

Original paper

Archives of Psychiatry Research 2021;57:81-92

DOI:10.20471/may.2021.57.01.10

Received August 25, 2020, accepted after revision November 10, 2020

Verbal Memory Functions in Patients after the Ruptured and Unruptured Cerebral Aneurysm Surgery

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Abstract - A cerebral aneurysm is a bulge in the wall of a brain blood vessel with a risk to rupture. It occurs in about 2% of the population, somewhat more often in women. Most aneurysms are located in the anterior circulation area. Aneurysm rupture is relatively rare and accounts for 5% of all cerebrovascular brain incidents. Ruptured and asymptomatic/unruptured aneurysms are often treated surgically at the Department of Neurosurgery, Medical School University of Zagreb. The study included 134 patients after cerebral aneurysm surgery during the last 10 years, and neuropsychological testing was performed on average 77 days after surgery. The average age was 52 years and they completed an average of 12 years of education. In the group of patients included in this study, 40.3% of them were operated after ruptured, and 59.7% for unruptured cerebral aneurysm. Most aneurysms were located in the middle cerebral and anterior communicating arteries. With regard to lateralization, there was an equal number of aneurysms located in the right and left hemisphere and bilaterally (on the anterior communicating artery). As part of regular neuropsychological assessment, tests of verbal learning and memory (numerical, logical and mechanical memory) were applied. The aims of the study were to find out whether patients operated for ruptured cerebral aneurysms show greater verbal memory impairments than patients operated for unruptured cerebral aneurysms and whether there was the significant effect of lateralization of aneurysm (to check the interaction effect of both rupture and lateralization on those functions). The results obtained show that, even though there are no statistically significant differences between groups of patients that underwent surgery for ruptured and unruptured brain aneurysm, patients show a trend of somewhat better results on most of the verbal memory functions after surgery for unruptured brain aneurysm. The results show statistically significant difference between groups of patients that underwent surgery for ACoA aneurysm and those with right lateralized cerebral aneurysms on most of the trails on AVLT test. Also, patients with operated ACoA aneurysm have significantly worse scores in learning process (AVLT 3 and AVLT 4) and especially on short-term and long-term verbal memory than the patients who were operated for left or right lateralized aneurysm.

Key words: cerebral aneurysm, ruptured cerebral aneurysm, unruptured cerebral aneurysm, verbal memory, lateralisation

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Introduction

Cerebral aneurysm (also intracranial or brain aneurysm) is a bulge in the wall of an artery or blood vessel in the brain with a risk to rupture. There are three types of cerebral aneurysms: the most common type is a saccular (which occurs in 90 percent of cerebral aneurysms) followed by two other types, fusiform and dissecting aneurysms. Cerebral aneurysm is relatively common in humans, with incidence ranges from 10 to 16 per 100000, it occurs more frequently in females and with the highest incidence of rupture between the ages of 40 and 70 [1-3]. It occurs more frequently in arteries located in the front part of the brain. Approximately 85% - 95% of all aneurysms develop at the anterior portion of the cerebral arterial supply [1,4]. The anterior communicating artery (ACoA) is one of the most common locations of cerebral aneurysm and it is the most frequent location of cerebral rupture and subarachnoid hemorrhage (SAH) [3], which is frequently correlated with cognitive decline. The incidence rate of SAH is 8 of 100 000 per year [5]. In patients with SAH the death rate is almost 50%, while approximately 30% of the survivors suffer from some neurological impairment [6].

However, patients surviving SAH often experience cognitive dysfunction demonstrated on standardised neuropsychological tests despite the absence of neurological deficits [7-20]. The objective of neuropsychological evaluation is to identify cognitive, emotional and behavioural sequels of cerebral dysfunctions according to Halligan and associates [21]. Therefore, neuropsychologist have a multiple role which includes determination of cognitive and conative changes and monitoring the patient's recovery, especially in different stages of neuropsychological re-

habilitation [22]. General neuropsychological deficits within SAH and aneurysm treatment include verbal and visual memory impairments as well as visuoperceptive and visuospatial constructive deficits, impairment of psychomotor speed, language disabilities, mental flexibility and personality changes [15,23-25], but the most common cognitive deficits include memory deterioration, executive function impairment, spatial deficits and aphasia as well as personality changes [15,19,26-28].

