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INFLUENCE OF COGNITIVE AND MOTOR ABILITIES ON THE LEVEL OF CURRENT FUNCTIONING IN PEOPLE WITH MULTIPLE SCLEROSIS

VPLIV KOGNITIVNIH IN MOTORIČNIH SPOSOBNOSTI NA STOPNJI TRENUTNEGA DELOVANJA PRI OSEBAH Z MULTIPLO SKLEROZO

Sanela SLAVKOVIC[1*], Spela GOLUBOVIC[1], Matilda VOJNOVIC[2], Congor NADJ[3]

[1]University of Novi Sad, Faculty of Medicine, Department for Special Rehabilitation and Education, Hajduk Veljkova 3, 21000 Novi Sad, Serbia
[2]University of Novi Sad, Faculty of Medicine, Department of General Medicine, Hajduk Veljkova 3, 21000 Novi Sad, Serbia
[3]University of Novi Sad, Faculty of Medicine, Department of Neurology, Hajduk Veljkova 3, 21000 Novi Sad, Serbia

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ABSTRACT

Introduction: Multiple sclerosis (MS) results in a wide range of disabilities. The effects of cognitive and motor dysfunctions are significant and affect level of functioning in people with MS.

Objective: The aim of the research was to determine the common contribution of neurological, motor and cognitive status to the overall functioning of MS patients.

Method: The sample consisted of 108 subjects with RRMS. The instruments used in the research included: The General Questionnaire, the World Health Organization Disability Assessment Schedule, the Audio Recorded Cognitive Screen, Paced Auditory Serial Addition Test, the Nine Hole Peg Test, the 25 Foot Walk Test, and the Expanded Disability Status Scale.

Results: Subjects with a mild neurological deficit had a higher level of current functioning in all domains (a lower WHODAS 2.0 score) than subjects with a moderate neurological deficit ($r=0.43$, $p<0.001$). We found a positive correlation between the level of cognitive impairment and motor deficits of both upper and lower extremities and the level of neurological deficit ($p<0.001$). Subjects with lower neurological deficits had significantly lower WHODAS 2.0. scores, i.e. better motor abilities of both upper and lower extremities than subjects with moderate neurological deficits ($p<0.001$). The greatest contribution to explaining the overall level of current functioning of people with MS had subjects' age, cognitive abilities and motor abilities of the upper extremities.

Conclusion: Inverse relationship of neurological, motor and cognitive status affects the overall daily functioning of people with MS, requiring planning of comprehensive programs in the rehabilitation of people with MS.

Keywords:
multiple sclerosis, motor abilities, cognitive abilities, functional status

IZVLEČEK

Uvod: *Multipla skleroza (MS) se kaže v širokem naboru nezmožnosti. Učinki kognitivnih in motoričnih nezmožnosti so znatni in vplivajo na stopnjo delovanja pri osebah z MS.*

Namen: *Cilj raziskave je določiti pogost doprinos nevrološkega, motoričnega in kognitivnega statusa k splošnemu delovanju bolnikov z MS.*

Metode: *Vzorec je vključeval 108 oseb z RRMS. Orodja, ki so bila uporabljena v raziskavi, so naslednja: Splošni vprašalnik (General Questionnaire), Lestvica ocenjevanja zmanjšanih zmožnosti (WHODAS), presejalni test Audio Recorded Cognitive Screen (ARCS), test Paced Auditory Serial Addition Test (PASAT), Test devetih zatičev (Nine Hole Peg Test), test časovno omejene hoje 25 Foot Walk Test in Razširjena lestvica stopnje prizadetosti (Expanded Disability Status Scale, EDSS).*

Rezultati: *Osebe z blago obliko nevrološke pomanjkljivosti so pokazale višjo stopnjo trenutnega delovanja na vseh področjih (nižji rezultat WHODAS 2.0) kot osebe z zmerno nevrološko pomanjkljivostjo ($r = 0,43$, $p < 0,001$). Med stopnjami kognitivne prizadetosti in motorične pomanjkljivosti obeh zgornjih in spodnjih okončin ter stopnjo nevrološke pomanjkljivosti smo odkrili pozitivno korelacijo ($p < 0,001$). Osebe z nižjo nevrološko pomanjkljivostjo so imele občutno nižje rezultate vprašalnika WHODAS 2.0, tj. boljše motorične sposobnosti obeh zgornjih in spodnjih okončin kot osebe z zmerno nevrološko pomanjkljivostjo ($p < 0,001$). Največji doprinos k pojasnjevanju splošne stopnje trenutnega delovanja oseb z MS so imele starost oseb, njihove kognitivne sposobnosti in motorične sposobnosti zgornjih okončin.*

