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Anomia Treatment in Patients with Herpes Simplex Encephalitis: Single-Subject Study

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Original Article

Abstract

Introduction: Herpes simplex encephalitis (HSE) virus is the most severe and debilitating inflammatory disease in the central nervous system (CNS). Anomia is one of the most common language disorders in patients with HSE. No study has been done on naming treatment in patients with HSE. This study aims to compare the effect of the Semantic Feature Analysis (SFA) and Phonological Components Analysis (PCA), as naming treatments, in two patients with HSE virus, who had different degrees of naming problems, to find the most optimal anomia treatment.

Materials and Methods: The design of the current study was ABACA reversal single-subject. Two patients with HSE underwent speech therapy at Kashani Hospital, Isfahan, Iran. After determining the baseline, to treat the naming problem, the first patient was first treated with PCA and then SFA, and the second patient was first treated with SFA and then PCA. The naming ability of the patients was collected in two baseline phases, two treatment phases, and finally follow-up phase. To analyze all the five-phase, within- and between-condition visual analyses were implied for (a) relative, (b) absolute, (c) median, (d) mean level change, stability envelope, and trend. Besides, the effect size involving percentage of non-overlapping data (PND) and percentage of overlapping data (POD) were calculated in trained words.

Results: The within-condition analysis of patient one showed 100% of the data of each phase, while for patient two, all data except the B phase were in the stability envelope. All details about the within-condition analysis of both patients showed different trends according to the order of treatments. Between-condition analysis of patient one exhibited the total PND of all phases was 100%, in contrary to less than 70% in patient two. In both patients, the improvement caused by SFA was greater than PCA. Additionally, the maintenance after SFA was more than PCA. The order of treatment presentation as providing PCA then SFA were statistically more effective.

Conclusion: SFA and PCA could potentially improve the naming ability in HSE patients with anomia. Both mentioned treatments have significant effects on the increase of naming scores. As the treatment program presented SFA then PCA, respectively, we saw less maintenance in naming scores. On the other hand, providing the reverse sequence, PCA then SFA, exhibited an excellent improvement in naming scores and also more maintenance happened.

Keywords: Encephalitis; Herpes simplex; Semantic features analysis; Phonological component analysis; Anomia

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Introduction

Herpes simplex encephalitis (HSE) is the most severe and debilitating inflammatory disease in the central nervous system (CNS) (1, 2). Severe viral encephalitis and meningoencephalitis occur by a direct attack of the herpes virus to the brain (1, 3). HSE is associated with high levels of morbidity and mortality (1, 2). Annually, about 1 in 250000 to 500000 cases are infected with this virus (4, 5). The development of medical sciences in the field of

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antiviruses, such as acyclovir, has helped to reduce the mortality rate, but a significant number of people who have survived from the HSE virus have kept living whilst suffering from long-term cognitive deficits. Consequently, these long-term cognitive deficits were made it impossible to return to the daily life activities in these patients (2). The HSE virus has a variety of severe effects on the brain hemispheres (6). The pathology of the lesion in five patients with HSE virus displayed that the most abnormality was in the sensitive areas of the grey matter of the temporal lobe, which includes the anterior region of the lateral part of the temporal lobe, temporal pole, and middle temporal cortex including the amygdala, hippocampus, entorhinal cortex, and the insular cortex (6). The complications of neurological damages persist after treatment in approximately 60% of patients with HSE, which can lead to mild to severe disabilities. Clinical signs of the virus include headache, lethargy, confusion, personality changes, behavioral changes, central neurological symptoms (in the temporal lobe), fever, decreased level of consciousness even coma, focal neurological symptoms, and seizures. In addition, if the temporal lobe in the dominant hemisphere gets involved, the aphasia will also indicate (7). The complexity of differential diagnosis of meningoencephalitis makes it difficult to diagnose the true cause of the disease in these patients. The delay in diagnosis will be associated with a poor prognosis, as it leads to delay in the initiation of treatment and thus to deterioration of the general condition of the patient (1, 7).