The nature and severity of the cognitive impairment mainly depends on the location of the aneurysm [18]. The rupture of ACoA often causes persistent memory deficits (with impaired anterograde memory as the most consistent findings) and personality changes, while ruptures of aneurysms of the internal carotid (ACI) or middle cerebral artery (ACM) often results with aphasic, spatial and memory impairments [18]. Fontanella and associates confirmed memory impairment as the most common deficit occurring after ACoA aneurysm surgery [29]. Long-term memory (both verbal and visual) becomes significantly deficient, while short-term memory can remain intact or only mildly damaged. However, as Bellebaum and associates state, most studies comparing the neuropsychological performance of ACoA patients and patients with ruptured aneurysms in other locations did not yield consistent differences between these two groups [24]. Furthermore, tests of executive functions did not differentiate patients with anterior and posterior lesions [24]. Neuropsychological deficits can persist even after a year and more following the insult [15,24]. Several studies found that 30% to 55% of patients have deficits in one or more cognitive domain 1-7 years after surgical treatment of ruptured aneurysms [26,30].

Ljunggren and associates found neuropsychological deficits, with memory loss being the most common, in 83% of patients tested 3 to 5 years after SAH (significant changes also have been found in intellectual functions, visual and spatial abilities, speed and formation of ideas with following changes in social activities, emotional control and mood) [26]. Meta-analysis from Al-Khindi and associates, in which they analysed the results of 61 studies confirmed severe memory (approximately 60%), executive functions (up to 75%) and speech (up to 75%) deficits due to aneurysmal SAH [31]. However, most studies of cognitive function after SAH have attributed cognitive impairments to the cerebral damage caused by the bleed rather than the effect of the surgery [15,32,33]. Hillis and associates found cognitive impairments in patients 3 months after unruptured intracerebral aneurysms (UIA) treatment similar as those seen after SAH from a ruptured cerebral aneurysm [34]. Also, Ohue and associates suggested that neuropsychological outcomes following surgery of UIA were not satisfactory, particularly in view of significant memory deficits occurring after surgery [35]. On the other hand, Otawara and associates report opposite results; the patients treated with surgery for non-ruptured aneurysms did not develop any cognitive disorders after operative procedure [36].

The aim of our study was to investigate memory deficits in Croatian patients operated for ruptured and unruptured cerebral aneurysms at Department of Neurosurgery, Medical School University of Zagreb.

The objective was to find out whether patients operated for ruptured cerebral aneurysms show greater memory impairment than patient operated for unruptured cerebral aneurysms and to find out if there is sig-

nificant effect of lateralization of aneurysm on cognitive impairment (to check the interaction effect of both rupture and lateralization on those functions).

Subjects and Methods

Subjects

The study included 134 patients after the brain aneurysm surgery in time period 2010-2019. There were 34 or 25,4% male and 100 or 74,6% female patients, with the mean age of 51,6 (19-69) and with the mean of 12,0 years of education. In the group of patients included in this study, after the ruptured aneurysm surgery there were 54 or 40,3 % (19 male, 35 female) and 80 patients or 59,7% were operated after unruptured aneurysm surgery (15 male, 65 female).

As regards the localization the most of the aneurysms were on ACM (76 – 56,7%), followed by ACoA (37 – 27,6%), ACI (9 - 6,7%) and ACA (5 – 3,7%) and artery pericalosa 3 -2,2%). There were only one on ACoP, ACP, AB and callousal artery. There were 16 (11,9%) patients with multiple aneurysms. As regards lateralization, there were 36,6% aneurysms in right and 35,1% in hemisphere and 28,4% bilateral (ACoA). As regards lateralization, in the group of patients after the ruptured aneurysm surgery there were 15 in left and 15 in right hemisphere and 24 bilaterally sited, while in the group of patients who underwent surgery of asymptomatic/unruptured aneurysm there were 32 in left, 34 in right and 14 bilaterally sited.

Measuring instruments

The following types of memory were investigated: numerical memory or memory of numbers, working memory or repeating num-

bers backwards, verbal-mechanical memory or memory of a list of words, verbal-logical memory or memory of stories. These types of memory were assessed by the following tests: Wechsler Memory Scale (WMS) and Auditory-Verbal Learning Test (AVLT).

a) Wechsler Memory Scale (WMS). Numerical memory or memory of numbers was assessed by numerical memory subtest that is part of the WMS, and it consists of numbers that have to be repeated forward (measure of numerical memory) and backwards (measure of working memory) [37]. Maximum possible score in forward memorizing numbers is 9, and 8 for backward memorizing. Total score equals the sum of forward and backward number memorizing scores. In our study, the numerical and working memory results were presented and analysed separately.