Zaključek: *Inverzni odnos nevrološkega, motoričnega in kognitivnega statusa splošno vpliva na vsakodnevno delovanje oseb z MS, zahteva načrtovanje celostnih programov pri rehabilitaciji oseb z MS.*

Ključne besede:
multipla skleroza, motorične sposobnosti, kognitivne sposobnosti, status delovanja

***Corresponding author:** Tel.: + 381 637 705 188; E-mail: sanela.slavkovic@mf.uns.ac.rs

1 INTRODUCTION

Multiple sclerosis (MS) is a chronic, demyelinating, and degenerative disease of the central nervous system (CNS). It can be said that the disease has a "thousand images" because it affects many functions and results in a wide spectrum of disabilities (1). According to Kurtzke's latest global MS prevalence scale, in most of Europe it has a moderate prevalence (38–70/100.000 of the population) (2) occurring in the 20–40-year age group (3). It is a challenge for researchers, doctors and other members of healthcare teams to understand how to treat people with MS.

As a result of the disease, many symptoms can occur that manifest in cognitive and motor impairments, the effects of which are great and affect functioning of people with MS. It is only when they become noticeable that rehabilitation strategies are employed in treating deficits. In the management itself, over 30% of people with MS report the need for a multidisciplinary approach (4). Although most MS symptoms can be objectively evaluated, very often they are based on the patient's subjective sense of illness (5). Problems that are not recognized timely may reduce the overall functioning of the patient and lead to serious consequences. Ten years after the diagnosis, 50–80% of the patients will no longer work (6) or have mood impairments, which will all affect the performance of their daily living activities (7).

Difficulties with cognitive functioning can become a significant problem affecting both the patient and his/her family members (8). Research has shown that the presence of cognitive impairment is a significant source of social disability (9, 10). Cognitive impairment is present in up to 65% of people with MS (1). Severity and type of cognitive impairment are individual. Cognitive dysfunction can develop at any time during the course of MS, regardless of the form of the disease, and may be associated with both mild and severe neurological deficits (11–14). People with MS with cognitive impairment usually less frequently participate in social activities and require more personal support than those with the same level of motor problems who are cognitively preserved (1). People with MS are less physically active compared to the general population (15, 16) and, therefore, a person with low level of physical activity is considered to have a sedentary lifestyle (17). Mobility problems lead to reduced activity (overall participation), while maintained mobility (walking ability) facilitates performance of daily activities and social activities with family and friends (18). Very often, patients themselves notice their reduced capacity for walking (19). Progression of the disease further worsens and reduces speed of gait, as a result of increased spasticity and other indicators of impaired motor control (20). With time, people with MS recognize difficulties in different motor skills involved to perform daily activities, such as, for example, climbing the stairs (19).

Furthermore, manual skills are considered essential for successful performance of daily tasks (21). Having problems in this field, the patient's level of independence in everyday activities, social participation and the overall quality of life are reduced (22).

MS is an unpredictable disease and it is a challenge for patients to cope with unstable and uncertain disease courses and reduced functional ability. Therefore, early recognition of symptoms and early intervention are very important. The primary objective of our research was to determine common contribution of neurological, cognitive and motor status on the overall functioning of MS patients.

2 METHOD

2.1 Participants

The sample consisted of 108 subjects diagnosed with MS aged 20–53 (Mean=39.86 years, SD=8.20 years).

The inclusion criteria were: the diagnosis of MS based on McDonald's criteria (23), relapsing-remitting form of the disease (RR MS), age 18–55 years, and EDSS score (24) 0–5.5.

Time from the diagnosis ranged from 1 to 26 years. A detailed overview of the demographic characteristics of the sample is shown in Table 1.

Table 1. Demographics of the study sample.

