

Neuropsychological tests in a group of patients with ischemic heart disease

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Summary

Aim. Ischemic heart disease (IHD) tops the list of sick and death rates all over the world. IHD brings the risk of central nervous system disturbances. On the other hand lower neuropsychological tests results enable to predict cardiac relapse. We assess the neuropsychological function such as working memory and executive functions, associated with prefrontal cortex activity, as well as direct and delayed verbal memory in patients with ischemic heart disease vs. healthy subjects.

Methods. The following neuropsychological tests were applied in the study for evaluation of cognitive functions: the Wisconsin Card Sorting Test (WCST) and the Rey Auditory Verbal Learning Test (RAVLT).

Results. In the patients with IHD a significant intensification of cognitive dysfunctions (working memory and executive dysfunctions also immediate and delayed memory was observed in comparison with the control group of healthy subjects.

Conclusions. Cognitive dysfunctions are widespread effect among IHD patients. Working memory and executive functions disturbances are especially dangerous in this group because can result in problems with understanding, learning new information and difficulties in following medical recommendations which may cause consecutive hospitalizations. The seriousness of cognitive disturbances consequences motivate to evaluate all patients and initiate neurocognitive rehabilitation programs when needed.

Key words: ischemic heart disease, neuropsychological dysfunctions, working memory disorders

Introduction

Ischemic heart disease (IHD) is one of the major factors of death and disability rates of people in Poland and all over the world. Cardiac vascular and cerebrovascular diseases are linked etiologically, which causes that the heart disease often increases the risk of CNS complications. Gradual occlusion of the arteries leading to coronary heart disease often affects the brain vascular occlusion causing a gradual loss of brain tissue

and cognitive deficits. In the IHD changes in brain functioning occur, mainly due to hypoxia, which is one of the main factors of cognitive dysfunction in patients. IHD can increase the risk of cognitive dysfunction, and at the same time, according to studies, the reduced neuropsychological result of the testing can predict occurrence of coronary events. Cognitive disorders may therefore be an independent risk factor for ischemic heart disease, comparable in terms of the predictive value with other risk factors for heart attack such as: left ventricular ejection dysfunction or high cholesterol levels [1].

Widely reported in the literature are cases of damage to the central nervous system as a result of cardiac surgery. Brain tissue is very sensitive to ischemia, therefore damage to the even a small area of the brain which are at risk of coronary artery revascularization surgery (CABG), can cause neurological symptoms, cognitive impairment or mental state disorders of patients, which often leads to difficulties in rehabilitation and return to daily activities [2]. Some data from the literature show that even 80% of CABG patients experience various cognitive dysfunction [3]. The specificity and severity of neuropsychological dysfunction after CABG have been the subject of many studies. The authors found that in a few to several days after the surgery, slightly to moderately severe symptoms of disorders of memory and learning, attention, visual-spatial perception and psychomotor speed occurred. Brain dysfunctions often are not specific and are „spilled”. Jodzio [4] showed a positive long term effects of CABG on cognitive functioning. After 6 months from the operation the subjects were characterized by better performance on neuropsychological tests (visual memory, reasoning by analogy, motor speed, attention) compared to tests from a few days after surgery. It is believed that the positive effect of CABG is associated with improvement in the oxidation of brain, heart and improved systemic blood distribution. This reflects the general improvement in health, fitness and well-being of patients.

Etiological factors of cognitive dysfunction in cardiac patients include: high blood pressure, atherosclerosis, peripheral artery disease, myocardial infarction cardiac arrest. These factors often occur in a person simultaneously, which poses a problem in a differentiation of their particular role in the etiology of neuropsychological disorders.

Cognitive impairment of cardiovascular origin are acute or chronic in nature. Acute character is typical for ischemic stroke, which can lead to severe hypoxia of the brain, causing a mental deterioration and dementia changes. Another cause of acute cerebral ischemia is myocardial infarction, often associated with cardiac arrest. In these patients, most often occur amnesic symptoms and executive disorders; disturbances of consciousness, difficulty in learning, focal deficits (as apraxia, alexia or agraphia) may also appear, in addition to frequent disorders of behavior and emotional problems [3, 5]. Cognitive dysfunction and myocardial infarction may occur in an individual independently of each other, but several studies show their causal relationship [6, 7].

Chronic nature of cognitive impairment occurs in ischemic heart disease, these include primarily the weaker: selective attention, visual memory, the ability to understand the analogy and psychomotor speed. As indicated by latest research results by Almeida [8] in patients with heart failure and in patients with ischemic heart disease, in neuroimaging deficits in gray matter of the brain are observed, particularly in the prefrontal and temporal-peritral lobe areas, which may result in, among others, memory disorders.

Often in the literature reports of cognitive dysfunction in patients with IHD concerning short-term verbal memory and verbal learning, short-term visual-spatial memory and abstract thinking are found [5, 6, 9]. Risk factors for coronary heart disease, especially high blood pressure, can have a damaging impact on specific areas of the frontal cortex, associated mainly with executive functions [10].