Verbal-logical memory is measured by the WMS subtest of logical recalling. The subtest contains two short stories and a defined number of points (score) is given to each separate unit of the story. A maximum number of points is 20. In our study, only one story was read and patients were asked to recall the story immediately upon its reading (short-term memory) and at the end of neuropsychological assessment (long-term memory).

b) Verbal-mechanical memory was assessed by the Auditory-Verbal Learning Test (AVLT), meant for evaluation of short-term memory, learning curve, learning and memorizing strategies, retroactive and proactive interference and long-term memory [38]. The test contains of two lists of 15 words. The study participant is verbally presented list A for five times and after each presentation the participant

is asked to repeat all the words he/she can remember. The results obtained after reading the fifth list indicates memory capacity, and the results from 1 to 5 repetitions show the learning curve. The sixth and seventh repetitions are the measure of short-term and long-term memory, respectively. The result for each word reproduction is total number of repeated words in a trial period.

Procedure

Neuropsychological assessment was conducted in a time period 1-6 month ($M=77$ days) after the operation of cerebral aneurysm at Department of Neurosurgery, Medical School University of Zagreb, during the time period 2010-2019. Neuropsychological assessment was carried out by an experienced psychologist and included clinical interview and neuropsychological tests described above, as a part of large neuropsychological assessment.

Windows package for statistics was used on data analysis; descriptive statistics and multivariate analysis of variance (MANOVA) as main statistical data processing were used.

Results

Overall number of patients and their number by relevant groups (ruptured and unruptured aneurysms), as well as descriptives for different measures of verbal memory are shown in Table 1. For a clearer overview, the results for AVLT across levels of independent variables have also been shown in Figure 1.

As it can be seen in Table 2, MANOVA showed a statistically significant multivariate main effect of lateralization, with 16.5% of variance explained. The main multivariate ef-

Table 1. Descriptive statistics for AVLT, numbers forwards and backwards and verbal-logical memory of groups of patients with differently lateralized ruptured and unruptured cerebral aneurysms

		rupt				nrup				total		
		dex	sin	ACoA	total	dex	sin	ACoA	total	dex	sin	ACoA
avlt1	M	6.87	6.53	6.43	6.20	6.94	6.83	6.25	9.95	6.92	6.73	6.36
	SD	2.2	1.25	1.8	1.82	1.66	1.85	1.6	3.04	1.82	1.66	1.71
	N	15	15	21	51	33	29	12	74	48	44	33
avlt2	M	8.47	8.8	8.57	11.35	9.61	9.31	8.75	9.35	9.25	9.14	8.64
	SD	2.42	2.24	1.66	2.19	1.52	2.22	1.36	1.81	1.90	2.22	1.54
	N	15	15	21	51	33	29	12	74	48	44	33
avlt3	M	10.33	10.33	9.67	10.63	11.09	10.69	9.17	10.62	10.85	10.57	9.48
	SD	2.94	2.26	2.37	2.24	1.59	2.29	2.21	2.07	2.10	2.26	2.29
	N	15	15	21	51	33	29	12	74	48	44	33
avlt4	M	11.27	10.53	10.24	10.06	12	11.55	10.42	11.57	11.77	11.20	10.30
	SD	2.37	2.03	2.28	2.49	1.95	2.01	2.27	2.07	2.10	2.05	2.24
	N	15	15	21	51	33	29	12	74	48	44	33
avlt5	M	12.27	11.27	10.76	6.59	12.85	12.34	11.17	12.38	12.67	11.98	10.91
	SD	2.58	1.67	2.1	1.77	1.73	2.04	2.41	2.03	2.02	1.97	2.18
	N	15	15	21	51	33	29	12	74	48	44	33
avlt6	M	10.67	8.93	8.62	9.31	10.91	9.93	8.75	10.18	10.83	9.59	8.67
	SD	2.97	3.35	2.97	3.15	2.48	2.95	3.25	2.87	2.61	3.09	3.03
	N	15	15	21	51	33	29	12	74	48	44	33
avlt7	M	9.73	8.8	7.62	8.59	10.42	10.21	8	6.78	10.21	9.73	7.76
	SD	3.15	3.1	3.54	3.36	2.6	3.17	3.33	1.72	2.77	3.18	3.42
	N	15	15	21	51	33	29	12	74	48	44	33
nf	M	5.86	6.36	6.20	6.15	6.19	6.43	6.27	6.30	6.09	6.40	6.23
	SD	0.86	1.39	1.32	1.22	0.79	1.03	0.65	0.87	0.82	1.15	1.12
	N	14	14	20	48	31	28	11	70	45	42	31
nb	M	4.07	4.93	4.60	4.54	4.61	4.82	4.55	4.69	4.44	4.86	4.58
	SD	1.21	1.33	1.27	1.29	0.92	0.98	0.69	0.91	1.03	1.09	1.09
	N	14	14	20	48	31	28	11	70	45	42	31
vlog	M	10.29	9.79	8.75	9.50	9.97	9.86	7.45	9.53	10.07	9.83	8.29
	SD	2.49	3.68	2.84	3.03	3.25	3.60	2.81	3.41	3.01	3.58	2.85
	N	14	14	20	48	31	28	11	70	45	42	31