		Frequency	%
Gender	Male	38	35.2
	Female	70	64.8
Living arrangement	With parents	19	21.8
	With relatives	1	1.1
	Alone	8	9.2
	With a partner	11	12.6
	With partner and child/ren	46	52.9
	Alone with child/ren	2	2.3
Other's support	No	78	72.2
	Yes	30	27.8
Residence	Urban	70	64.8
	Rural	38	35.2
Marital status	Single	26	24.5
	Married	69	65.1
	Separated	2	1.9
	Divorced	5	4.7
	Nonmarital cohabitation	4	3.8
Work status	Full-time	26	24.3
	Part-time	4	3.7
	Freelance	2	1.9
	Student	3	2.8
	Retired	47	43.9
	Unemployed due to illness	12	11.2
	Unemployed for other reasons	12	11.2

2.2 Instruments

The current functioning was assessed using the 36-item self-reporting version of the World Health Organization Disability Assessment Schedule (WHODAS 2.0) (27), which covers the following six domains: Cognition, Mobility, Self-care, Getting along, Life activities, Participation.
Motor function was evaluated using the 9 Hole Peg Test (9HPT) and the 25 Foot Walk Test (25 FWT). The 9HPT possesses good validity and sensitivity in detection of even the slightest impairments in function of the arm (28, 29) and was, therefore, chosen to assess manual dexterity, and it represents a good measure of defining the degree of dysfunction of upper extremities. The 25 FWT evaluates the function of lower extremities and gait and is a good instrument for the assessment of gait in MS patients (30).

Cognitive abilities were assessed using two instruments. The Audio Recorded Cognitive Screen (ARCS) (31) is a screening instrument used to detect cognitive impairment or dementia. The components of the ARCS statistically significantly correlate with conventional neuropsychological tests. The ARCS has a good validity and reliability (31), as well as excellent sensitivity (92%) and specificity. The other instrument used was the Auditory Serial Addition Test – PASAT (32), which measures cognitive function in the sense of auditory information processing speed, attention, and calculation ability.

Neurological deficit was evaluated using the Expanded Disability Status Scale (EDSS) (24). On the basis of EDSS scores, all subjects were divided into three groups: without neurological deficits (EDSS 0–1.5) – 22 subjects (20.4%); mild neurological deficits (EDSS 2–3.5) – 61 subjects (56.5%); and moderate neurological deficits (EDSS 4–5.5) – 25 subjects (23.1%).

2.3. Statistical Analysis

All statistical data analyses were performed using SPSS Statistics for Windows, Version 21.0. We used descriptive statistics, Pearson correlation coefficient and Hierarchical regression analysis. Also, a multiple regression analysis was used to verify the relationship between EDSS subscales and the results to WHODAS. T-test and one-way ANOVA were used to test group differences. Hierarchical regression analysis was used in order to determine the effect of predictors on functioning of subjects with MS. We used a step-by-step approach; in the first stage, the socio-demographic predictors were entered; then, in each further stage, one pre-correction variable was included in the model. In the second stage, the scores from the PASAT test were used as predictors, in the third ARCS performance scores, in the fourth step the new neurological deficit was included as a predictor variable and, in the last two stages, estimates of the motor status of the upper and lower extremities were consecutively included.
The missing data treatment was performed using k-nearest neighbour model in R, which occurred only among a few examinees. To calculate effect size within the model, we used an effect size calculator for hierarchical multiple regression (25), after which we calculated post-hoc statistical power for HMA (26).

The statistical significance of each independent variable was obtained using beta coefficients and values $p<0.05$ were considered statistically significant.

3 RESULTS

The socio-demographic variables were an important segment in the results. In our sample, most subjects (69.5%) earned their income through salaries and pensions. As regards social activities, the largest number of subjects (86%) did not have a hobby. The WHODAS 2.0 scores showed that our subjects had the most problems in the domains of Participation, Mobility, Life Activities (Domestic) and Cognition (Table 2). The least problems were reported in the domain of Self-Care.

Table 2. WHODAS 2.0 total score and individual domain scores.

