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Cognitive impairment and functional ability in the acute phase of ischemic stroke

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Abstract. – OBJECTIVE: Acute ischemic stroke significantly affects cognitive efficiency and functional ability, primarily physical ability. Decreased cognitive efficiency is often in correlation with decreased functional ability following an ischemic stroke. The aim of the study was to determine whether there is cognitive impairment in patients with preserved physical ability in acute ischemic stroke, and if so, determine whether there is a significant correlation with the functional, i.e. physical status.

PATIENTS AND METHODS: The study included a total of 80 subjects: 40 subjects (26 male and 14 female) in the acute phase of ischemic stroke and 40 healthy subjects (20 male and 20 female) with no history of neurological disease. Both groups were matched with regard to basic sociodemographic characteristics. The cognitive status was evaluated using a comprehensive neuropsychological battery, while physical status was assessed using the modified Rankin scale. Cognitive performance was presented using the following seven cognitive domains: executive function, immediate recall, delayed recall, speech, divergent thinking, attention and concentration, and visual-constructive performance.

RESULTS: The two groups differed in all the studied cognitive domains, with acute ischemic stroke subjects achieving poorer results. There was no correlation between the cognitive status and the functional, i.e.physical ability in the acute ischemic stroke group.

CONCLUSIONS: The results showed significant impairment in all cognitive domains in the acute phase of ischemic stroke, regardless of the preserved functional, i.e. physical ability of these patients.

Key Words:
Acute ischemic stroke, Cognitive impairment, Functional and physical ability.

Introduction

Cognitive impairment is a frequent and often neglected consequence of the acute phase of ischemic stroke[1-3]. In addition to being associated with increased mortality and functional disability[4], the very presence of cognitive impairment often affects the functional outcome more than the physical disability[4,5]. The prevalence of cognitive impairment in the first month after the stroke ranges from 10-82%, which primarily depends on the criteria that are used to define cognitive impairment, and on subject selection[6]. In the first three months, cognitive impairment is found, on the average, in 30% of the patients who had suffered an ischemic stroke[7,8], whereas long-term decrease in cognitive efficiency is registered in 12-52% of patients who had suffered a cerebrovascular incident[9-12], which is significantly higher than the age-related cognitive decline, found in 5-10% of adults[13]. Cognitive impairment found in the first three months after the stroke in patients aged 55-85 most often occurs in one or two cognitive domains (62% and 32%, respectively)[14]. The cognitive domains primarily affected are short-term memory (31%), long-term memory (23%), constructive and visual-spatial functions (37%), executive functions (25%), and aphasia (14%)[14]. Some studies indicate that as many as 90% of the patients show some form of cognitive impairment in the first few weeks after the stroke[15-17]. It is considered that ischemic stroke primarily affects attention, speech/language abilities, delayed recall, and executive functions[18-21]. Cognitive impairment in the acute phase of ischemic stroke is inevitably associated with the localization of the lesion[22] and the severity of the stroke[2], where patients with a higher degree of functional disability and more severe stroke show more pronounced cognitive impairment, both in the acute phase and during follow-up. However, the existence of cognitive impairment in patients with acute ischemic stroke who have "a good outcome", i.e. minor functional, primarily physical, disability immediately after the stroke, are rarely studied. If there is cognitive

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impairment in these patients, the question is whether it correlates with functional, i.e., physical, disability. The main goal of the study was to determine whether there is cognitive impairment in patients with a high degree of functional ability in the acute phase of ischemic stroke and whether a specific neuropsychological profile can be registered.

Patients and Methods

Sample

The study included 40 (26 male and 14 female) patients with acute ischemic stroke, aged 45-78, of different educational levels. The inclusion criterion was the diagnosis of the first clinically verified acute ischemic stroke. The diagnosis of acute ischemic stroke was established on the basis of clinical symptomatology and neuroradiological findings obtained with computed tomography. Only hospitalized patients were included. The exclusion criteria were: data on a previous (clinically verified) stroke, presence of sensory or motor aphasia or severe dysphasia, paralysis of the dominant hand, subjects whose first language was not Serbian, visual and hearing impairment that prevented the completion of test tasks, impairment of consciousness, previous psychiatric disorders, and total Mini Mental State Examination score under 15. On the modified Rankin Scale (mRS), the subjects scored between 0-4. Given that the mRS score is usually divided into two categories, 0-3 (mild to moderate disability) and 4-5 (severe disability), whereby the patients with scores 0-2 are independent and do not require the assistance of others, most of the patients in the study were functional and independent.

The control group comprised 40 (20 male and 20 female) healthy volunteers aged 45-82, of different educational levels. The inclusion criteria were absence of neurological disease and no history of depressive disorder, visual or hearing impairment, or deficits in the motor function of the dominant hand. The subjects whose first language was not Serbian were excluded. Controls were randomly selected, and the exclusion criteria were the same as for the study group.

