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NONVERBAL MEMORY CAPACITY IN PERSONS WITH EPILEPSY IS ASSOCIATED WITH DEPRESSION RATHER THAN ANXIETY

Krunoslav Matešić[1], Meri Tadinac[2] and Hrvoje Hećimović[3]

[1]Department of Psychology, Catholic University of Croatia, Zagreb, Croatia;
[2]Department of Psychology, Faculty of Humanities and Social Sciences, University of Zagreb, Zagreb, Croatia;
[3]Clinical Department of Neurology, Sestre milosrdnice University Hospital Centre, Zagreb, Croatia

SUMMARY – Epilepsy is characterized by repeated epileptic seizures, which are manifested in various ways and depend on the location and size of foci in the brain. Long-term seizures with secondary generalization can cause memory problems. Numerous studies demonstrate the connection of memory damage and lateralization in medial temporal lobe epilepsy (TLE). However, the results were not always consistent with the material-specific memory model. A possible explanation for these inconsistent data is the insufficient control of psychological variables that can affect memory. In most of the previous studies in persons with epilepsy, they were not controlled for their emotional states such as anxiety and depression. We used the Rey Complex Figure Test (RCFT) as a measure of visual memory, Beck's depression inventory as a measure of depressive symptoms, and the State-Trait Anxiety Inventory as a measure of anxiety in 57 consecutive participants. Our aim was to investigate whether there is difference in visual memory with respect to the left and right TLE, and whether the participants of different gender with higher anxiety and depression rates would achieve different results on visual memory. Persons with lower levels of depression achieved better scores in the Immediate and Delayed recall subtests of the RCFT. We also explored the potential gender differences. Testing differences between the persons with higher and lower anxiety levels did not reveal any significant differences in any of the measures tested.

Key words: *Epilepsy, temporal lobe; Memory; Pattern recognition, visual; Anxiety; Depression; Neuropsychological tests*

Introduction

Epilepsy is a chronic neurologic disorder that has complex interference with social, vocational and psychological functioning. Epilepsy is characterized by repeated epileptic seizures, which are manifested in various ways and are dependent on the location and size of epileptic region in the brain. Some studies have shown that longer duration of epilepsy with frequent secondary generalization may cause memory problems[1-3]. Studies of the cognitive function in people with temporal lobe epilepsy (TLE) are numerous due to the importance of the temporal lobe structures in cognition. The material-specific memory model has been drawn from the observations of Milner[4], who found that postoperative lesion in the left medial temporal lobe caused problems with verbal memory, while lesion in the right medial temporal lobe damaged memory for the non-verbal tasks.

Research suggested a relationship between memory damage and lateralization of medial temporal lobe[5-7], but the results were not always consistent with the material-specific memory model[8]. There is a stronger link between deficits in verbal memory and TLE in the language-dominant hemisphere[9], while evi-

Correspondence to: *Krunoslav Matešić, PhD*, Department of Psychology, Catholic University of Croatia, Ilica 242, HR-10000 Zagreb, Croatia
E-mail: krunoslav.matesic@unicath.hr
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dence for link between the right temporal lobe and nonverbal memory is inconsistent.

In nonverbal memory tests, the first phase includes either intentional or unintentional learning of nonverbal stimuli, and some form of recall is assessed in the second phase. One of the most common diagnostic tests for visual memory is the Rey Complex Figure Test (RCFT)[10]. Several studies confirmed that patients with left TLE performed better in the recall test of the RCFT compared to those with right TLE[11-13], whereas others found no differences[13-15]. These studies tested patients before surgery for TLE and none of them showed that patients with left TLE had worse nonverbal memory scores. One proposed explanation for these data was inadequate control of psychological variables that can affect memory, such as anxiety and depression. Brain laterality differences between genders have also been documented. The women over men advantage in verbal abilities may reflect stronger lateralization of the language towards the left cerebral hemisphere[16]. Gender difference in visuospatial processing due to lateralization of the brain is more complex because of inconsistent data. Some studies found evidence for differences in laterality between men and women when processing visuospatial information[16], while others failed to show differences between sexes[17].

