ORIGINAL ARTICLE

Attention and executive functions in microsurgically treated patients after subarachnoid hemorrhage

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ABSTRACT

Objectives: This research aimed to assess attention and executive functions in subarachnoid hemorrhage (SAH) patients.

Methods: The prospective, controlled, longitudinal study was conducted. There were two groups of patients (SAH and lumbar microdiscectomy groups), and all of them were operated on by a single neurosurgeon (KD) in the same institution. Preoperatively, SAH patients were in the Hunt-Hess Grade I and II. They did not develop any focal neurological deficit or hydrocephalus postoperatively. The patients were tested in 2-time points: 15 and 45 days after microsurgery with a battery of tests and questioners consisting of the Trail Making Test, the Sustained Attention to Response Task, the Hayling Sentence Completion Test, The Attention/Concentration test of Attention, the Wechsler Adult Intelligence Scale (verbal part). Results between groups were compared (sex, age; years of education and verbal IQ).

Results: It was found the presence of lower attention and executive function test scores in the SAH group of patients with a trend of improving during the time.

Conclusion: The detailed neuropsychological assessment of operated patients who sustained SAH and were without the focal neurological deficit postoperatively, showed declination in their attention and executive function with a trend of cognitive recovery as time passes by.

Key words: Attention, executive functions, neuropsychological assessment, subarachnoid hemorrhage

Introduction

Cognitive dysfunctions after subarachnoid hemorrhage (SAH) are well documented. Attention, memory and other cognitive functions are very important for SAH patient rehabilitation and their return to normal life. Numerous clinical studies showed that cognitive deficits in these patients depend on a large number of factors, which includes the effects of hemorrhage and secondary brain ischemia, surgical performance,[1] timing of surgery,[2,3] anatomical location of the aneurysm,[4] family, friends and medical staff support,[5,6] utilization of endovascular or microsurgical clipping options.[7] The study of Ropper and Zervas[8] pointed out that 25% of patients, year after successful treatment of ruptured intracranial aneurysm, have psychological and emotional deficits. The research of Ogden *et al*.[9] shows that the high percentage of patients demonstrated some mild to moderate psychosocial impairments. Hütter and Gilsbach[10] concluded that a good neurological outcome does not exclude the persisting neuropsychological deficits. Some other results [9, koso-dizdarević] show that the severity of SAH is the most important factor related to cognitive dysfunction. Hillis *et al*.[11] examined patients with unruptured and ruptured aneurysm. Both groups performed significantly below published norms on many of the neuropsychology tests after surgery. On the other hand, Otawara *et al*.[12] found that microsurgery of the unruptured intracranial aneurysm did not influence the cognition. Samra *et al*.[4] presented that cognitive improvement that is present after 3 months, with a plateau between 9 and 15 months, was not affected by the location of the aneurysm. Many studies enrolled the patients with cognitive impairment who harbored the anterior communicating artery (ACoA) aneurysms.[13-15] However, cognitive results from these studies were very similar with cognitive dysfunctions found in the patients with aneurysm on other arteries. Lloyd *et al*.[7] examined the difference between cognitive function and quality of life among patients treated by endovascular coiling

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and those treated by microsurgical clipping. The conclusion was that endovascular treatment and microsurgery had the similar impact on health-related quality of life and cognitive function. Patients in both groups demonstrated a significant decline in cognitive function. The goal of the study that conducted by Tuffiash *et al*.[15] was to identify changes in cognitive function associated with surgical clipping of the unruptured intracranial aneurysm. They found no evidence of subtle cognitive deficits resulting from aneurysm clipping alone, suggesting that the common impairments after surgery for ruptured aneurysms are due to SAH itself, complications of SAH such as vasospasm or hydrocephalus, or preoperative stroke. Chan *et al*.[16] concluded that in patients with ACoA aneurysm, endovascular coiling demonstrated significantly fewer severe cognitive deficits than surgical clipping.

The goal of this research was to assess attention and executive functions in SAH patients after microsurgical clipping and to compare their cognition with the cognition of the control group of patients treated by microdiscectomy due to lumbar disk herniation. In above-mentioned studies, researchers used the control group of healthy patients. The variables that partially caused the difference in cognitive functions between clinical and healthy groups could have been an anxiety or depression because of hospitalization. That is the reason why we use hospitalized patients as a control group. Cognitive abilities of these two groups were tested in 2-time points: 10–12 days after the surgery and 46 days after the surgery.

