Comparing Of Learning And Memory Functions Of Patients With Prodromal Vascular Dementia And Prodromal Alzheimer's Disease With Healthy Control Group

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Abstract
It is known that learning and memory impairments are at the forefront in both patients with prodromal Alzheimer's dementia (pAD) and those with prodromal vascular dementia (pVD). In pAD, learning and memory impairments are predominantly prominent. On the other hand, pVD is characterized by impairments in various areas, mainly in the executive functions. This is a preliminary study aimed at comparing the learning and memory functions of patients diagnosed with pVD and pAD in terms of their incidental recall, delayed recall, and learning.
A total of 100 adults, comprising 42 females and 58 males participated in the study. A total of 26 patients with a clinical diagnosis of pAD (N = 14) and pVD (N = 12) were compared with 74 cognitively healthy people.
The scores for pAD and pVD groups were significantly lower than those of the healthy individuals, and the pAD group achieved the lowest scores in all the trials. The scores of the pVD group were lower than those of the healthy group but higher than those of the pAD group. The number of learning trials were higher than that of control group for both pAD and pVD. In other words, pAD and pVD groups needed more learning trials to remember. Overall, pVD group was able to learn more materials compaired to pAD.
The findings of this study could be considered as useful in differentiating the two groups for neuropsychological evaluation.

Keywords: Cognitive dysfunction, memory, learning, prodromal Alzheimer's dementia, prodromal vascular dementia.

1. Introduction

Although Alzheimer's disease (AD) constitutes more than half of the dementia cases, cerebrovascular events are viewed as the second reason that leads to cognitive impairment and dementia. It has been stated that the cognitive impairments, the existence of dementia, and the functional impairment in AD

begin in the prodromal or the pre-clinical phase before the period during which these symptoms are clearly observed (1). Longitudinal follow-up studies of population-based, community-dwelling individuals have shown that cognitive impairment can be detected well before the onset of dementia symptoms (2). Therefore, it is extremely important to identify the cognitive impairments before the functional losses begin to present themselves.

Consistent with the new approach proposed by Dubois et al, the revised criteria for the clinical diagnosis of AD proposed by the National Institute on Aging and Alzheimer's Association also considered a symptomatic pre-dementia phase of AD referred to as "mild cognitive impairment due to AD" (3,4). The International Working Group research criteria allow the diagnosis of AD in the prodromal phase before patients have developed dementia (5); these criteria require evidence of both specific clinical features and biomarkers supported by neuroimaging and/or biochemical methods. In this study, the first group of patients has been termed as pAD and the second group of patients as pVD.

In patients with vascular dementia, executive dysfunction (slow information processing, impaired ability to change from one task to another, and impaired ability to retain and process information) is more characteristic than memory and language deficits (6,7). Attention, executive function, language, visuospatial abilities, memory, and learning can be affected to different extents and in various combinations depending on the size and localization of the cerebrovascular lesion (7-9).

When considered from the perspective of memory and learning difficulties, in pAD, there are difficulties related to the remembrance and acquisition of information (10), while in pVD, there are retrieval difficulties and episodic memory is better preserved than that in AD (6,11-13). On the other hand, it has been stated that there are memory impairments in the prodromal phase of vascular dementia as well (14), and that there are overlaps with regard to the neuropsychological profiles of both groups (15). This study aims to distinguish the pAD and pVD groups in terms of their memory and learning profiles.

2. Methods and Materials

A total of 100 adults, comprising 42 females and 58 males, aged between 50 and 80 years (mean age = 67.82 ± 7.96 years; mean duration of education = 10.53 ± 4.70 years) participated in the study. A total of 26 patients with a clinical diagnosis of pAD (N = 14) and pVD (N = 12) were compared with 74 cognitively healthy people. Participants were diagnosed with pAD and pVD at the neurology department of Mersin University Hospital. All subjects had undergone extensive medical screening at enrolment. A medical history, neurological examination, brain scans (CT or MRI and SPECT), and blood screening tests for dementia were performed for all participants. Diagnoses were made according to the criteria suggested by Dubois et al. based on the previous Peterson criteria termed as mild cognitive impairment (1). The participants in the non-demented control group were all individuals who were residents of Mersin with no evidence or complaints of memory loss. The participants in this group were chosen among people who had similar age range and educational characteristics with those of the patient groups. The demographic characteristics and the neuropsychological test scores of all participant groups are shown in Table 1. The participants were respectively administered the Standardized Mini-Mental State Examination (SMMSE) (16,17) and the Three Words -Three Shapes (3W3S) test (18).

The 3W3S test is a short and moderate level memory and learning test and could be easily applied to groups with low education. In addition, there is an adaptation study of this test, which offers normative data for our country (19). The test allows the evaluation of both verbal and non-verbal memory. The materials used for this test involve a card on which there are three shapes and three words, and a second card on which there are the target shapes and words and distracters for the recognition trial. The test contains trials for copying, incidental recall, retrieval after 15 min, and recognition trials. Each trial is scored in accordance with both the words and the shapes. To those participants who cannot exhibit adequate learning in the incidental recall trial, the stimuli are shown again, which allows to assess whether the learning has increased. The repetitions determine the acquisition score of an individual's learning.

All participants provided their informed consents. Our study was approved by the local ethics committee of Mersin University Medicine Faculty (date: August 17, 2017, number: 78017789-050.01.04-521126).