Our aim was to investigate whether there was a difference in visual memory with respect to the left *versus* right TLE, gender, and level of anxiety and depression.

Patients and Methods

Patients

We examined 57 consecutive patients at the Zagreb Epilepsy Center, Sestre milosrdnice University Hospital Centre from Zagreb. The mean age of study patients was 32±13.4 (range 17-67) years, 58% (n=33) of them women (Table 1). Patients with brain lesions such as cerebral tumors, malformations of blood vessels, congenital developmental disorders and mental retardation were excluded from the study. All patients had partial epileptic seizures originating from temporal lobe, based on their medical history, prolonged electroencephalography and brain magnetic resonance imaging. During the interview, the patients did not complain of comorbid diseases and no clinical symptoms of the possible comorbidities were observed.

Table 1. Gender and lateralization of epilepsy foci distribution in the sample

		Lateralization		Total
		Right	Left	
Gender	Men	10	14	24
	Women	17	16	33
Total		27	30	57

Instruments

I Visual memory testing

The Rey Complex Figure Test is a standardized neuropsychological assessment tool designed to measure visuospatial construction ability and visual memory in persons with brain damage[10]. The examinees are asked to reproduce a complex line drawing, first by copying it freehand (testing their recognition), and then by drawing it from memory. This results in two measures: Immediate Recall and Delayed Recall. Immediate Recall is done 15 minutes after the copying, and Delayed Recall is done 30 minutes after Immediate Recall. Various cognitive abilities are needed for correct performance, and the test evaluates different functions such as visuospatial abilities, memory, attention, planning, and working memory (executive functions)[13].

II Depression assessment

The Beck Depression Inventory (BDI-II)[18] is a self-report scale containing 21 items which are used to assess the severity of depressive symptoms and as a measure of depression. It has been widely used in patients with TLE[18].

III Anxiety assessment

The State-Trait Anxiety Inventory (STAI) consists of two self-report scales intended to determine anxiety as a trait and as a state[19]. The State Anxiety Scale (S-scale) employed in this study consists of 20 statements used to assess how the subject feels "now, at this moment", and it has been extensively used in epilepsy patients[19].

Procedure

The study was carried out from September 2013 to February 2015. All participants signed an informed consent issued by the Hospital Ethics Committee.

They completed the RCFT, BDI and STAI. The whole procedure lasted for about 50 minutes.

Statistics

We used factorial 2x2 ANOVA to test for statistical significance between two independent variables, both at two levels. We used the non-parametric Mann-Whitney U-test for cases that we could not provide parametric analysis due to small group samples. The Mann-Whitney U-test uses the sum of ranks to determine whether two samples are grouped in a population with the same median. The level of statistical significance was set at $p<0.05$. Statistical analysis was performed using the IBM SPSS Statistics 20. In our study, adjustment for gender was performed.

Results

Immediate Recall and Delayed Recall

The means and standard deviations for RCFT Immediate Recall according to sex and lateralization of focal epilepsy are shown in Table 2.

To examine differences between patients with right and left TLE with respect to gender, 2x2 ANOVA with gender (men, women) and lateralization of epilepsy (left, right) as independent variables and RCFT Immediate Recall as a dependent variable was performed. Two-way ANOVA showed neither significant main effects of gender and laterality, nor their interaction.

The means and standard deviations for RCFT Delayed Recall by gender and lateralization of focal epilepsy are shown in Table 3.

Table 2. RCFT Immediate Recall by gender and lateralization in persons with temporal lobe epilepsy

Lateralization		Mean	SD	n
Right	Men	63.50	12.946	10
	Women	66.29	34.723	17
	Total	65.26	28.318	27
Left	Men	73.29	45.008	14
	Women	91.25	56.813	16
	Total	82.87	51.582	30
Total	Men	69.21	35.141	24
	women	78.39	47.710	33
	Total	74.53	42.765	57

RCFT = Rey Complex Figure Test; SD = standard deviation

Table 3. RCFT Delayed Recall by gender and lateralization of epilepsy with means and standard deviations (SD) for correct responses

Lateralization		Mean	SD	n
Right	Men	36.70	18.500	10
	Women	31.76	14.368	17
	Total	33.59	15.856	27
Left	Men	37.57	14.463	14
	Women	31.31	13.174	16
	Total	34.23	13.915	30
Total	Men	37.21	15.885	24
	Women	31.55	13.588	33
	Total	33.93	14.734	57

RCFT = Rey Complex Figure Test

To examine differences between patients with right and left TLE with respect to gender, 2x2 ANOVA with gender (men, women) and lateralization of epilepsy (left, right) as independent variables and RCFT Delayed Recall as a dependent variable was performed. Two-way ANOVA showed neither significant main effects of gender and laterality, nor their interaction.