Characteristic	N	Min	Max	Mean	SD	Skewness	Kurtosis
Cognition	108	0	100.00	23.90	24.27	0.97	0.02
Mobility	108	0	100.00	26.45	23.14	0.74	0.03
Self-care	108	0	75.00	9.25	16.17	2.16	4.37
Getting along	108	0	75.00	16,03	20.07	1.40	1.11
Life activities - domestic responsibilities	108	0	100.00	25.99	23.71	0.83	0.39
Life activities - leisure, work and school	84	0	68.75	13.20	12.16	1.64	4.68
Life activities	108	0	81.25	22.12	18.44	0.90	0.56
Participation	108	0	84.38	28.12	19.46	0.78	0.17
WHODAS 2.0 score	108	0	65.97	21.19	15.40	0.81	0.04

Age has a low to moderate positive correlation with the total WHODAS 2.0 score (r=0.27, p<0.05) and the domains of Participation (r=0.19, p<0.05), Self-Care (r=0.25, p<0.01), Life Activities (r=0.21, p<0.05) and Getting Along (r=0.35, p<0.01), indicating that older subjects had more difficulties in the specified domains, i.e. they had higher WHODAS 2.0 scores in these domains. The time passed since diagnosis has a low but significant positive correlation with the domains Getting Along (r=0.29, p<0.01), Participation (r=0.21, p<0.05), and the total WHODAS 2.0 score (r=0.28, p<0.01).

The average achievement on the 9HPT, performed with the dominant hand, was 22.69 seconds (SD=9.90), and with the non-dominant hand it was 24.92 (SD=9.48 seconds). On average, male subjects had worse results with the dominant hand compared with the norm for the general population by 7.62 seconds, while the deviation in women was 3.99 seconds. Poorer achievement on the 9HPT was recorded in subjects with longer disease duration (r=0.27, p<0.001) and in older subjects (r=0.31, p=0<0.001), but with very low correlations.

The average value on the 25FWT was 5.49 (SD=2.81 seconds). Again, there was a statistically significant positive but low correlation with disease duration (r=0.36, p<0.001) and age (r =0.24, p<0.001).

The average score for all subjects on the PASAT was 43.52 (SD=19.84); 21 (19.4%) subjects had problems in cognitive functioning. The ARCS showed that 38.3% of subjects fell into the cognitive impairment category, and another 37 (34.6%) had deficits of a single function, i.e. visuospatial abilities. The subjects with cognitive deficits were older (t=-2.91, p<0.001) and/or with longer disease duration (t=-2.82, p<0.001).

We confirmed our assumption that there was a low negative but significant correlation between the level of current functioning as measured by the WHODAS 2.0 and the level of EDSS score in patients with MS (r=0.34, p<0.001). The results showed a significant difference between the three groups of subjects categorized according to neurological deficits in relation to the WHODAS 2.0 attainment test (F=8.92, p<0.001). The findings suggested that subjects without neurological deficits had significantly lower scores (Mean=13.62, SD=12.03) on the WHODAS 2.0 compared to subjects with moderate neurological deficits (Mean=30.85, SD=16.13). In addition, the difference between subjects with mild neurological deficits (Mean=19.96, SD=14.37) and those with moderate neurological deficits was also significant. Subjects with mild neurological deficits had a better functional status than subjects with pronounced neurological deficits.

When we analysed all the EDSS subscales together, we found these subscales to be significant predictors of WHODAS 2.0 scores (R^2=0.233, F=3.297, p<0.01), significant partial contributions to the prediction of the WHODAS 2.0 score for the functions of the pyramidal system (ß =0.34, p<0.05) and the bladder and the bowels (ß=0.24, p<0.05). The higher scores for these functions were associated with poorer current functioning.

The second assumption of our research was that there was a positive correlation between the level of cognitive impairment and the level of neurological deficits in patients with MS. There was a significant but low negative correlation between the EDSS and PASAT scores (r=-0.25, p<0.001). Higher scores on the EDSS were associated with lower PASAT scores. The same finding was obtained for the ARCS (r=-0.34, p<0.001).

The association between cognitive and motor abilities and the current functioning of our subjects was tested with the Pearson coefficient of linear correlation. The total ARCS, 9HPT and 25FWT scores significantly correlated with all WHODAS 2.0 domains and total score, except for the domain that identifies difficulties in life activities – work/school (Table 3). These correlations range from weak to moderate, indicating that the level of achievement in WHODAS 2.0 scales is negatively correlated with ARCS score and positively correlated with the motor abilities of upper and lower extremities.

Table 3. Correlation between cognitive and motor functioning and WHODAS 2.0 domains and total score.