Methods

In this study, we controlled factors as age (there were no patients beyond 60 years and there was no difference between control and experimental group), years of education, anesthesia, emotional and stress factors of being hospitalized, verbal intelligence, sex, premorbid loss of consciousness, premorbid neurological or psychiatric illness, Hunt-Hess (HH) grade (only Grades 1 and 2), considering that all that factors can be variables that can influence or moderate results on cognitive function's tests. As far as we know, there was no research conducted by the control group of hospitalized subject that would give us an opportunity to exclude a factor of hospitalization on cognitive functions.

Subject characteristics

Two groups of patients were examined: 12 patients (7 male and 5 female), diagnosed with aneurysmal SAH treated with surgery and 12 patients after discus hernia surgery (5 male and 7 female).

All patients, in the time of testing, were middle-aged (ME =45,92, SDE =8,81; MK =45, 50, SDK =12, 59; t = 0.094, df =22, P = 0.926), with similar level of education measured with years of school (ME =10,67, SDE = 1,97; MK = 12,17, SDK = 1,80; t = −1.947, df = 22, P = 0.064) and with similar level of verbal intellectual skills measured with subtests Wechsler Adult Intelligence Scale (WAIS) – comprehension (ME = 20,83, SDE = 4,324; MK = 21,83, SDK = 4,726; t = −0.541, df = 22, P = 0.594) and WAIS – Similarities (ME = 19, 08, SDE = 2,811; MK = 20,25, SDK = 3,079; t = −0.969, df = 22, P = 0.343).

Following local Institutional Review Board/Ethics Committee approval, all subjects that match criteria during the 2 years of research were tested. They were all treated by a single neurosurgeon (co-author) at the Department of Neurosurgery, Clinical center University of Sarajevo. Criteria were: Age <60 years; lost of consciousness shorter than 10 min; good general health condition; all patients in the experimental group were HH Grade 1 or 2; all patients had excellent neurological postoperative recovery; all patients were right-handed, and all were operated by the single neurosurgeon; all patients in the experimental group were operated on through the same surgical approach (pteryonal craniotomy with transsylvian route.

Psychological assessment

In 1st time point, we used: Questionnaire to collect basic information to the patient and the Trail Making Test (TMT) test of attention. In 2nd time point, we again use TMT, which gave us an opportunity to follow improvement with patients, and we use other cognitive tests: The Sustained Attention to Response Task (SART), Hayling Sentence Completion Test (HSCT), Attention/Concentration (AC) test of attention, WAIS (Comprehension) and WAIS (Similarities) and Alcohol Use Disorders Identification Test (AUDIT).

The TMT is a test of scanning and visuomotor tracking, divided attention, and cognitive flexibility. It is given in two parts, A and B. Slowed performance on TMT Part B relative to TMT Part A signals impaired ability to execute and modify the plan.[17] The SART is a continuous performance test developed by Robertson *et al.*[18] and involves the withholding of key presses to rare (one in nine) targets. The HSCT measures verbal response initiation and suppression.[19] Patients with frontal lobe lesions need more time than control participants in finding a word far from the semantic field that normally completes the sentence.[20] The verbal part of WAIS[21] was used to assess verbal intellectual function. AC test of attention is a continuous paper-pan performance test where subject is asked to cross letter C each time when he/she noticed that letter in A4 paper among all other letters. The 10-item AUDIT;[22] was administered to assess alcohol use.

Statistical analysis

SPSS 17.0 (IBM company, Chicago, IL) software was used in the statistical treatment to the data. For tests used in both time periods, we used mixed two (repeated measures for time: Spot 1 vs. spot 2) × 2 (SAH vs. DH) ANOVA (multiple analyses of variance). For additional tests used during 2nd time period, we use *t*-test. As an index of effect size, we report ^{2}h that can vary between 0 and 1. When ^{2}h >0.15 effects are considered "large" in magnitude, and when ^{2}h 0.06 effects are "medium."

Results

Visuomotor tracking and initiation (TMT A), cognitive flexibility (TMT B, Hayling) and attention (SART, AC)

Factorial analysis of variance (2 × 2) for dependent variable cognitive attention and initiation [Table 1] we have determined shoed statistically significant effects of factor Group (F = 16,103, $P = 0.001$) and time ($F = 6{,}471$, $P = 0.019$), while the effect of interaction factor time × group is on the edge of statistical significance ($F = 4{,}215$, $P = 0.052$). Those that have undergone SAH surgery needed significantly more time for TMT A test than those with DH surgery. Furthermore, both groups needed more time to solve TMT A in first than in the second measurement. *T*-test for repeated measures has confirmed that this change is statistically significant for the experimental group ($t = 2{,}414$ df = 11 $P = 0.034$), but not for the control group ($t = 0.803$ df = 11 $P = 0.439$). Cognitive flexibility (TMT B)