Immediate and Delayed Recall depending on depression

The mean result on the BDI-II as a measure of depression was 7.46±6.52. The cut-off point for high depression listed in the BDI-II Manual is 13. However, Oliveira *et al.*[20] state that the cut-off point for patients with epilepsy should be set at 15, thus distinguishing more clearly between depressed and non-depressed patients. Our cut-off score was 15. A relatively smaller number of highly depressed individuals were present in our sample (n=9), while much more individuals had low depression levels (n=48).

In order to examine whether the patient level of depression was related to their performance on memory tasks, we performed the nonparametric Mann-Whitney U-test because of the small number of participants with a higher level of depression. Table 4 shows descriptive values for visual memory for the low and high depression groups and the significance of differences between the two groups, as determined by the Mann-Whitney U-test.

Significant differences in visual memory were found for both Immediate Recall and Delayed Recall;

Table 4. Descriptive values of visual memory tests in relation to the degree of depression and results of testing differences using Mann-Whitney U-test

	BDI-II ≤14 (n=48)		BDI >14 (n=9)		Mann-Whitney U-test
	M	D	M	D	
RCFT T-values Immediate Recall	36.71	20.00	25.11	20.00	75.00**
RCFT T-values Delayed Recall	35.58	20.00	25.11	20.00	89.00**

*p<0.05; **p<0.01; RCFT = Rey Complex Figure Test; BDI II = Beck Depression Inventory; M = arithmetic mean; D = median

Table 5. Descriptive values of executive functions testing and visual memory with regard to anxiety levels (STAI-S) and results of testing differences by Mann-Whitney U-test

	STAI-S ≤39 (n=50)		STAI-S >40 (n=7)		Mann-Whitney U-test
	M	D	M	D	
RCFT T-values Immediate Recall	34.3800	20.00	38.4286	34.00	219.50
RCFT T-values Delayed Recall	33.6000	20.00	36.2857	28.00	205.00

RCFT = Rey Complex Figure Test; STAI-S = State-Trait Anxiety Inventory (S-scale); M = arithmetic mean; D = median

highly depressed participants (n=9) achieved lower results that those (n=48) with low depression levels.

Immediate Recall and Delayed Recall depending on anxiety

Anxiety was assessed using the State-Trait Anxiety Inventory (STAI), which yields two results, i.e. anxiety as a trait and anxiety as a state. Anxiety as a state (STAI-S) is an anxiety that is measured at a given moment, and this score was used as a measure of anxiety. Contrary to the usual findings[19], we found no gender differences.

The cut-off value of 40 points was used to distinguish less anxious participants from the highly anxious ones, as suggested by the STAI Manual. There were 50 less anxious participants and seven highly anxious ones. Table 5 shows the values of dependent variables in both groups. Using the Mann-Whitney U-test, we found no significant differences in visual memory between the high- and low-anxiety participants.

Discussion

Lateralization of epileptic region and gender of TLE subjects were not associated with Immediate Recall and Delayed Recall differences measured by the RCFT. This finding is in accordance with the majority of earlier studies[13-15]. However, some studies suggested lower results for Immediate Recall and Delayed Recall tasks on nonverbal material in patients with right-sided TLE. Frank and Landeira-Fernandez offer an explanation for the difficulty of reproducing this finding in our study, indicating that the figural stimulus used for testing nonverbal memory is not optimally constructed[21]. They suggest that figural stimuli can be verbalized and modified as linguistic stimuli, i.e. when participants are required to recall the elements of the RCFT, they may verbalize the figure before reproducing it. It seems that right and left TLE is affecting visual memory in the same degree, although the memory specific model implies that visual memory should be affected more in people with right TLE than in those with left TLE. Gender of the participants was not associated with visual memory in our study, although there is a research showing that men have different lateralization of the brain for the visuospatial processing[16]. It is possible that the measurement of visual memory with the RCFT is dependent on both hemispheres equally in men and women. So even with different brain lateralization, epileptic seizures are affecting structures needed for visual memory capacity in both genders.