Anterograde declarative memory deficits constitute a considerable part of the neuropsychological profile of a person affected by the HSE virus (5, 8, 9). Most studies exhibit varying degrees of memory deficits in these patients (5, 10). Many cases also show significant deficits in other brain areas such as language, executive function, or emotion control (2). Signs of aphasia in patients with HSE have high frequencies, which can affect various aspects of language, including speaking, listening, reading, and writing skills (2, 3). Reports indicate that anomia is one of the most common language disorders in these patients after infecting by the herpes meningoencephalitis virus (1). According to some evidence, other language defects are rarely seen in these patients (1). In patients with HSE, grey matter density is an indicator associated with scores displaying a decrease in verbal memory, as well as omission/error in naming pictures (2). Soares-Ishigaki et al (1) found that the sudden onset of language abnormality, aphasia, was an important sign of the HSE virus (1). Rehabilitation of these patients may be long-term (7), but early diagnosis of the virus allows for providing optimum criteria for the rehabilitation of language and cognitive problems in this group of patients (1). Therefore, anomia is one of the main problems of patients with HSE (11). Anomia dramatically reduces the speed and the fluency of speech (12). Besides, anomia has various clinical signs such as non-response, denial of the correct response, circumlocution, errors of a part of the whole word, and unintelligible speech products (12). Anomia has different treatments; a group of anomia treatments are facilitators which focus on a specific level of injury and attempt to improve the function of the naming mechanism, such as phonological and semantic therapies (12). On one hand, many naming treatments imply techniques trying to improve semantic processing representations (13). One of the most common of these approaches is Semantic Feature Analysis (SFA) (14). SFA is an effective and proven approach for treating naming problems (15). It has been used in various studies to treat anomia after stroke. SFA has had positive effects on the recovery of treated words, words that were trained with SFA, and even untreated words, words that were not trained by SFA (15). SFA is based on the theory of spreading activation in which words are organized in a semantic network (15). When a concept is activated, the activation is propagated to nodes connected to the concept, emitting the same features straightaway (15). Once the features of a particular word are activated, it reaches the threshold level for word production; thus, the production of the correct word is more likely to occur (15). On the other hand, Phonological Components Analysis (PCA) is a recent phonological approach to treat naming disorders (16). This approach has a similar structure to SFA and focuses on the phonological features of words to facilitate word-level processing (16). A review of the literature shows that both SFA and PCA approaches, depending on the degree of patient's naming difficulties, have been effective in improving the naming ability of patients with aphasia (17–19). Except for Del Grosso et al.'s case report (11), no study has been conducted to investigate the effect of treatments for language deficits in these patients; however, there are some studies which have described language features after being infected with HSE (1, 2, 6). Besides, no study has been done on naming treatment in patients with HSE. This study aims to compare the effect of the SFA and PCA, as naming treatments, in two patients with HSE virus, who have different degrees of naming problems, to find the most optimal anomia treatment.

Materials and Methods

The present study with scientific code 196092 was approved by the Student Research Committee of Isfahan University of Medical Sciences, Isfahan, Iran. Participation in this study was performed with the ethical consent of patients' family.

Participants: This study selected two patients with HSE based on the following inclusion criteria: (1) receiving a diagnosis of HSE by a neurologist, (2) having HSE in the acute stage of the disease, (3) being over 18 years old, (4) receiving a diagnosis of aphasia by Persian version of Bedside Aphasia Battery (20) by getting 76 scores or higher, (5) being a native Persian speaker, (6) having anomia as the main complaint, (7) having no cognitive problem by getting above 22 scores in Mini-Mental State Examination (MMSE) test, (8) not receiving any other anomia treatment, and (9) taking no drugs that affect their language function. Exclusion criteria included: (1) being bilingual, (2) having another illness associated with HSE, and (3) refusing to continue during treatment. Overall, both participants had been infected with HSE for more than one year and had received a short course of cognitive behavioral therapy (CBT) by psychologist before entering the study. Demographic characteristics of patients and scores of Persian Western Aphasia Battery (P-WAB) (20) are shown in table 1. Table 2 also displayed the linguistic profile of the participants based on the P-WAB.

Table 1. Demographic information of the participants

Assessment at the admission time	Patient 1 (M.H.)	Patient 2 (H.S.)
Age (year)	28	19
Education level	BSc student	BSc degree
Language	Persian	Persian
Hand superiority	Right	Right
MMSE	28	26
P-WAB	83	81

BSc: Bachelor of Science; MMSE: Mini-Mental State Examination; P-WAB: Persian Western Aphasia Battery