Factorial analysis of variance (2 × 2) for dependent variable cognitive flexibility measured with TMT B [Table 2], have determined statistically significant effects of factor Group ($F = 41{,}103$; $P < 0.01$) and time ($F = 19{,}566$; $P < 0.01$), as well as the effect of interaction factor factors ($F = 4{,}215$; $P < 0.01$). Those that have undergone SAH surgery needed twice as much time to solve TMT B test than those with DH surgery. Also furthermore, groups needed more time to solve TMT B in first than in the second measurement. *T*-test for repeated measures has confirmed that this change is statistically significant for the experimental group ($t = 3{,}957$ df = 11 $P = 0.002$). Values for the control group are also on the edge of statistical significance ($t = 2{,}124$ df = 11 $P = 0.057$).

Forty-five days after SAH and DH surgeries patients were tested with battery of tests for measurement of cognitive functions. We have used tests from the first measurement: TMT A and TMT B, but also four additional tests: HSCT, SART, AC, sub tests Comprehension and Similarities from WAIS. Results of those tests will be presented on following pages. Sustained attention, initiation, inhibition, vigilance and working memory Table 3 shows means, standard deviations and *t*-test for repeated measures for sustained attention, initiation, inhibition, vigilance and working memory [Table 3]. Descriptive statistical values, *t*-values and effect size on tests SART, Hayling test, AC and WAIS memory.

As Table 3 shows, there is statistically significant difference between the experimental and control groups on tests used during the second measurement. When compared with the control group, the experimental one shows statistically poorer result on the sustained attention test measured by SART and AC. Time reaction, measured in seconds on SART test, shows no difference between two groups. The experimental group also achieved the significantly poorer results on HSCT, used for the measurement of initiation, inhibition and evaluation of the supervision attention system.

Table 1: Descriptive statistical values for cognitive attention and initiation

Group	First measurement		Second measurement	
	Mean	SD	Mean	SD
Experimental group	86.08	37.98	60.33	22.66
Control group	40.00	17.62	37.25	16.41

SD – Standard deviation

Table 2: Descriptive statistical values for cognitive flexibility

Group	First measurement		Second measurement	
	Mean	SD	Mean	SD
Experimental group	180.92	60.00	125.92	33.95
Control group	69.17	24.55	59.42	23.82

SD – Standard deviation

Table 3: Descriptive statistical values, t-values and effect size on tests SART, Hayling test, AC and WAIS memory

	Group	Mean	SD		η^2
SART f^+	Experimental	10.33	6.29	t=1.675 (df=22; P=0.108)	
	Control	6.83	3.59		
SART f^-	Experimental	30.25	32.81	t=2.264 (df=22; P=0.034)	0.179
	Control	8.33	6.93		
SART total	Experimental	40.58	32.36	t=2.625 (df=22; P=0.015)	0.224
	Control	15.17	8.83		
SART rt	Experimental	519.71	134.04	t=0.972 (df=22; P=0.341)	
	Control	472.96	98.87		
Hayling 1	Experimental	0.91	0.15	t=4.160 (df=22; P=0.0001)	0.427
	Control	0.71	0.056		
Hayling 2	Experimental	2.98	1.88	t=3.602 (df=22; P=0.002)	0.359
	Control	1.01	0.197		
Hayling index	Experimental	3.24	1.82	t=3.273 (df=22; P=0.004)	0.338
	Control	1.42	0.28		
AC L	Experimental	39.42	2.78	t=−1.749 (df=22; P=0.094)	
	Control	40.83	0.39		
AC R	Experimental	40.00	1.86	t=−3.169 (df=22; P=0.004)	0.299
	Control	41.75	0.45		
AC total	Experimental	79.42	4.40	t=−2.465 (df=22; P=0.022)	0.205
	Control	82.58	0.67		
	Control	7.83	1.85		

SART – Sustained attention to response task; SART f+ – Sustained attention to response task false positive; SART f– – Sustained attention to response task false negative; SART total – Sustained attention to response task total; SART rt – Sustained attention to response task reaction time; Hayling 1 – Hayling sentence completion test part one, Hayling 2 – Hayling sentence completion test part two; Hayling index – Hayling sentence completion test relation between first and second part; AC L – AC attention test, number of crossed letter on the left side; AC R – AC attention test, number of crossed letter on the right side; AC total – AC attention test, total number of crossed letters; WAIS – Wechsler adult intelligence scale; AC – Attention/concentration; SD – Standard deviation

