verbal fluency deficits, poor sustained attention, impaired set-shifting, limited response inhibition, and weak problem solving and judgment in ALS patients [4]. Some of the mentioned problems in ALS patients show underlying cognitive and language impairments in substantial word finding processes [5]. Abrahams et al. in their study on ALS patients indicated that they have selective deficits on confrontation naming and letter fluency test, but their other executive function abilities were intact [3]. In several studies, it has been shown that one of the most consistent and prominent deficit in these patients is verbal fluency performance [2, 3, 5]. These patients have major impairment in letter fluency test, and also difficulty in category fluency [2]. But there is limited study on the underlying processes of naming function on ALS patients.

Verbal fluency tests are useful neuropsychological tests that have been used to investigate high-level language performances, and a variety of cognitive processes such as word knowledge, access to semantic memory, long-term verbal memory, attention [1, 2], speed of information processing, vocabulary size, working memory, inhibition of irrelevant words [6], and executive function. These tests are composed of semantic fluency test and category fluency test [7].

In order to understand the mechanisms involved in optimal word generation, the examiner should study the cognitive strategies used to complete the task successfully [8, 9]. Previous studies have demonstrated that ALS patients do not show normal performance in verbal fluency tests; however, there is no qualitative analysis in the output of verbal fluency tests in Persian ALS patients. Qualitative analysis on verbal fluency tests that was presented by Troyer has shown that words are generated in clusters, which means that when a participant is asked to produce words, he searches mentally in his vocabulary repertoire and immediately after identifying a category, word production within that category is commenced [7]. A subcategory is composed of semantically or phonemically related words that are known as clusters [7]. When a subcategory is exhausted, the efficient performance is to rapidly move to another subcategory and produce words within that subcategory [7, 10]. The process of shifting from one cluster to another is called switching [7]. These underlying components of verbal fluency performance (switching and clustering) can distinguish healthy control groups from patients with neurological disorders [9]. Clustering and switching are positively correlated with the total number of generated words [11, 12]. Each of these strategies is related to unique processes of the brain. The clustering of words is related to processes such as verbal memory, verbal storage and temporal function [9]. The other strategy, switching, requires the ability to engage in strategic search processes such as initiating, cognitive flexibility and mental shifting [7]. It appears that both clustering and switching tactics are highly active in semantic fluency, but switching is more significant in phonemic fluency performance [13]. It is evident that in patients with brain pathology such as Parkinson disease

[14], Huntington's disease, Schizophrenia, and patients with frontal and temporal lobe lesions [9], and ALS patients [7], verbal fluency performance is impaired. In Persian language, there are studies that investigated verbal fluency performance of neurogenic disorders like Alzheimer disease, Parkinson disease and Multiple Sclerosis (MS). In Persian speakers with Alzheimer disease, verbal fluency performance is disturbed [15], and there is no research regarding the underlying processes of verbal fluency function in Persian patients with Alzheimer. Also, Persian patients with Parkinson disease have disorder in both phonemic and semantic fluency functions and switching and clustering strategies in both of them [16, 17]. As well, Persian patients with MS have problem in verbal fluency performance [18]. Patients with MS show limited ability on switching and clustering values of semantic and phonemic fluency task. However, there is no study about verbal fluency performance of Persian patients with ALS. Also, there is little information about the underlying processes of verbal fluency performance of ALS patients in other languages [19].

Cognitive deficits of ALS patients present before the onset of motor symptoms, and there is an increasing recognition of the importance of drawing a broad spectrum of cognitive impairments in this population. Furthermore, awareness of the specific form of cognitive performance of these patients can help to predict the presence of ALS disease. Additionally, recognition, evaluation and management of cognitive deficits of ALS disease can have effect on the quality of life of patients, caregivers and their families [1].