WHODAS 2.0	ARCS score	9 HPT	25 FWT
Cognition	-0.31**	0.31**	0.27**
Mobility	-0.34**	0.56**	0.51**
Self-care	-0.28**	0.43**	0.30**
Getting along	-0.25**	0.34**	0.32**
Life activities	-0.24*	0.43**	0.32**
Life activities – domestic responsibilities	-0.29**	0.51**	0.36**
Life activities – leisure, work and school	-0.03	0.00	-0.00
Participation	-0.23*	0.35**	0.38**
WHODAS 2.0 score	-0.34**	0.48**	0.42**

** Correlation significant at p<0.01

* Correlation significant at p<0.05

In order to examine the common contribution of all predictor variables in explaining the overall functioning of MS patients, a hierarchical regression analysis was employed (Table 4). Models were constructed by firstly introducing socio-demographic variables and then individual variables of all studied domains (models are explained in method section).

Table 4. Hierarchical regression analysis: dependent variable – functioning of subjects.

Model	R	R^2	F	p	beta	p	95% CI
Step 1.	0.35	0.12	2.82	0.03			
AGE					0.24	0.03	0.51;2.66
Step 2.	0.51	0.26	5.40	0.00			
PASAT					-0.39	0.00	-23.94;-6.13
Step 3.	0.56	0.32	6.05	0.00			
PASAT					-0.32	0.00	-21.02;-3.56
ARCS					-0.26	0.00	-21.41;-4.70
Step 4.	0.57	0.32	5.23	0.00			
PASAT					-0.32	0.00	-19.74;2.77
ARCS					-0.25	0.01	-18.67;-2.06
Step 5.	0.65	0.43	7.09	0.00			
PASAT					-0.29	0.00	-18.09;-1.80
9HPT					0.40	0.00	-26.89;-6.59
Step 6.	0.66	0.43	6.25	0.00			
PASAT					-0.29	0.00	-17.90;-1.62
9HPT					0.39	0.00	-25.38;-3.88

Model 1: sociodemographic variables
Model 2: sociodemographic variables and PASAT
Model 3: sociodemographic variables, PASAT and ARCS
Model 4: sociodemographic variables, PASAT, ARCS and EDSS
Model 5: sociodemographic variables, PASAT, ARCS, EDSS and 9HPT
Model 6: sociodemographic variables, PASAT, ARCS, EDSS, 9HPT and 25FWT

Individual contributions of only statistically significant predictors are shown.

We used hierarchical regression analysis in order to determine the effect of a set of predictor variables on the functionality of people with MS. In the first step, we tested the predictive contribution of socio-demographic variables. The results show that socio-demographic variables explained 12% of the variance in the functioning of our subjects. By analysing the individual contributions of socio-demographic variables, it was found that only age had a significant contribution. With more advanced age, subjects had, i.e. lower level of overall functioning. In the second step, we added the PASAT variable, which led to a significant change in the explanation of the variance of social participation and explained 26% of the variance. When we consider contribution at an individual level within the model in step 2, we can see that the contribution of age is lost, whereas only cognitive abilities measured by the PASAT test have a significant predictor role.

In the third step, the ARCS total score model was included, changing the percentage of explained variance significantly, whereas PASAT and ARCS became the only predictors of the level of overall functioning of our subjects. The scores on both cognitive tests negatively correlated with the WHODAS 2.0 score, i.e. it was confirmed that a lower cognitive status was associated with a lower level of overall functioning of people with MS.

In the fourth step of analysis, we introduced the level of neurological deficit (EDSS score) as a predictor. The observed change in the prediction of the level of

functioning was not significant, and the percentage of the explained variance increased to 32%. Cognitive ability scores remained the only significant predictors.

In the fifth step, the score of motor abilities of the upper extremities was added. The observed change in the prediction of the level of functioning was significant, and the percentage of the explained variance rose to 43%. Significant variables noticed in this model were cognitive abilities, as assessed by the PASAT, and the motor function of upper extremities. The other predictors were not significant.

In the final model, the lower extremity motor function was added – the percentage of the explained variance remained the same, as well as the predictors of functioning.

Cohen's f2 effect size for our model was 0.75. Statistical power was tested post hoc, i.e. after performing analysis. For an effect size of 0.75, with a significance p-level of .05, and 108 participants, observed statistical power for our model was 0.99.