dex - group of patients with right lateralized cerebral aneurysm; sin - group of patients with left lateralized cerebral aneurysm; ACoA - group of patients with anterior communicating artery aneurysm; rup - ruptured aneurysm; nrup - non ruptured aneurysm; nf - results of WMS subtest Numbers Forward; nb - results of WMS subtest Numbers Backwards; vlog - verbal-logical memory (stories)

* $p < 0.05$; ** $p < 0.01$

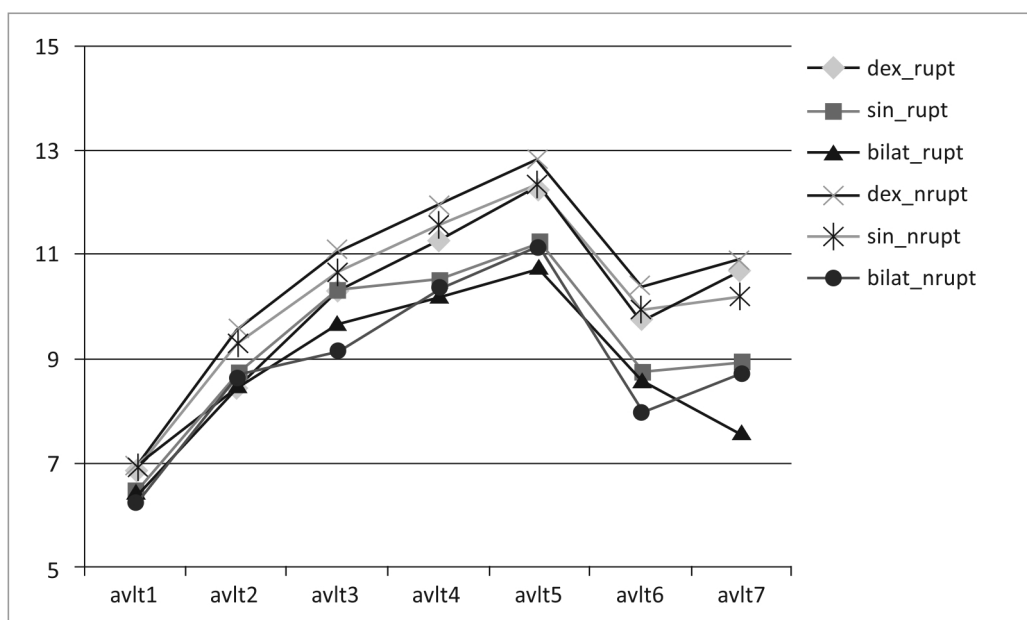


Figure 1. Learning curves (AVLT) for patients with differently lateralized ruptured and unruptured cerebral aneurysms.

fect of rupture, as well as multivariate interaction of rupture and lateralization have failed to reach statistical significance and explain 11.6% and 4.7% of total variance, respectively. Even though there are no statistically significant differences between groups of

patients that underwent surgery for ruptured (40.3%) and unruptured (59.7%) brain aneurysm, patients show a trend of somewhat better results on most of the verbal memory functions after surgery for unruptured brain aneurysm.