Previous research has clearly demonstrated the comorbidity of depression and anxiety with epilepsy[22-26]. Nine (15%) participants in our study were depressed, while seven (12%) had significantly elevated anxiety. Patients with lower depression levels performed better

in the Immediate Recall and Delayed Recall subtests of the RCFT. This is not surprising, as depression may have a direct effect on concentration, attention and memory[27,28].

The patients with low and high anxiety performed equally well on both recall tasks. This finding was contrary to our expectations, as we presumed that anxiety would be a contributing factor in lower achievement on visual memory tasks[29,30]. The lack of differences could be due to the small number of participants in the high-anxiety group. In one research, there was a link between lower results on the RCFT and people with generalized agoraphobia[31]. For performing well on the tests of visual memory, participants also need to have good motor skills, planning skills and speed in processing. Thus, it is possible that because of the different set of abilities needed to successfully reproduce visual memory tasks, maybe not only visual memory capacity but something additional can affect lower results in these tasks in people with TLE.

Besides the small number of participants in this study, it would be useful to have participants divided into groups based on age. The diagnostic tests we used are all performance based, so with older age there is a small but steady decline. Prospective studies with a greater number of participants are needed. Also, it would be useful to conduct longitudinal studies to reveal the possible decline in cognitive functions.

In conclusion, it appears that gender and anxiety level are not variables that significantly contribute to visual memory capacity, but possibly more specific anxiety measures would be needed in future studies. Furthermore, we found that people with TLE and greater depression achieved statistically significantly lower results on visual memory. Therefore, we recommend that future studies assessing visual memory in people with TLE also examine symptoms of depression.

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Sažetak

KAPACITET NEVERBALNOG PAMĆENJA KOD OSOBA OBOLJELIH OD EPILEPSIJE POVEZAN JE S DEPRESIJOM, A NE S ANKSIOZNOSTI

K. Matešić, M. Tadinac i *H. Hećimović*

Epilepsija je obilježena ponavljajućim epileptičnim napadajima koji se manifestiraju na razne načine ovisno o lokaciji i veličini žarišta. Dugotrajni napadaji sa sekundarnom generalizacijom oštećuju i produbljuju probleme s pamćenjem. Brojne studije su dokazale povezanost oštećenja pamćenja i lateralizacije kod epilepsije temporalnog režnja. Međutim, rezultati nisu uvijek bili sukladni modelu pamćenja specifičnog za materijal. Moguće objašnjenje ove nedosljednosti je nedovoljna kontrola psiholoških varijabla koje mogu utjecati na pamćenje. U većini prijašnjih studija s osobama koje boluju od epilepsije emocionalna stanja poput anksioznosti i depresivnosti nisu bila kontrolirana. U našem istraživanju smo primijenili Reyev test složenog lika kao mjeru vidnog pamćenja, Beckov inventar depresije (BDI) kao mjeru depresivnosti i Upitnik anksioznosti kao stanja i osobine ličnosti kao mjeru anksioznosti na 57 uzastopnih sudionika. Naš glavni cilj je bio ispitati postoji li razlika u vidnom pamćenju s obzirom na desnostranu i lijevostranu epilepsiju temporalnog režnja, rod sudionika te stupanj anksioznosti i depresivnosti. Sudionici s niskom razinom depresivnosti su postigli bolje rezultate na subtestovima Reyeva složenog lika te na neposrednom i odgođenom dosjećanju. Također smo istražili potencijalne spolne razlike. Nisu utvrđene razlike u vidnom pamćenju niti s obzirom na rod sudionika niti s obzirom na stupanj anksioznosti.

Ključne riječi: *Epilepsija temporalnog režnja; Pamćenje; Vidno pamćenje; Anksioznost; Depresija; Neuropsihološki testovi*