Table 1. The profile of participants' Persian aphasia test

Different parts of exam	The number of question		Patient one		Patient Two	
			+	*	*	+
Speech fluency	1-6	6	6	10	--	5
Word recognition	7-28	19	20	10	10	20
Recognition of body organs	29-38	10	10	10	10	10
Distinguish right and left limbs	46-39	8	8	10	10	8
Simple commands	47-51	5	5	10	10	5
Understand complex concepts	52-55	4	4	10	5	2
Understand the short story	56-59	4	4	10	10	4
Expression Fluency	60-71	12	6	5	10	12
Automatic speech	72-74	3	1	3	10	3
Remember to read melodic pieces	75-79	5	2	5	10	5
Words repetition	80-89	10	6	6	7	7
Phrases repetition	90-99	10	8	8	5	5
Word reading	100-109	10	10	10	5	5
One word answers	110-119	10	5	5	10	10
Looking and naming	120-144	25	3.2	3.2	2.8	7
naming	145-149	5	0	0	4	2
Oral reading sentences	150-159	10	4	4	4	4
Words and letters recognition	160-169	10	10	10	0	0
Phonetic association	170-177	8	10	10	10	8
Matching words with pictures	178-187	10	10	10	0	0
Reading Comprehension	189-197	10	10	10	6	6
Transcription	198-202	5	10	10	10	5
Performance when writing dictated letters and words	203-212	10	10	10	0	0
Performance when writing dictated sentences	213-217	5	10	10	0	0
Free writing	Due to the patient were disabled in writing, this subscale didn't assessed.	-	-	-	0	0

First participant: First participant (Table 1) had a history of one and a half years of HSE. Initially, the patient's cognitive problems were severe. In the P-WAB test (20), he received a lower score than the standard in the anomia section (6 out of 20), and in other areas of the P-WAB test, problems were observed (Supplement 1), but he mostly complained about his anomia.

Second participant: The second participant (Table 1) was infected with HSE for one year. Initially, the patient had cognitive and attention problems. Besides, in the P-WAB test (20), he received a lower score than the standard in the anomia section (7 out of 20). In addition, in other areas of the P-WAB test, some problems were obvious (Supplement 1); however, he complained mostly about his anomia.

Procedure: In the present study, the participants received program at Kashani Hospital, Isfahan, Iran. The design of the current study is single-subject reversal ABACA (21). In general, this study had five phases: 1) baseline, 2) treatment, 3) baseline, 4) treatment, 5) follow-up. Consequently, 28 data points were collected from the following method during the 5 phases.

Baseline phases: During this study, the assessment was performed by a trained speech-language pathologist (SLP), with 20 years' experience, via a naming subtest of P-WAB. The baseline determination was performed two times, one before and another between treatment phases. During baseline phases, which lasted for three weeks, one assessment session was done once a week; therefore, a total of three data points were obtained. Additionally, during the assessment, the patients' voices were recorded then scored by another SLP who was blind to the participants.

The criteria for picture selection: In the baseline phases, in order to determine the therapeutic and non-therapeutic pictures, 143 pictures were presented to the patients to name orally. These pictures were taken from a collection of adopted pictures in the Persian language (22). If the patients were able to name a picture in 10 seconds or in two of three assessment sessions, the picture was chosen as a therapeutic or trained picture. If the patient named a picture after ten seconds or was able to name it in only one-third of the baseline sessions, the picture was included in the non-therapeutic or untrained pictures set. In this way, 45 pictures were identified as therapeutic or trained pictures for the first participant and 36 for the second one. Then, these trained pictures were divided into three sets (the first participant with three sets of fifteen pictures and the second participant with three sets of twelve pictures). In both participants, the "Bird Story" was used as a control stimulus before and after the study to evaluate the "generalization effect" (20). This test assessed mental lexicon and was taken twice, one before the treatment sessions and the other after the last baseline session.

Treatment phases: Two treatments, PCA and SFA, were performed for both participants by a SLP with 6 years' experience. In the first one, PCA and then SFA were performed, and in the second one, the order of treatment was reversed. The treatment period lasted 17 weeks. In each treatment phase, 12 sessions were performed during four weeks, with three sessions in a week. In each session, a specific set of therapeutic pictures was practiced; after each of the three sessions of treatment, an assessment session was performed with non-therapeutic pictures. The voices of the participants were recorded during the exercises and then examined. Both SFA and PCA treatments were performed according to the treatment protocol of Boyle and Coelho (23) and Leonard et al. (16).

Follow-up phase: This phase lasted for three weeks. In each session, all trained and non-trained pictures were evaluated and a total of 6 data points were obtained for each patient.

"Bird Story" to investigate generalization: To investigate generalization, the "Bird Story", a part of Western Aphasia battery test- Persian version(20), was utilized(20). As mentioned before, it assessed mental lexicon and to some extend generalization.