Working memory is a short-term memory, which allows for the proper integration of the information, depending on the requirements of the situation, thus enabling on-line processes. The information about the currently performed activities are stored for some time in it. Working memory enables changes in action depending on the new rules and adaptation to the requirements of the environment [11, 12].

For the functioning of working memory is responsible prefrontal cortex of the brain [13]. It influences the control of the course and the synthesis of arbitrary, conscious, purposeful activities, at all levels of activity organization [14] which often in the literature is referred to as executive functions, which are a set of higher organized capabilities including: strategic planning, flexibility of thinking, self-regulation, behavior focused on achieving the goals and monitoring other cognitive processes [15]. Executive functions are involved in processes such as solving new problems in the environment, adaptive behavior (such as abstract thinking, creativity, introspection) or complex sequences of behavior that allow for the evaluation of the effectiveness of an individual's behavior [16]. Executive functions play the role of regulators of behavior. They do not take part in any specific form of information processing, but all dysfunction in their range leads to impairment of other cognitive processes [11].

The proper functioning of working memory is associated, apart from the prefrontal cortex, also with parietal cortex and subcortical structures: the hippocampus, thalamus and cerebellum. The hippocampus plays an important role in the regulation of emotions and motivation, memory, learning, and adaptation to changing environmental conditions.

Impaired executive function and working memory can cause problems with the generalization of knowledge and an impaired ability to flexible solve problems in response to stimuli from the environment and own organism. Working memory disorders can affect the functioning of the social and professional activities of patients, which is particularly evident in the impediment process of learning new behaviors.

The seriousness of these consequences, and incomplete and not always consistent data from the literature prompted us to conduct a study to determine the incidence and severity of cognitive impairment in patients with ischemic heart disease.

Material

The study included 111 patients (22 women and 89 men), aged 41–65 years (mean: 55.4 ± 5.6), with diagnosed ischemic heart disease. These were patients hospitalized in the 1st Department of Cardiology and Cardiac Surgery of Medical University of Łódź.

The study involved people who meet the criteria for ischemic heart disease according to ICD-10. Exclusion criterion was the presence of severe neurological disorders, previous head injury, serious mental illness and dementia, other severe somatic diseases, as well as addiction to psychoactive substances and alcohol.

45 patients (40%) of included in the study had had ischemic myocardial infarction, 24 subjects (22%) during the study were after recent myocardial infarction (to 7 days after infarction), 42 (38%) had never had heart attack. 55 (49%) patients had one myocardial infarction, 14 (13%), had two or more infarcts

The control group consisted of 50 people (10 women and 40 men) selected to suit the study group in terms of gender structure. The two groups did not differ significantly in age, gender and education (as determined by the number of years of education). All persons, both in the studied group and the control one, were qualified to the study after written consent to participate in it, after explaining the purpose and nature and the rules of conduct. The need to use medical data to analyze the results was emphasized.

The conduct of the clinical research was approved by the Bioethics Committee on Human Research of Medical University of Łódź (No. RNN/127/06/KE). Patients and healthy volunteers were informed about the study and its nature as well as of the applied research procedures and gave written consent to participate in it. The subjects were also informed that they could withdraw from the study at any time, without giving any reason, and without any consequence related thereto, as well as about the confidential nature of all the collected personal and medical data

Method

For the neuropsychological evaluation Wisconsin Card Sorting Test – WCST and Rey Auditory Verbal Learning Test – RAVLT were used.

WCST [17] is used to assess the severity of dysfunction of working memory and executive functions. In the study its computer version, Heaton, was applied, which allowed the comparison of he tested person data with standard norms for his/her age and education.

In the assessment of the results in this study were included:

- The percentage of perseverative errors – PE, indicating the rigidity of thinking, the tendency to perseveration response, even if the patient is aware of the ineffectiveness of such action.
- The percentage of nonperseverative errors – NPE, indicating a tendency to random, chaotic, less controlled reactions. Errors in this area may reflect the impaired attention and information processing.
- The number of correctly arranged categories – categories completed – CC, which is an indicator of the effectiveness of thinking.
- The number of trials needed for the first category arrangement (trials to complete 1st category – 1KA), which provides the ability to formulate a logical concept.
- The percentage of responses consistent with the concept of logic (conceptual level response – CON), reflecting the ability to maintain the logical rule of response and the use of new information with previous experience.

Rey Auditory Verbal Learning Test Re can assess verbal memory, auditory declarative memory performance, both immediate and delayed memory, and verbal learning performance. The examined person is presented five times a list of 15 words – list A

(trial A1–A5), which is recalled by the person immediately after reading it by the person examining. After completing this part of the test the person is presented a new list of words – a list B (trial B1), which is also recollected after a single hearing. Then, the subject is asked to recall previously memorized words from the presented list A (trial A6). After 20 minutes, a replay of the words from the list A occurs (sample A7).