Instruments

A comprehensive neuropsychological test battery was used to assess different aspects of the cognitive status. The following tests were used: Mini Mental State Examination (MMSE)[23]; Trail Making Test (TMT) Form A and B[24,25]; Phonemic and Categorial Fluency[26,27]; Rey Auditory-Verbal Learning Test (RAVLT)[28]; Rey-Osterrieth Complex Figure test (ROCF)[29,30]; Wisconsin Card Sorting Test (WCST)[31]; Boston Diagnostic Aphasia Examination (BDAE)-subtests Repetitive Speech, Complex Ideational Material, Commands[26]; Boston Naming Test (BNT)[32]; Wechsler Memory Scale-Revised (WMS-R) – subtests Digit Span, Mental Control, Spatial Span[33]; and the modified Rankin Scale (mRS)[34,35].

In order to present a clear overview of achievement on the applied test battery, most scores were reduced to cognitive domains. This was done using principal components analysis, while subsequent analyses used factor scores from the first main component of each of the cognitive domains, which are presented in Table I.

Procedure

The study was conducted at the Clinic for Neurology of the Clinical Center of Vojvodina, Serbia. An institutional Ethics Committee had approved the study and all the subjects had signed an informed consent. Patients in the acute phase of ischemic stroke underwent neurological examination, CT or MRI of the brain, assessment of the functional status and of the presence of risk factors for cerebrovascular disease, as well as neuropsychological assessment. The study included patients whose first ischemic stroke occurred in different zones of brain irrigation. Neurological examination was performed by the admitting physician, a neurology specialist, immediately after hospital admission. Neurological status was assessed using the NIHSS scale for assessment of stroke severity. Functional status was assessed immediately before hospital discharge. Neuropsychological testing was performed during hospital treatment in the acute phase of ischemic stroke, i.e. within the first four weeks after the onset of stroke (not before day 10 or after day 28). Neuropsychological testing included assessment of attention and concentration, verbal and visual memory, visual-spatial and visual-constructive abilities, executive functions, and speech/language functions. The same neuropsychological battery was used on control subjects.

Statistical Analysis

The results were analyzed with SPSS 16.0 software package (SPSS Inc., Chicago, IL,

Table I. Neuropsychological tests/variables comprising the cognitive domains

Cognitive domains	Neuropsychological tests/variables
Executive functions	TMT B – Total reaction time, WSCT – Number of categories, Perseverative errors, Perseverative responses, Correct answers, Wrong answers
Immediate recall	Subtest Digit span and Spatial span from WMS-R
Delayed recall	ROCF – 45 minutes, RAVLT – A7 list, Recognition list of A
Divergent thinking	Phonemic fluency test, Categorical fluency test
Visual-constructive performance	ROCF – copy – summary score
Speech	BNT – Correct answers, BDAE – Subtests Repetition of Phrases and Sentences, Complex ideational material, Commands comprehension
Attention	TMT A – Total reaction time, Index of concentration from WMS-R, subtests Digit span – forward and Spatial span – forward

USA). Qualitative data were analyzed using a chi-square test. Quantitative data were represented using arithmetic means and standard deviations. Principal components analysis was used to reduce the main group of variables. Differences between the groups were studied using analysis of variance and *t* test, while the correlation between predictor variables and criterion variable was assessed using multiple regression analysis. The p value < 0.05 was considered statistically significant.

Results

Chi-square test and Student's *t*-test were used to determine whether the groups significantly differed in their main sociodemographic characteristics. It was found that the patients with acute ischemic stroke and healthy controls did not differ in gender [χ^2 (1, N = 80) = 0.021; $p > 0.1$], level of education [χ^2 (3, N = 80) = 0.881; $p > 0.1$], marital status (χ^2 = 3.875; df =3; $p > 0.1$), or age [Levin F = 0.080; $p > 0.1$; t (78) = 0.282; $p > 0.1$].

The significance of differences between the patients with acute ischemic stroke and healthy controls in the domain of executive functions was analyzed using Student's *t*-test for independent samples (Table II). The independent variable was presented by the presence or absence of acute ischemic stroke, while the dependent variable was operationally defined by the factor score on the first main component of each of the cognitive domains. Since Levene's test for homogeneity of variances showed that variances of the dependent variable on the subsamples were not homogeneous, we applied the *t*-test for non-homogeneous variances.

It was found that the groups significantly differ in all the studied domains of cognitive status, with the acute ischemic stroke group showing poorer performance than the control group.