4 DISCUSSION

In our research, it was found that the domains most commonly affected in MS patients are participation, mobility, life activities and cognition. Each of the domains will be discussed separately and then the interdependent relationship between the functioning domains of this population will be compiled.

Social life and social participation are influenced by physical, social, environmental and personal factors (33). Changes that occur within the course of the main disease are dynamic. After they have been diagnosed with MS, people tend to experience fear, uncertainty, social isolation from friends and changes in the quality of life (34, 35). In this context, it is important to discuss a few, in our opinion, most important findings. Given that our subjects did not have severe disabilities and considering the age structure of the sample, it is worrying that only 32 subjects were employed and 47 (43.9%) had already been retired due to MS. Regardless of the severity of neurological deficits, it is necessary to provide a support system for the patients in order for them to maintain active participation in society. Already in the last century it was found that the functional damage that is common in MS included difficulties in independent purchasing, home maintenance, clothing, driving and using public transport (36), which consequently reduced the level of social participation. Nearly 30% of our subjects had support and help in everyday activities.

The total WHODAS 2.0 score in our study was 21.19, which indicates that disability was not a pronounced problem in our subjects. In an Italian study, the total WHODAS 2.0 score was 22.93 for persons with disabilities (37). We can conclude that with disease progression the WHODAS 2.0 score rises.

In our study, on the WHODAS 2.0, subjects had the most difficulties in the domains of Participation, Mobility and Life Activities (domestic responsibilities) and the least difficulties in the domain of Self-Care. Considering that the scores grouped around higher values, we can conclude that our subjects had not yet developed a disability that would have interfered with their overall functioning. Of significance is the finding that less severe neurological deficits were associated with a higher level of functioning, indicating that the dimensions of neurological status are predictors of patients' functioning in different domains of life. This finding is in accordance with current literature data (38). We also confirmed that there were significant differences between subjects without, with mild and moderate neurological deficits with regard to level of functioning, thereby proving the initial hypothesis of our research that with progression of MS the overall functioning of the patients decreases. Previous studies have shown that transition of the EDSS score from 1.0–3.0 to 3.5–5.5 significantly affects all aspects of functioning (39) and that, therefore, the patients require support in these processes.

Manual abilities and gait are significant predictors of perceived difficulties in daily activities in patients with MS who do not have motility problems (40). According to Lamers and associates (41), the general muscular strength of the upper extremities is strongly associated with the 9HPT measures of the capacity of upper extremities, and damage to bodily functions and structures and the level of disability of upper extremities are strongly associated with participation in community. Given that with advanced age and longer disease duration motor abilities worsen, it is necessary to integrate their screening into MS management protocols. Similar findings were reported by the authors of a Swedish study (42). They found that better results on the 9HPT were associated with a higher level of social participation and that gait and manual skills had a better discriminatory and predictive value than cognitive measures.

In our study, we also confirmed that cognitive impairment is registered in older subjects and in subjects with longer disease duration, which points to the importance of screening cognitive abilities after the diagnosis of MS has been established. The overall prevalence of cognitive dysfunction in our subjects was similar to those in other published studies, i.e. up to 70% (1). However, the significant negative correlation we obtained between the total EDSS score and the cognitive function measures should be considered with caution, since it is not always the case.

It has long been established that MS patients with cognitive impairment less frequently participate in social activities compared with those with only motor disability (9). Considering the costs that such monitoring implies, contemporary science offers a potential solution; use of computerized assessment techniques such as ARCS.

In this study, we tested the significant contribution of predictor variables in explaining the degree of current functioning and found that age and performance on cognitive ability tests, the upper extremity ability test and gait test are significant predictor variables, while neurological deficit itself, as measured by the EDSS, is not a significant predictor of the overall functioning in people with MS.

5 CONCLUSION

Since interdependence of neurological, motor and cognitive status of MS patients affects the overall daily functioning, comprehensive rehabilitation program and psychosocial support for patients with MS should be carefully planned.

CONFLICTS OF INTEREST

The authors report no conflicts of interest.

FUNDING

The study has received no funding.

ETHICAL APPROVAL

The research was approved by the Ethics Committee of the Clinical Centre of Vojvodina and the Ethics Committee of the University of Novi Sad, Faculty of Medicine.

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