Results

To analyze all the five phases in both patients, within- and between-conditional visual analyses were implied for relative, absolute, median, mean level change, stability envelope, and trend. Besides, the effect size involving percentage of non-overlapping data (PND) (24) and percentage of overlapping data (POD) (25) was calculated. The results of the within-conditional analysis in trained words in the first patient (Figure 1, Table 3) and the second patient (Figure 2, Table 4) and also the between-conditional analysis of both patients in trained words (Table 5) have been presented below, separately.

Patient 1

Within-condition analysis in the trained words: According to table 3 and figure 1, 100% of the data of each phase were in the stability envelope. The relative level change of each phase exhibited that in the first baseline (A1), the patient naming score did not change, but in the other phases, changes were positive. The absolute level change in each phase displayed that in the first baseline (A1), the

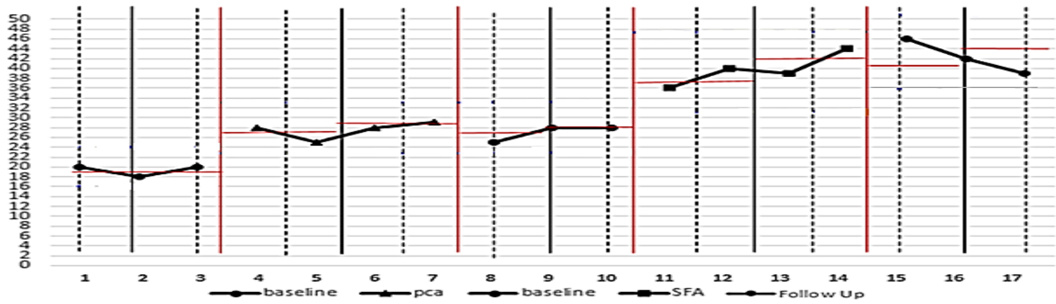

Figure 1. Naming accuracy in trained items for patient one

The vertical red line separates the phases. The vertical black line divides the data of each phase into two halves. Vertical black dotted line defines the middle session of each part. The horizontal red line indicates the trend line.

patient's naming score did not alter, but in the treatment phase B (PCA), the second baseline (A2), and also the treatment phase C (SFA), these alternations were positive while in the follow-up phase were negative.

Between-condition analysis in trained words: The trend direction of the first baseline remained constant (Figure 1). The trend of the phases B (PCA), the second baseline (A2), and the phase C (SFA) was upward, but in the follow-up was downward. 100% of the data points of each phase were in the stability envelope; therefore, data were reliable.

Patient one's relative level changes (Table 5) between phases A1-B improved his naming ability by 7.5 scores. These changes between phases B-A2 were decreased by minus two degrees, then they were increased from A2 to C by 9.5 degrees. Finally, they decreased from C to the follow-up by 1.5 degrees. Patient one's absolute level changes also exhibited that his naming ability was improved by 8 scores between phases A1-B (Table 5). These changes were decreased by minus four degrees between phases B-A2. From A2 to C, these changes were raised by 8 degrees and from C to the follow-up, they were declined by 2 degrees.

The comparison of mean changes between phases depicted that providing both treatments increased the mean scores of patients' naming compared to the previous baseline; however, the SFA increased the mean more than the PCA. Moreover, the transition from the treatment phase to the baseline caused a decrease in the patients' naming performance, but the rate of decline was greater after the end of PCA.

Table 3. Within-conditional visual analysis of variables in the patient one-trained pictures

Case 1	A	B	A	C	A
Median	20	28	28	39.5	42
Mean	19.33	27.50	27.00	39.75	42.33
Range	18-20	25-29	25-28	36-44	39-46
Stability chamber	16.0-24.0	22.4-33.6	22.4-33.6	31.6-47.4	33.6-50.4
Stability envelope (%)	100	100	100	100	100
The range of changes in stability chamber	Stable	Stable	Stable	Stable	Stable
Alternation changes					
Relative alternation changes	0	2.0	1.5	4.5	3.5
Description of alternation changes	Improvement in anomia	Improvement in anomia	Improvement in anomia	Improvement in anomia	Without changes
Absolute alternation changes	0	1	3	8	-7
Description of alternation changes	Without changes	Improvement in naming	Improvement in naming	Improvement in naming	Deterioration in naming
Trend					
Trend direction	Equal	Ascending	Ascending	Ascending	Descending
Trend description	Unchanging in naming	Improvement in naming	Improvement in naming	Improvement in naming	Deterioration in naming
Stability	Stable	Stable	Improvement in anomia	Stable	Stable
Percentage of data in stability chamber	100	100	100	100	100