Table 1. Demographic variables and mean scores and standard deviations of 3W3S performances for each condition (for words and shapes)

	Healthy		pAD		pVD	
	Mean (SD)	Min-Max	Mean (SD)	Min-Max	Mean (SD)	Min-Max
Education	11.05 (4.22)		8.86 (5.70)		10.50 (6.05)	
Age	66.08 (6.02)		71.93 (6.33)		68.50(10.95)	
SMMSE	26.80 (2.22)		25.25 (3.46)		26.00 (3.81)	
3W3S trials						
Copy						
Shapes	14.62 (.871)	10 – 15	13.21 (3.92)	0 – 15	13.58 (1.16)	11 – 15
Words	14.95 (.28)	13 – 15	13.71 (3.98)	0 – 15	14.92 (.28)	14 – 15
Incidental recall						
Shapes	12.11 (3.52)	0 – 15	5.86 (6.18)	0 – 15	8.83 (5.84)	0 – 15
Words	11.74 (3.85)	0 – 15	5.86 (5.86)	0 – 15	8.25 (6.77)	0 – 15
Acquisition						
Shapes	13.83 (2.35)	0 – 15	5.82 (5.49)	0 – 14	9.0 (5.77)	0 – 15
Words	13.15 (3.73)	0 – 15	7.91 (7.62)	0 – 15	8.57 (8.01)	0 – 15
LearningTrials	1.04 (0.19)	1 – 2	2.14 (1.09)	1 – 4	1.83 (0.38)	1 – 2
Delayed Recall						
Shapes	13.16 (3.03)	0 – 15	7.08 (6.65)	0 – 15	9.92 (5.90)	0 – 15
Words	11.66 (4.49)	0 – 15	5.31 (6.55)	0 – 15	9.33 (7.06)	0 – 15
Recognition						
Shapes	14.73 (1.40)	5 – 15	12.14 (4.25)	5 – 15	13.75 (2.26)	10 – 15
Words	14.26 (2.43)	0 – 15	10.36 (4.98)	0 – 15	10.42 (6.20)	0 – 15

3. Results

Table 1 presents the mean scores and the standard deviations of the 3W3S test performances under each condition (for words and shapes) for the healthy control and the pAD and pVD groups. A one-way ANOVA test was conducted for evaluating the differences between the groups. Significance levels were interpreted using Bonferroni corrections for multiple pairwise comparisons. The ANOVA results showed that under the copy condition, the performance of the pAD group was worse than that of the healthy control group for shapes (P =.013) and words (P =.015). Under the incidental recall condition, the pAD (P =.000) and the VCI (P =.041) groups performed worse than that of the healthy control group for shapes. The pAD (P = .000) and the VCI (P = .042) groups also performed worse than that of the healthy control group for words. Following the incidental recall trial, when the learning trials were continued and the acquisition scores were examined, it was observed that the performances of the pAD (P =.000) and the pVD (P =.001) groups were worse than those of the healthy control group for shapes; the performances of the pAD (P =.003) and the pVD (P =.044) groups were also worse than those of the healthy control group for words.

Under the delayed recall condition (15 min), the performances of the pVD group were worse than those of the healthy control group for shapes (P =.031). The performances of the pAD group were worse than those of the healthy control group for shapes (P =.000) and words (P =.001). Among the distractors that were applied immediately after the delayed recall condition to recognize the target stimuli, both groups received lower scores than those of the healthy control group. When the results were examined, it was observed that the pAD and the pVD groups received different scores than those of the healthy control group; however, the scores of these two groups did not show a statistically significant difference when compared between each other. The average scores of the pVD group were still higher than those of the pAD group.

4. Discussion

This study compared the scores of three groups, namely, pAD, pVD, and the healthy control. The lowest scores among the subscores of the 3W3S test were taken from the incidental recall condition. In other words, this phase that evaluates to what extent the individuals could remember the encountered stimuli without showing a conscious effort was the most difficult phase for all the groups; however, as expected, the lowest scores were observed in the pAD group. The scores of the pVD group were higher than those of the pAD group, but they were lower when compared to those of the healthy control group. Weintraub

et al (18) indicated that this stage was similar to the forgetfulness in daily life and showed impairment with aging. It was also observed that the number of learning trials that were applied to patients for better learning after the incidental recall in both the pAD and the pVD groups was higher than that for the control group; in other words, these two groups needed more learning trials to remember the materials in question. However, as expected, the pVD group was able to learn more materials and remember them, and the amount of remembering and learning for the pAD group was lower. In a similar vein, several findings in the literature mention that the verbal learning and memory performance of patients with vascular cognitive impairment are better than those of patients with pAD and that their memory losses are generally related to recall and retrieval (11,14,15).

When examined from the standpoint of verbal and nonverbal modalities, the two groups of patients performed poorly in the verbal modality of the recognition experiment, whereas they did not differ in the incidental and delayed recall attempts of verbal modality.

The most important limitation of this study is the low number of samples in the patient groups. Therefore, the findings of this study could be considered as only preliminary. On the other hand, the comparison of different types of dementia in terms of memory and learning functions could provide useful information with regard to differentiating them in neuropsychological assessment. Future work with larger samples may provide more insights into whether this test shows a certain pattern in different groups. Regarding the conclusion, we can say that repeated learning is a useful method for pVD but not for pAD.

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