However, various researches have shown that the performance on verbal fluency tests is influenced by language and culture [20]. There is no study on verbal fluency performance of Persian speakers with ALS. Therefore, the main aim of this study is to explore verbal fluency performance of Persian ALS patients. The results of this study at first are useful for understanding the profile of verbal fluency performance of ALS patients (one of their cognitive function) and also it will be useful for speech and language therapeutic decision makings. In other words, when the framework of this function is clear, the clinician can decide to improve the aspects that are responsible for naming deficits of ALS patients.

Methods

Design

It was a cross-sectional, analytical-descriptive study. The way for matching groups was paired matching method.

Participants
Participants with ALS:

Fifteen patients (11 male, 4 female) with ALS were included in this study. These patients were chosen from ALS clinic of Hazrat-e-Rasoul-eAkram hospital in Tehran. No patient had dementia, a history of head injury in the last 10 years, stroke, long-term use of alcohol or

drug addiction, epilepsy or other neurological disease, and taking antidepressant medication. All patients were right handed. They were all Persian speaking. Patients with evidence of respiratory weakness in the interview session were excluded from the study. Patients were excluded if the severity of bulbar muscles involvement prevents them from speaking. Neurological data were taken from the records of the patients' clinic visit nearest to the time of testing.

Healthy controls (HCs):

Fifteen healthy (11 males, 4 females) age, sex, education matched (paired matching) controls were included in this study. They were all Persian speaking and right handed. No participant had a history of head injury in the last 10 years, stroke, long-term use of alcohol or drug addiction, epilepsy or other neurological disease, and taking antidepressant medication.

This study was approved by the Iran University of Medical Sciences research ethics committee and Informed consent was obtained from all individual participants included in the study. This research was financially supported by the Vice Chancellor for Research at Iran University of Medical Sciences.

Instrument

For this study, Persian verbal fluency test [21] was performed in the participants. This test has two sections and a special method for analyzing scores that is explained on scoring test results section. The study was conducted in a quiet room in the hospital. For recording participant's responses, MP3 player was used and for calculating the time of their responses, a chronometer was used.

Phonemic Fluency Test:

Consistent with standard instruction, [21] the participants were told to produce as many words as possible beginning with "F", "A" and "S", within 1 minute for each letter. Participants were not allowed to use proper nouns, such as people's, city and country names or same words with different suffixes. The following instructions were given: I will give you a letter, then you will try to produce quickly as many words as you can which are initiated with that letter within one minute. Please be careful you can't produce proper nouns or same words with different suffixes. For instance, if I said "M" you can tell magazine, machine, etc., but you shouldn't say Mashhad, Maryam, Malaysia (proper nouns), or same words with different ending". Then if participants understand these instructions, they would be asked to do the main test letters ("F", "A" and "S").

Semantic Fluency Test:

The participants were instructed to produce as many words as they can in one minute from a specific category (animals and fruits).

Scoring Test Results:

For scoring test results, according to the manual of test (that is excluded from Troyer scoring method for verbal fluency test) [21], the total number of words for each subtest was counted. Then, for semantic fluency section, words within each category (animals/fruits) were categorized in terms of their categorization method (birds, aquatics …/citrus, dried fruits …). The categories and subcategories of each section are explained in the manual of verbal fluency test [21]. This procedure was repeated for phonemic fluency section in that words were categorized for each letter (F, A, S) in terms of their phonological features within a proper cluster. The number of switches is equal to the number of clusters minus one, and the cluster size is equal to the number of words within each cluster minus one, and finally the mean cluster size is equal to the Total cluster size divided by the number of clusters [21].

Data Analysis

Statistical analyses were done using SPSS (Version 16.0. Chicago.SPSS.Inc.). Description of data in each group was explored with descriptive statistics section of SPSS 16 software. Shapiro-Wilk test was conducted for exploring the distribution of data. Due to the fact that the data distribution was normal ($p{\geq}.05$), independent T-test was used to compare verbal fluency performance between these two groups.

Results

Demographic Features of Participants

The 15 patients and 15 HCs did not differ in age, gender or education level. They had been educating for five to sixteen years. They were between 40 and 65 years old (Table 1).