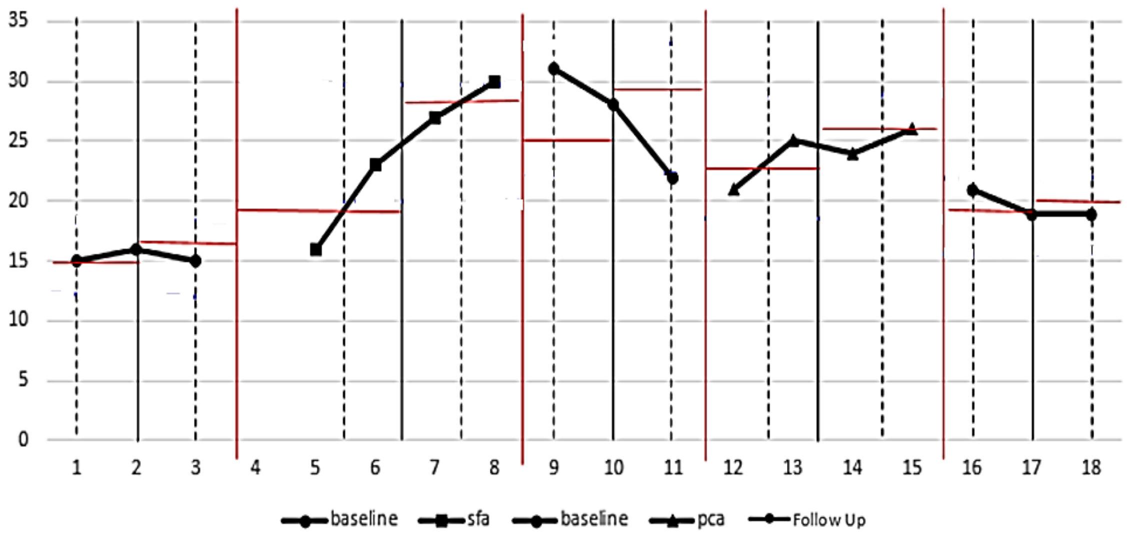

Figure 2. Naming accuracy in trained items for patient two

The vertical red line separates the phases. The vertical black line divides the data of each phase into two halves. Vertical black dotted line defines the middle session of each part. The horizontal red line indicates the trend line.

Additionally, PND was used to evaluate the effect size. The results exhibited that PND of A1 and B were 100%; thus, PCA was quite effective because it was more than 70% (26).

The PND of A2 and C were also 100%; therefore, SFA was quite effective. As a result, the total PND of all phases were 100%; accordingly, the treatment sequence, PCA then SFA, in the first patient was quite effective.

"Bird Story" analysis: To investigate generalization, the "Bird Story", in Western Aphasia test was utilized (20). According to its results, patient one had gotten a 28% score before the treatment period and reached 40% after that. It means that patient one showed a 12% increase in mental lexicon.

Patient 2

Within-condition analysis in the trained pictures: 100% of the data of phases A1, A2, C, and follow-up were in the stability envelope, but about phase B, it was 75% (Figure 2).

Table 4. Within-conditional visual analysis of variables in the patient two- trained pictures

Case 2	A	B (SFA)	A	C (PCA)	A
Median	15.0	25.0	28.0	24.5	19.0
Mean	15.3	24.0	27.0	24.0	19.6
Range	15-16	16-30	22-31	21-26	19-21
Stability chamber	12.0-18.0	20.0-30.0	22.4-33.6	19.6-29.4	15.2-21.8
Percentage of data in stability chamber	100	75	100	100	100
Change ranges in stability chamber	Stable	Unstable	Stable	Stable	Stable
Alternation changes					
Relative alternation changes	0.5	9.0	4.5	3.0	1.0
Description	Improved	Improved	Improved	Improved	Improved
Absolute alternation changes	0	14	9	5	2
Description	Unchanged	Very improved	Improved	Improved	Less improved
Trend					
Direction	Equivalent	Ascending	Descending	Ascending	Descending
Description of trend direction	Stability in naming ability	Increase in naming ability	Deterioration of naming ability	Increase in naming ability	Deterioration of naming ability
Stability	Stable	Unstable	Stable	Stable	Stable
Percentage of data in stability chamber	100	75	100	100	100