Discussion

According to current researches and theoretical presumptions, we have assumed that patients, after clipping of ruptured intracranial aneurysm causing SAH, will experience certain cognitive dysfunction. We have also presumed that average cognitive function test during the first measurement will be poorer than tests results achieved during the second measurement, which implies that cognitive functions will recover in time. Results of cognitive function tests in patients after surgical treatment of aneurysm causing SAH have been compared with results of patients who have undergone lumbar disk microsurgery. Hospital time, stress, pre and postoperative anxiety and depression as well as postoperative recovery could represent variables that would influence results on the cognitive function test, which has not been controlled in researches before. In order to control the influence of such variables, we choose the control group that has experienced general anesthesia and was operated on at the same Neurosurgical Department. Data analysis indicates cognitive dysfunction in SAH patients. According to Lezak[23] TMT is a test of scanning, visuomotor tracking, divided attention and cognitive flexibility. It is a test of complex visual scanning where motor abilities, such as motor speed and agility, significantly influence test results. The same way as all other tests that include motor speed and attention this one is very sensitive to the brain damage.[23] Factorial analyses of variance have confirmed that patients with aneurysm surgery needed significantly more time to solve TMT An and TMT B test. Patients with SAH diagnosis that have undergone aneurysm surgery and have been tested on 12th and 46th day after the surgery had significantly poorer results on TMT test than patients tested on 12th and 46th day after microdiscectomy. Effects of group, time and interaction time × group are significant for TMT A and TMT B test. According to [Figures 1 and 2] functions measured with TMT A and TMT B improved in time, but such improvement is different for experimental and control group. Difference between first and second measurement for the control group is small and not significant, while the difference between two measurements for the SAH group is much higher and significant. All participants have been, in average, tested with an extended battery of tests for neuropsychological assessment of cognitive functions 46 days after surgery and 34 days after first testing. Apart from tests that have been used during first measurement, such as attention assessment, initiation and inhibition, cognitive flexibility, visuomotor activities, we have used additional test for assessment of sustained attention, verbal initiation, inhibition, vigilance, working memory and verbal intellectual abilities. Table 3 indicates that there is statistically significant difference between the experimental (SAH) and control groups with regard to sustained attention where reaction time and sustained attention were measured with SART test. Reaction time needed for completion of a task is slightly longer for the experimental group, but such difference is not significant. Total number of mistakes between control and experimental group is significantly different. Another test that measures attention and also represents a test of continued performance is AC test. Table 3 indicates difference in the total number of crossed letters C. If we observe closely the number of crossed letters C on left and on the right side of the paper, we see that the difference is not significant for the left side of the paper, but it is for the right one. Therefore, if we are to observe the number of crossed letters C on the right side of the paper, we can notice that patients undergone aneurysm surgery make more mistakes in this task and have significantly poorer sustained memory and tracking. In our sample of patients with aneurysm surgery, we have had seven patients with aneurysm on right and five patients with aneurysm on the left side of the brain, which is not significantly large sample for us to test significance of such difference between these two groups with regard to their performance on cognitive tests. The HSCT is a measure of response initiation and response suppression and is used for assessing supervisory attentional system.[19] This function is controlled by the frontal lobe.[24] Our results indicate that patients after aneurysm surgery have extended reaction time on first and second part of the test (initiation and inhibition)

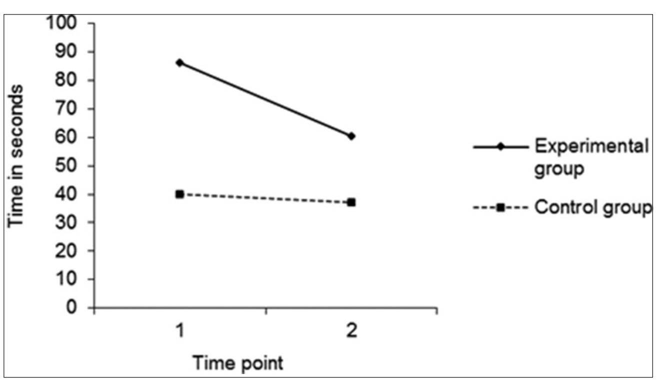

Figure 1: This graph shows significant changes in time for the experimental group (ΔMe = 25, 75; ΔMk = 2, 75) than for the control one