Table 2. MANOVA results for AVLT and WMS measures for groups of patients with ruptured and unruptured aneurysms with different lateralization

	Wilk's λ	F	df	sig	partial η^2
Lateralization	0.698	1.828	22	0.02	0.165
Rupture	0.884	1.217	11	0.285	0.116
Lateralization*Rupture	0.908	0.457	22	0.983	0.047

Lateralization - multivariate main effect of lateralization; rupture - multivariate main effect of rupture; lateralization*rupture - multivariate interaction effect of lateralization and rupture, * $p < 0.05$; ** $p < 0.01$

Table 3. F-values of univariate effects with corresponding Post-hoc results

	lateralization	rupture	Lateralization*rupture	Post-hoc
AVLT1	0.906	0.035	0.156	/
AVLT2	0.445	2.750	0.590	/
AVLT3	3.309**	0.233	0.716	bilat<dex**
AVLT4	3.348**	2.530	0.344	bilat<dex**
AVLT5	5.360*	3.107	0.266	bilat<dex*
AVLT6	4.873*	0.670	0.244	bilat<dex*
AVLT7	4.906*	1.944	0.260	bilat<dex* bilat<sin**
nf	1.205	0.613	0.198	/
nb	3.601	0.356	1.040	/
vlog	2.35**	0.655	0.377	/

Lateralization - univariate main effect of lateralization; rupture - univariate main effect of rupture; lateralization*rupture - univariate interaction effect of lateralization and rupture; * $p < 0.05$; ** $p < 0.01$

Further analysis included univariate effects of independent variables in order to determine possible impact of lateralization. In Table 3 obtained F-values and relevant post-hoc results showing the direction of those differences are presented. As it can be seen, there is a univariate main effect of lateralization on third (AVLT3), fourth (AVLT4), fifth (AVLT5), sixth (AVLT6) and seventh (AVLT7) trail on AVLT. Other measures do not differ significantly.

Our results show statistically significant difference between groups of patients that underwent surgery for anterior communicating artery aneurysm and those with right lateralized cerebral aneurysms on most of the trails on AVLT. More precisely, group with an anterior communicating artery aneurysm scored on average 1.37 (SD=0.50; $p < .05$), 1.47 (SD=0.49; $p < .05$), 1.76 (SD=0.46; $p < .01$), 2.17 (SD=0.66, $p < .01$) and 2.45 (SD=0.70; $p < .01$) points less than the group

with right lateralized cerebral aneurysm on AVLT3, AVLT4, AVLT5, AVLT6 and AVLT7, respectively. Also, the group with anterior communicating aneurysm scored 1.97 (SD=.71; $p < .05$) points less than the group with left lateralized cerebral aneurysm. In other words, patients with operated bilateral aneurysm (ACoA) had significantly worse scores in learning process (AVLT 3 and AVLT 4) and especially on short-term and long-term verbal memory than the patients who were operated for left or right lateralized aneurysm.

Discussion

As in studies already mentioned in introduction and according to some other, memory deficits in patients after ruptured brain artery aneurysm and following SAH, as like as in patients with unruptured aneurysms, present the most common deficits [39-41]. Furthermore, Liacona and associates found

significant memory deficits in patients after surgical treatment of ACoA aneurysm [39]. Such findings were also reported by Stefanova and associates who cited that patients after ACoA aneurysm surgery had deficit of verbal-mechanical short-term and long-term memory following surgical procedures [42].

Even though our study hadn't yield up statistically significant differences in memory deficits between groups of patients with ruptured and unruptured brain aneurysms, we did find that patients show a trend of somewhat better results on most of the verbal memory functions after surgery for unruptured brain aneurysm. Our findings are somewhat in concordance with findings from studies by Otawara and associates, as well as by Hilis and associates, who concluded that, although patients who underwent operation of ruptured aneurysms perform below published norms on many neuropsychological tests, in a minority of patients significant impairments can be seen [7,34].

However, the other finding of this study was the influence of lateralization that is somewhat in concordance with other research in this field that was conducted on the similar group of patients [43]. In our research, patients with operated ACoA (bilateral aneurysm) had significantly worse short-term and long-term verbal memory than the patients who were operated for either left or right lateralized aneurysm. These results are similar to those reported earlier.

Regarding to the type of treatment, some studies supports evidence to favourable outcome following endovascular coiling treatment rather than surgical clipping [44,45]. On the other hand, Bonares and associates in their systematic review cited that although treatment for unruptured intracranial aneurysms allays anxiety, it also results in an ob-

servable decline in cognition and daily functioning, and that the decision to treat an unruptured intracranial aneurysm ought to add more weight to the neuropsychological, psychosocial, and functional profiles of these patients [46]. Regarding to that, Bonares and associates did the meta-analysis on the effects of unruptured intracranial aneurysms (UIA) treatment on general cognition with an emphasis on 4 specific cognitive functions: verbal and visual memory, visuospatial functions, and executive functions [47]. The results showed that the treatment of an UIA does not seem to affect long-term cognitive functions. However, these findings should be taken with caution due to paucity of studies addressing this issue.