SFA: Semantic feature analysis; PCA: Phonological components analysis

Table 5. The state comparison between two patients

Clients						One					Two	
Change trend												
Trend						Positive					Negative	
Change stability						Unstable to stable					Stable to stable	
	A_1 to B	B to A_2	A_2 to C	C to A_3	A_1 to B	B to A_2	A_1 to B	B to A_2	A_1 to B	B to A_2	A_2 to C	C to A_3
Changes in related alternation level	15.5 to 19.5	28.5 to 25.0	29.5 to 22.5	25.5 to 19.0	19.0 to 26.5	28.5 to 26.5	15.5 to 19.5	28.5 to 25.0	15.5 to 19.5	28.5 to 25.0	29.5 to 22.5	25.5 to 19.0
Absolute alternation changes	15 to 16	30 to 31	22 to 21	26 to 21	20 to 28	29 to 25	15 to 16	30 to 31	15 to 16	30 to 31	22 to 21	26 to 21
Median changes	15.3 to 24.0	24.0 to 27.0	27.0 to 24.0	24.0 to 19.6	20.0 to 28.0	28.0 to 28.0	15.3 to 24.0	24.0 to 27.0	15.3 to 24.0	24.0 to 27.0	27.0 to 24.0	24.0 to 19.6
Mean changes	15.0 to 25.0	25.0 to 28.0	28.0 to 24.5	24.5 to 19.0	19.5 to 27.5	27.5 to 27.0	15.0 to 25.0	25.0 to 28.0	15.0 to 25.0	25.0 to 28.0	28.0 to 24.5	24.5 to 19.0
PND (%)						37.5					100	
POD (%)						62.5					0	

PND: Percentage of non-overlapping data; POD: Percentage of overlapping data

Patient's relative level change of each phase indicated that in all phases, the patient's naming score was positive. Moreover, the absolute level changes in each phase showed that these scores did not alter in the first baseline (A1). In contrast, in the first treatment phase B (PCA), second baseline (A2), and treatment phase C (SFA), the score was absolutely positive but it was decreased in the follow-up phase (Table 4).

Between-condition analysis in the trained pictures: The trend in the first baseline was flat (Figure 2) but in phase B (PCA) was ascending. While the trend in the second baseline (A2) was descending, in the phase C (SFA) and the follow-up was ascending. All data except phase B were in the stability envelope.

In case of changes in the relative level between A1-B phases, the patient's naming ability indicated 4 degrees improvement. This change between B-A2 phases was decreased to -3.5, and from A2 to C decreased to -7. Additionally, these changes from C to the follow-up phase decreased to -6.5 (Table 5).

(Figure 2) but in phase B (PCA) was ascending. While the trend in the second baseline (A2) was descending, in the phase C (SFA) and the follow-up was ascending. All data except phase B were in the stability envelope.

Regarding the changes in the patient's absolute level between A1-B and B-A2, it had an increase by 1 score. This alternation from A2 to C decreased by one degree and also decreased by five scores from C to the follow-up (Table 5).

The comparison of mean changes between phases exhibited that the SFA treatment increased the mean scores of patients' naming ability compared to the previous baseline. In contrast, the transition from PCA to the third baseline in addition to the transition from the third baseline to follow-up reduced the mean score at naming. Similarly, the results were the same for the median.

Investigating the PND results showed that the PND of A1 and B was 75%; therefore, the SFA was statistically effective because it was more than 70%. On the other hand, the PND of A2 and C was 0%; therefore, PCA was statistically ineffective. The total PND of the phases was 37.50%. Thus, this treatment sequence in the second patient was not effective.

The comparison of mean change level between phases showed that providing PCA reduced the naming score mean of the second patient in comparison to the previous treatment phase (SFA). Furthermore, the transition from PCA to follow-up led to a more reduction in the mean. Examination of PND results showed that the PND of SFA and PCA phases was 0%; thus, PCA was not statistically effective because it was less than 70%. Therefore, this treatment sequence was not statistically effective in the second patient.

"Bird Story" analysis: Similarly, patient two had displayed a 36% score in the mentioned story before the treatment period and reached a 48% score after that. It means that the second patient showed also a 12% increase in mental lexicon.

Discussion

There is a lot of evidence in case of the effectiveness of phonologically- and semantically-based treatments such as PCA and SFA in anomia rehabilitation in patients with stroke (16, 17, 27-29). On the one hand, there are some researches about the language problems like anomia and some kinds of language therapy in patients with HSE. On the other hand, the lesion in patients with stroke is local and subsequently, the patient with aphasia experiences some degrees of damage in special part of his/her brain like dominant language hemisphere, mostly in Broca's or Wernicke's area (30, 31), while in patients with HSE, the lesion as mentioned before involved diverse parts of his/her brain (1, 2, 7). On the other hand, there is no study which investigates the effects of both SFA and PCA on HSE patients with anomia.