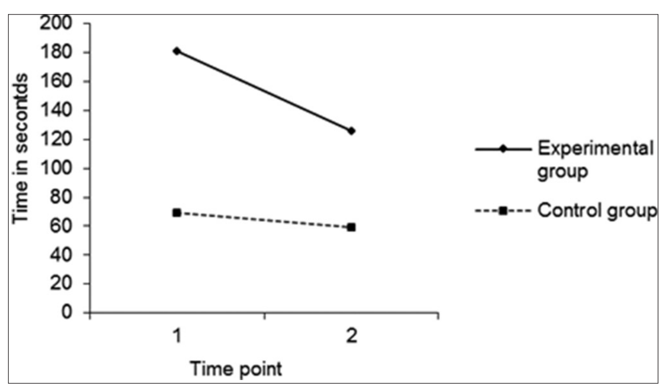

Figure 2: Bigger and more significant changes in time for the experimental group (ΔMe = 55; ΔMk = 9, 75) compared with the control group

and ratio between these two measures is significantly higher for experimental (SAH) than for the control group. Such difficulties result in slow reaction time for giving simple answers, inability to inhibit dominant response and supervision attention system disorder. Altogether, this result shows disorder of executive functions. Size of the effect is largest for HSCT that measures initiation, inhibition and is presumably measure of supervision attention system. Results that prove damaged function of visuomotor memory, divided attention, cognitive flexibility, sustained attention, verbal initiation, inhibition and vigilance for persons that have undergone aneurysm surgery is in accordance with results of many other authors whose results also indicate a disorder of cognitive functions for aneurysm surgery patients.[9,10,11] Cognitive functions will recover in time, which can be concluded from this research and from researchers of other authors that have tested cognitive functions in two or more time periods.[25] Due to the presence of the control group that has also undergone general anesthesia and operative stress, we can conclude that the reason for poorer results on cognitive ability tests is SAH and aneurysm surgery. Other researchers that have included structural and functional brain scans could not explain or find any correlation of cognitive deficit. Even if there was a possibility to find areas in the brain affected with blood circulation disorder, there was no correlation between location or brain hemisphere affected with aneurysm and cognitive dysfunction.[26] The SPECT study conducted by Tooth *et al*.[27] identified a large common area of subcortical hypoperfusion in the SAH patient undergone surgery. Authors of this study suggest a possible link between reduced subcortical function and the extent and severity of cognitive deficits. Nozaki *et al*.[28] determined cholinergic dysfunction in patients with cognitive impairment after SAH based on the pupillary response to tropicamide. There is also an ongoing debate on mechanisms responsible for the recovery of cognitive functions of stroke patients. Ponsford[29] presumes that this includes different biological processes. Recovery that happens after several days is related to temporary structural damage such as vascular disruption or edema.[29] Our research also pointed out that cognitive dysfunction in SAH patients after aneurysm clipping will decrease in time. Clearly, the cause of cognitive deficit in these patients is not defined but there was certainly some connection with previously mentioned biochemical processes within the brain. However, these and other results should emphasize the need for a neuropsychological assessment of patients after neurological surgeries so that the appropriate professional help could be provided. Many authors agree that due to such cognitive deficits, it is hard for patients to return to their normal daily routine[6] while Suarez[30] believes that neuropsychological evaluation is necessary in first 3 months after the stroke. Cognitive dysfunction symptoms that were detected in our research in people undergone aneurysm surgery and SAH may prevent patients from going back to work, socialize and have the same quality of life as before the surgery. Rehabilitation of SAH patients depends upon our ability to recognize their problems and understand if and how cognitive deficits influence patients' daily lives. If such deficits are permanent and appear even after rehabilitation, the patient could be suggested to adopt new lifestyle and job. Patients with the memory disorder can be included in memory rehabilitation programs. According to Wilson[29] memory rehabilitation, should not be focused upon the improvement on the test score for memory or any other neuropsychological functions. There are several basic steps in memory rehabilitation process, including: Assessing memory and memory deficit, providing relevant information to patients and family, agreeing on therapy goals and specific problems that will be treated, choosing suitable external or internal strategies for a specific problem, teaching clients different strategies and evaluating effects of the treatment.[29] Many authors emphasize the importance of support of community, family and work colleagues.[9]

Obviously, neuropsychological assessment and treatment have to be an essential part of any recovery process for patients with SAH, including the initial phase (after aneurysm rupture and surgery). Early rehabilitation has to be available for all patients. During discharge rehabilitation, team must inform patient and family on future treatment, continuous cognitive and behavioral therapy and social rehabilitation. It is also important to have additional assessment that will enable the rehabilitation team to re-evaluate patient's recovery, social behavior and gather necessary information that will help them plan all rehabilitation stages during SAH recovery. Improvement in daily practice with patients undergone aneurysm surgery will not be possible without thorough research on cognitive deficit causes.

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