Due to some methodological issues that weren't included in this study, such as general effects of neurosurgical operation, type of treatment/operation and perioperative management, presence and size of SAH, time span from surgery to neuropsychological testing, compliance with physician's instructions, family support, etc., further studies need to be carried. When interpreting the results, it is important to take into account that this is a relatively small sample, which is also the main limitation of this research. In addition, the number of participants in individual subgroups (e.g., ruptured and non-ruptured aneurysms located in the left or right cerebral hemisphere or bilaterally) is unequal and insufficient. This prevents strong conclusions about possible intergroup differences.

Conclusion

Even though there are no statistically significant differences between groups of patients that underwent surgery for ruptured and unruptured brain aneurysm, patients

show a trend of somewhat better results on most of the verbal memory functions after surgery for unruptured brain aneurysm.

The results show statistically significant difference between groups of patients that underwent surgery for anterior communicating cerebral aneurysm and those with right lateralized cerebral aneurysms on most of the trails on Auditory-Verbal Learning Test. Also, the group with anterior communicating aneurysm scored few points less than the group with left lateralized cerebral aneurysm. In other words, patients with op-

erated bilateral aneurysm (ACoA) had significantly worse scores in learning process and especially on short-term and long-term verbal memory than the patients who were operated for left or right lateralized aneurysm.

Acknowledgements

None.

Conflict of Interest

The authors report no conflict of interest.

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Verbalna memorija u bolesnika nakon operacije rupturirane i nerupturirane cerebralne aneurizme

Sažetak - Cerebralna aneurizma je proširenje cerebralne krvne žile kod kojeg postoji vjerojatnost rupture. Javlja se u oko 2% populacije, nešto češće kod žena, a većina je smještena je u području prednje cirkulacije. Ruptura aneurizme je relativno rijetka i predstavlja 5% svih cerebrovaskularnih moždanih incidenata. U klinici za neurokirurgiju Medicinskog fakulteta Sveučilišta u Zagrebu često se operativno liječe rupturirane, ali i asimptomatske/nerupturirane aneurizme. U ovo istraživanje uključeno je 134 bolesnika operiranih u zadnjih 10 godina, kod kojih je neuropsihologijsko testiranje provedeno u prosjeku 77 dana nakon operacije. Prosječna životna dob ispitanika je bila 52 godine te u prosjeku imaju 12 godina školovanja. U skupini bolesnika uključenih u ovo istraživanje 40.3% bolesnika operirano je nakon rupture aneurizme, a 59,7% bolesnika operirano je zbog nerupturirane aneurizme. Najviše je aneurizmi bilo smješteno na srednjoj mozgovnoj i prednjoj komunikantnoj arteriji. S obzirom na lateralizaciju, bio je podjednak broj aneurizmi smještenih u desnoj i lijevoj hemisferi odnosno bilateralno (na prednjoj komunikantnoj arteriji). U okviru redovne neuropsihologijske obrade primijenjeni su testovi verbalnog učenja i pamćenja (numeričko, logičko i mehaničko pamćenje). Cilj istraživanja bio je ustanoviti postoji li razlika u deficitima verbalnog pamćenja u bolesnika nakon operacije rupturiranih i nerupturiranih aneurizmi te postoji li značajan učinak lateralizacije aneurizme (provjeriti interakcijski učinak rupture i lateralizacije na te funkcije). Dobiveni rezultati su pokazali da, iako

nisu utvrđene statistički značajne razlike između skupine bolesnika operiranih nakon rupturirane aneurizme i nerupturirane aneurizme, u većini ispitivanih funkcija bolesnici nakon operacije rupturirane aneurizme postižu nešto niže rezultate. Rezultati pokazuju statistički značajnu razliku između skupina pacijenata koji su operirani zbog ACoA aneurizme i onih s desnim lateralnim cerebralnim aneurizmama na većini ponavljanja na AVLT testu. Također, pacijenti s operiranom ACoA aneurizmom imaju značajno lošije rezultate u procesu učenja (AVLT3 i AVLT4), a posebno na kratkotročnom i dugoročnom verbalnom pamćenju od pacijenata koji su operirani zbog aneurizme smještene u lijevoj ili desnoj mozgovnoj hemisferi.

Ključne riječi: cerebralna aneurizma, rupturirana cerebralna aneurizma, nerupturirana cerebralna aneurizma, verbalno pamćenje, lateralizacija