In this reversal single-subject study, these two treatments were separately provided for two patients with HSE, over 18 years old, and consequently the within- and between-condition analysis as well as PND were investigated to find the effects of each treatment in addition to different sequences of treatment presentation.

Patient one: Within-condition analysis of the first patient (A-PCA-A-SFA-follow-up) in the trained pictures exhibited that the data of each phase had complete stability; therefore, they were reliable. As well, the relative level change displayed that the naming ability was remained unchanged in the first baseline, but it was improved in other phases. Besides, absolute change level showed that this ability in the first baseline remained unchanged but in the PCA, the second baseline (A2), and the SFA was developed. However, in the follow-up, this ability was deteriorated.

Between-condition analysis also showed that the patient's naming status in the first baseline (A1) was steady due to the lack of treatment. The trend of the patient's naming performance in phases B (PCA), second baseline (A2), and phase C (SFA) showed naming improvement, but in the follow-up phase, there was a drop in naming ability.

Relative level change between adjacent phases demonstrated that the ability to name improved upon receiving PCA, but after completing the PCA and not receiving any treatment, the naming ability was lowered. This result is in line with a previous study by Howard et al. (32) who reported that phonetic cues could be effective in naming in comparison to the unavailable treatment. Moreover, with SFA, the naming ability showed a great improvement while this progress was more than this amount from A1 to PCA, which means SFA is more effective than PCA. From the C phase (SFA) to the follow-up, this ability became weak. This deterioration was less than the amount of the transition from PCA to the second baseline. This may conduct a better maintenance of SFA than PCA. The results of Howard et al. study showed that providing phonological cues had a strong but immediate and short-term effect on aphasic participants with anomia, while they were less likely to name the items 30 minutes after practice. Semantic representation exercises, on the other hand, make a significant improvement in word access that can remain up to about 24 hours.

Furthermore, absolute level change between adjacent phases pointed out that the naming ability was enhanced by PCA, while it deteriorated after finishing PCA. After SFA, naming ability recovered greatly. Besides, this change from SFA to follow-up caused a slight advancement in naming ability, which might indicate the effect of SFA that was maintained. As well, this enhancement showed the maintenance of the entire treatment sequence in the first patient. This result is similar to Neumann's study (33) which reported the greater maintenance by SFA over PCA among his aphasic participants with mild anomia.

The comparison of mean changes between phases similarly clarified that providing both treatments improved the patient's naming ability compared to the previous baseline, but SFA made improvement more than PCA. The transition from the SFA to the baseline lowered naming performance. This frequency was lower than the decrease after PCA; thus, less maintenance occurred after PCA.

According to PND, presenting the treatment sequences as PCA then SFA showed that it was effective (PND over 70%). Additionally, the large difference between PND and POD indicates the high impact of the treatment. The mean of follow-up phase scores after SFA exhibited that maintenance was occurred, whereas no maintenance was observed after PCA. Further, follow-up phase showed that this treatment sequence resulted in the maintenance of the treatment. Moreover, as a result, SFA treatment in the first patient apparently was more effective than PCA.

The interpretation of all visual indicators revealed that patient one had a better naming status after receiving SFA and maintained his ability better after the end of it, while after PCA, the maintenance was not observed. As a result, the treatment sequence in patient one was apparently more effective than patient two, with reverse treatment sequence.

Patient two: According to the results, within-condition analysis showed that the data of all phases, except B, were completely reliable. Relative level change in each phase displayed that the patient's naming ability improved in all of phases. However, the absolute level change exhibited that this ability in the first baseline remained unchanged, but in the treatment phase B (SFA), second baseline (A2), treatment phase C (PCA), and follow-up, it improved to varying degrees.

Secondly, between-condition analysis of the trained pictures explained that the naming status had stability in all phases except phase B (SFA); it means that most data were reliable. Moreover, the trend in the first baseline showed any change due to the absence of the treatment. In contrast, in the phase B (SFA), naming was improved. This ability in the second baseline and phase C (PCA) raised. But, in the follow-up, there was a drop due to not receiving treatment.

Relative and absolute level changes between adjacent phases showed that this ability was improved upon receiving SFA, and it was reduced after SFA. It has also shown a lot of decline with PCA. In the C phase to the follow-up, a decrease in naming ability was also observed. These changes also indicate less maintenance of PCA than SFA in the second patient.