Multiple regression analysis was used to study the correlation between the seven domains of cognitive status and the degree of functional, i.e. physical disability, as assessed by the mRS. It was found that the degree of functional, i.e. physical disability was not correlated with the group of predictors, i.e., the cognitive domains [R = 0.531, R^2 = 0.282, F (7.32) = 1.803, p = 0.120], and none of the domains was identified as a partially significant predictor: executive functions (β = 0.377, p = 0.114), immediate recall (β = 0.095, p = 0.802), visual constructive performance (β = –0.267, p = 0.239), attention (β = 0.075, p = 0.859), speech (β = –0.428, p = 0.105), delayed recall (β = –0.251, p = 0.192) and divergent thinking (–0.062, p = 0.772).

Discussion

The findings indicate that the group of patients in the acute phase of ischemic stroke showed a general decline in cognitive efficiency in all studied cognitive domains. Furthermore, no correlation was found between the degree of functional, primarily physical disability and cognitive performance. In the present study, functional disability was assessed using the modified Rankin scale, which is primarily a global functional

Table II. Differences between the groups in the cognitive domains.

	Acute ischemic stroke group		Healthy control group		
Cognitive domains	Mean	Standard deviation	Mean	Standard deviation	*t* test
Executive functions	–0.331	1.096	0.441	0.642	3.688**
Immediate recall	–0.250	0.917	0.333	1.024	2.507*
Delayed recall	–0.273	1.023	0.363	0.856	2.757**
Divergent thinking	–0.228	1.047	.305	.858	2.272*
Visual constructive performance	27.575	8.154	32.783	3.300	–3.660**
Speech	–0.359	1.150	0.479	0.430	4.227**
Attention	–0.348	0.925	0.464	0.916	3.652**

*p level < 0.05, **p level < 0.01.

health scale, with an emphasis on physical disability[36]. The majority of patients in the study (90%) scored 0-2 on the scale, which implies independent functioning, whereas only 10% scored 3 (7.5%) and 4 (2.5%), which implies mild and moderate disability, respectively. Therefore, it can be said that the patients had preserved functional, i.e. physical ability; namely they had "good recovery". The assumption that "good recovery" implies preserved cognitive efficiency is the reason why so few studies have dealt with this correlation. Planton et al[37] found that patients with ischemic stroke who were considered asymptomatic due to their good functional outcome had deficits in several cognitive domains, which negatively affected their return to daily activities. The study also found decreased efficiency in several cognitive domains in patients with good recovery. A general decline in cognitive efficiency in all studied domains indicates a great susceptibility of cognitive functions to the acute phase of ischemic stroke. This finding disproves the common belief that stroke that does not lead to serious functional, i.e. physical, disability and whose intensity is not expressed by high scores on the clinical scales for assessment of stroke severity is not associated with significant cognitive impairment. The absence of the correlation between severe functional, i.e. physical disability and cognitive efficiency indicates in fact that the tendency of clinicians to draw conclusions on the cognitive status based solely on the physical/motor status is often erroneous and without merit.

The comprehensiveness of the registered cognitive impairment suggests that the acute phase of ischemic stroke in itself has certain characteristics that are not always and exclusively related to lesion location, brain hypoperfusion, stroke severity, and the degree of physical disability. The reason for this frequent disregard of the comprehensiveness of cognitive impairment in the acute phase of stroke may be found in the researchers' tendency to choose instruments typical for cognitive screening, most frequently the MMSE test. These instruments are often not sensitive enough to register the presence of subtle cognitive impairment[38], which consequently leads to a false conclusion that there is no such impairment. Only a thorough neuropsychological battery may provide a true insight into the condition of cognitive efficiency in the acute phase of ischemic stroke[37,39]. Furthermore, the analysis of the findings obtained in the present study shows that the general decrease in cognitive efficiency in the acute phase of ischemic stroke does not allow for identification of a specific neuropsychological profile characteristic of vascular pathology. Such a profile would reflect dominant deficits in the domains of attention, speech and language, delayed recall, and executive functions[18-21]. In addition to these domains, decreased efficiency was also registered in the domains of immediate recall, divergent thinking, and visual-constructive abilities, which underlines the negative effect of the acute phase of ischemic stroke on cognitive efficiency. For this very reason, early detection of cognitive impairment is of paramount importance, since it allows early recognition of the patients that demand a follow-up and, if needed, early rehabilitation treatment of cognitive functions. On the other hand, the cognitive status largely reflects the success of the treatment and possibility to rehabilitate these patients, and its assessment is, therefore, increasingly considered

a mandatory part of the diagnostic protocol in the acute phase of stroke[40]. Since cognitive impairment is associated with a higher mortality rate and a poorer functional outcome, which is often more disabling than the physical disability itself[41,4,5], early assessment of the cognitive status, even in patients with good physical ability, seems obligatory.

The limitations of the study can also be considered as recommendations for future studies, namely increasing the sample, choosing patients with similar lesions in the same zone of irrigation of a certain blood vessel, with neuropsychological testing of all patients being conducted at the same time (e.g. the 14th day) after the stroke.

Declaration of funding interests

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Conflict of Interest

The Authors declare that they have no conflict of interests.

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