Data Analysis Results
Total fluency scores:

The ALS patients generated significantly fewer words on both phonemic ($P{\leq}0.05$) and semantic fluency measures ($P{\geq}0.05$) compared to HCs (Table 2).

Phonemic fluency. ALS patients generated fewer numbers of clusters compared to the HCs (P=0.000; Table 2). ALS patients also generated fewer switches between clusters (P=0.006) than the HCs. But the mean cluster size did not differ significantly between ALS patients and HCs (P=0.886).

Table 1: Demographics for ALS and healthy controls

	ALS	HC
Gender (M/F)	11/4	11/4
Age (yrs)	54	54
Education (yrs)	12	12

ALS = Amyotrophic Lateral Sclerosis. HC = Healthy Controls

Table 2: Means for ALS patients and healthy controls for phonemic and semantic fluency scores

	ALS	HCs	P value
Phonemic fluency			
Total score	15.33 (7.10)	23.36 (7.64)	0.00
Mean cluster size	0.614 (0.624)	0.65 (0.70)	0.88
Switches	9.86 (5.57)	16.53 (6.65)	0.00
Number of clusters	9.86 (5.57)	19.53 (6.65)	0.00
Semantic fluency			
Total score	24.46 (8.02)	32 (8.10)	0.01
Mean cluster size	1.00 (0.844)	1.35 (0.86)	0.27
Switches	12.66 (2.66)	15.33 (4.46)	0.05
Number of clusters	12.66 (2.66)	17.33 (4.46)	0.00

ALS = Amyotrophic Lateral Sclerosis. HC = Healthy Controls. Standard deviations in parenthesis. P values are reported for total ALS versus HC

Semantic fluency. ALS patients generated fewer numbers of clusters compared to the HCs (P=0.002; Table 2). ALS patients also generated fewer switches between clusters (P=0.050) compared to the HCs. But the mean cluster size did not differ significantly between ALS patients and HCs (P=0.273).

Discussion

Our results confirm the impairment of verbal fluency performance in ALS patients, which are consistent with the results of Abraham et al. [22], Evdokimidis [23], Murphy et al. and Murphy et al. [24, 25].

In this study, the patients showed some deficiencies in phonemic fluency performance, which are consistent with the findings of Abraham and his colleagues [3] and Lepaw et al. [19] that showed that ALS patients had deficit on phonemic fluency task. According to the findings of our study, ALS patients also display some deficiencies in semantic fluency performance, which are consistent with the findings of Abraham and his colleagues [2] and Lepaw et al. [19].

Statistical analyses show that the total number of words generated in the phonemic and semantic fluency are significantly different between ALS and HCs, and HCs perform better. Phonemic fluency lies on the frontal lobes [26] and it has been said that cognitive flexibility and executive functioning is mediated by frontal lobes. So the difference in performance might be explained by an impaired executive functioning, which makes shifting and search strategy more difficult. For exact conclusion in this field, a research can be conducted on the relationship of phonemic fluency performance and cognitive flexibility and executive functioning in ALS patients.

Mean cluster size and the number of clusters and switches are the most qualitative way of measuring. In our study, the number of clusters and switches was significantly different between ALS and HCs. These findings were according to our expectations, because ALS patients have impairment in "organization of thinking" [5]. These findings are in accordance with a study held by Lepaw et al., which showed that ALS patients have problems in cluster numbers of phonemic fluency task, and cluster numbers and switches between semantic clusters of semantic fluency task. But unlike