The comparison of mean changes between phases showed that SFA increased the mean scores of patients' naming score compared to the previous baseline, while PCA decreased this ability compared to the previous baseline. This ability also was decreased in transition from PCA to follow-up. This result is also true for the median.

Between-condition analysis of adjacent phases in all visual indicators exhibited that the second patient had a better naming status after receiving SFA and retained his ability better after the end of this treatment sequence, while after PCA, there was a greater decrease in comparison to after SFA. Therefore, SFA was effective in the second patient but PCA was less effective. The maintenance occurred after SFA but did not occur after PCA. Totally, this treatment sequence was not effective in the second patient.

The PND results similarly explained that in the second patient, treatment sequence of SFA then PCA was ineffective (PND less than 50%). After SFA, the ability to name was retained, while after PCA, this ability declined sharply and was not maintained. The observation of the follow-up phase also exhibits that this treatment sequence did not lead to the maintenance of improvement. Finally, the SFA in the second patient was more effective than PCA.

Theoretical principle: Regarding the effect of treatment sequence in patients one and two, it can be concluded that the treatment sequence, PCA and then SFA, is statistically more effective. Although it seems that there is not any research about the naming treatment in patients with HSE, there are a lot of studies about the effects of SFA and PCA in patients with aphasia (16, 34), in which they have exhibited the effectiveness of the two mentioned treatments with the different degrees of improvement and different levels of maintenance and generalization to untrained items (35, 36).

Altogether, the effectiveness of these two methods in improving the naming ability of patients with HSE can be justified by the Hebbian learning principle (37-39). According to this principle, neurons that are activated together also communicate with each other (37-39). Therefore, activating phonological or semantic networks to retrieve word names can lead to a connection between them. As a result, by repeating and practicing, this connection is strengthened and the naming ability is improved.

Limitations

It is important to explain that the small sample size of this study, two participants, may restrain the generalization of the results to a larger group of HSE patients. However, results of this study can be considered as a trigger point for next researches.

Recommendations

Further studies are required to clarify the effect of semantic- and phonological based approach, such as SFA(13), PCA(16), Response Elaboration Training (RET)(44), Gestural Facilitation of Naming (GES)(38), contextual repetition priming treatments(41), Verb Network Strengthening Treatment (VNeST) (43,45), Errorless Naming Treatment (ENT)(38) and , etc. on naming ability via different doses and sequences of treatment programs rehabilitations in patients with HSE with different degrees of anomia..

Conclusion

The results of this study, conducted for the first time, revealed that SFA and PCA, anomia treatment approaches, could potentially improve the naming ability in HSE patients with anomia. As mentioned before, both treatments have significant effects on the increase of naming scores. Additionally, this is in line with previous studies (29, 40-42) which mentioned that PCA and SFA could have a significant effect on improving the naming scores of anomic patients with aphasia. This improvement was due to the enhanced representation of word form. It is also possible that both methods can strengthen the mapping between semantics and phonology (29, 40-42).

On the one hand, the sequence of treatment presentation is notable. As the treatment program presented SFA then PCA, respectively, we saw less maintenance in naming scores. On the other hand, providing the reverse sequence, PCA then SFA, exhibited an excellent improvement in naming scores and also more maintenance happened. This result is in line with Coelho et al. study about SFA effect on aphasic patients with anomia. It mentioned that while only a small number of words were trained, the generalization to untrained words was more considerable. The influence of generalization in their study also was maintained for two months after finishing treatment (14). According to Edmonds et al. study, this generalization maybe is due to the effect of other generalization mechanisms besides semantic generalization (43).

Generally, the different sequence of anomia treatment programs makes significant changes in the naming performance of these two patients. SFA is based on the theory of spreading activation (15) in which providing some characters for a target word activates the semantic network for it. Therefore, it is more likely that the item will be activated by more threshold level which is required for retrieving the correct word.

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The study was approved by Institutional Ethics Committee of Isfahan University of Medical Sciences, and the patients' parents consented to the use of data anonymously

Authors' Contribution

Both authors contributed to all processes of this article entailing writing the proposal, design, data collection, data analysis, writing the manuscript, and revision. Both authors approved the version to be published. Both authors are responsible for all facets of the work to ensure the accuracy and integrity of all questions. The authors appropriately reviewed and resolved the total parts of the article.

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Conflict of Interest

There is no declaration in this study.

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