their results that showed that ALS patients have problem in cluster value of phonemic fluency task; our results indicated that these patients do not have problem in this performance [19]. This conflict in the present study and Lepaw et al. study can be due to the differences in Persian and English language features. In other words, there is difference between the frequency of words that start with letters "F", "A", and "S" in Persian and English language. It seems that in English language, evaluation of phonemic fluency performance with letters "F", "A, and "S" has a diagnostic value but for Persian language it is obscure that it has a diagnostic value [27]. In other words, in English prompts are chosen, in part, because there are large numbers of English words available in each phonemic category and these potential responses include many high-frequency words (hence words likely to be known to all participants regardless of age or educational level) and these words fall into clusters sharing phonemic features. Hence, individual variation in total scores as well as clustering scores can be meaningfully interpreted as representing how efficiently individuals are able to search through a mental lexicon, a mental lexicon can be reasonably assumed to be highly similar across participants. Normal Persian speakers (in this study) produce less words than English (in Lepaw et al. study) on phonemic fluency task (total score in phonemic fluency task in English: 40; total score in phonemic fluency task in Persian: 23), but mean phonemic cluster size in English for normal participants is 3.8 while in Persian this value is 0.65 (number of clusters: 19.53, and number of switches: 16.53), therefore, it seems that with letters "F", "A", and "S" for Persian language, words don't fall into clusters. Hence, it may not be meaningful to compare phonemic fluency performance of Persian speakers with these letters, and it may be better to compare the performance of Persian speakers with ALS with other letters that are suitable for this task in Persian language. Mardani et al. in their research show that letters are effective factors on the performance of Persian speakers on phonemic fluency task [27]. In this study the researchers use from "F", "A" and "S" letters for evaluation of phonemic fluency performance due to standard manual of test in Farsi [21], but it seems that it has no diagnostic value. Therefore in future studies, it has to select appropriate letters for Persian language and then compare phonemic

fluency performance of ALS patients and HC.

Dadgar et al. evaluated verbal fluency performance of Persian patients with Parkinson disease. They indicated that patients with Parkinson disease have disorder in both phonemic and semantic fluency functions and switching and clustering strategies in both of them [16, 17]. Their findings are along with our results in ALS disease, and it seems that verbal fluency is under effect to neurological disease in Persian language. In their study, letters "F", "A" and "S" were selected for phonemic fluency measurement too. In their results, the total number of words on phonemic fluency task of normal participants was close to our results for normal participants (total score in phonemic fluency task in normal Persian speakers in Dadgar et al. study was 22.24 and it is 23 in the present research). It can eliminate any doubt about sampling errors in the present study and confirm the need to select appropriate letters in Persian language.

Ebrahimipour et al. in their study on verbal fluency performance of patients with Multiple Sclerosis (MS) in Persian language indicated that these patients have problem in this performance [18]. Patients with MS show limited ability on switching and clustering values of semantic and phonemic fluency task. These findings in other neurological disorders on Persian speakers can show that Persian verbal fluency test is also sensitive to neurological problems, but for distinguishing neurological diseases from the aspect of switching and clustering values, at first, it has to review the Persian version of verbal fluency test (at the phonemic fluency subtest items).

The total number of clusters can be seen as a measure of cognitive flexibility, and mean cluster size is seen as an indicator for the retrieval ability [28]. Therefore, it seems that ALS patients have deficit in cognitive flexibility, but their retrieval ability is spared.

The ability to create clusters, including producing subcategories, depends on verbal memory and word storage [28]. The ability to shift between clusters is dependent on cognitive abilities such as strategic search, set shifting and cognitive flexibility [28]. Thus the results stated above show that in ALS patients, semantic fluency performance declined and this might also imply that the underlying involved processes such as memory and executive functioning have declined.

Verbal fluency and its component processes are sensitive to the presence of most forms of brain damage, traumatic brain injury, diffuse cerebral illness and neurodegenerative disorders and understanding of neurological dysfunction forms [29].

Conclusion

Verbal fluency tests useful method for drawing a model of neurological dysfunction in ALS patients. In this study, the researchers attempted to present and explain a cognitive linguistic performance of ALS patients. It is recommended that researchers, draw a comprehensive clinical profile of cognitive and linguistic performance of ALS patients in a wider sample size, that is useful for diagnostic assistance criteria and is beneficial for intervention suggestions.

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