All statistical calculations were performed using the statistical packages Statistica and SPSS. Continuous variables (age, duration of education, the results of psychological tests) were presented as mean and standard deviation (SD) or median with interquartile range (IQR), depending on the nature of the variable distribution verified using the Shapiro-Wilk test. In the case of normally distributed variables Student's t-test and analysis of variance (ANOVA) with post-hoc test of Tukey were used. Alternatively, non-parametric tests were used: nonparametric analysis of variance Kruskal-Wallis test with post-hoc Mann-Whitney U with Bonferroni correction for comparisons between subgroups. The correlation analysis was performed using C Pearson's correlation test or Spearman rank correlation, depending on the type of the variables and their distribution.

Results

In the tables the following markings of variables were presented:

WCS – PE – percentage of perseverative errors;

WCST – NPE – percentage of nonperseverative errors;

WCST – CC – number of categories completed;

WCST – CON – percentage of conceptual level responses;

WCST – 1KA – number of trials to complete 1st category;

RAVLT A 1–A7, B1 (Rey Auditory Verbal Learning Test – RAVLT). Trials A 1–A7, B1.

Group of patients with ischemic heart disease was compared with the control group in terms of the results obtained in the test WCST. People with ischemic heart disease received statistically lower ($p < 0.01$) results in the subtests, WCST – PE, NPE – WCST, WCST – CC ($p = 0.0152$), WCST – CON, WCST – 1KA., The results are shown in Table 1.

Table 1. Wisconsin Card Sorting Test results in the studied and control group

	Studied group N = 111		Control group N = 50		Significance p
	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	
WCST-PE	13.8±7.4	12.0(9.0–16.0)	8.4±3.0	8.0(6.0–10.0)	0.0000
WCST-NPE	13.2±6.6	12.0(9.0–16.0)	7.9±2.6	8.0(6.0–9.0)	0.0000
WCST-CC	5.1±1.5	6.0(4.0–6.0)	5.9±0.3	6.0(6.0–6.0)	0.0152
WCST-CON	66.4±16.2	72.0(56.0–78.0)	80.7±6.8	80.0(76.0–86.0)	0.0000
WCST-1KA	19.8±19.5	14.0(13.0–19.0)	13.2±4.1	12.0(11.0–13.0)	0.0000

IQR – interquartile range; SD – standard deviation; N – sample size; p – probability value for the Mann-Whitney U test

Results of the Rey Auditory Verbal Learning Test obtained in the studied group were compared with those in the control group. The examined group had significantly lower scores on scales of Rey Auditory Verbal Learning Test i.e. in trials: A1 ($p < 0.001$), A2 ($p < 0.05$), B1 ($p < 0.01$), A6 ($p < 0.05$), A7 ($p < 0.001$). The results are shown in Table 2.

Table 2. Rey Auditory Verbal Learning Test results (1–7 trials) in the studied and control group

	Studied group N = 111		Control group N = 50		Significance
	Mean \pm SD	Median (IQR)	Mean \pm SD	Median (IQR)	p
RAVLT–A1	4.9 \pm 1.4	5.0(4.0–6.0)	6.1 \pm 0.8	6.0(6.0–7.0)	0.0000
RAVLT–A2	6.8 \pm 1.9	7.0(5.0–8.0)	7.4 \pm 1.1	8.0(7.0–8.0)	0.0362
RAVLT–B1	4.7 \pm 1.5	5.0(4.0–6.0)	5.3 \pm 0.9	5.0(5.0–6.0)	0.0062
RAVLT–A6	7.8 \pm 2.5	8.0(6.0–9.0)	8.7 \pm 1.8	9.0(7.0–10.0)	0.0208
RAVLT–A7	7.2 \pm 2.8	7.0(5.0–9.0)	8.8 \pm 2.0	9.0(7.0–10.0)	0.0004

IQR – interquartile range; SD – standard deviation; N – sample size; p – probability value for the Mann-Whitney U test

Comparing the patients from the studied group in terms of occupational status it was indicated that non-working patients obtained a lower results in trials A1 ($p < 0.05$), A2 ($p < 0.001$) and A6 ($p < 0.005$) and A7 ($p < 0.05$) RAVLT (Table 3).

Table 3. Rey Auditory Verbal Learning Test results (1–7 trials) of working and non-working patients from the studied group

	Working group N = 50		Non-working group N = 61		Significance
	Mean \pm SD	Median (IQR)	Mean \pm SD	Median (IQR)	p
RAVLT–A1	5.3 \pm 1.4	5.0(4.0–6.0)	4.6 \pm 1.4	5.0(4.0–5.0)	0.0242
RAVLT–A2	7.5 \pm 1.8	7.0(6.0–9.0)	6.2 \pm 1.7	6.0(5.0–7.0)	0.0006
RAVLT–A6	8.4 \pm 2.6	8.5(7.0–11.0)	7.3 \pm 2.3	7.0(6.0–9.0)	0.0310
RAVLT–A7	7.8 \pm 3.1	7.0(6.0–10.0)	6.7 \pm 2.4	7.0(5.0–8.0)	0.0352

IQR – interquartile range; SD – standard deviation; N – sample size; p – probability value for the Mann-Whitney U test

Table 4 shows the correlation between demographic data (age, years of education) and the results of neuropsychological tests. Time of education negatively correlated with PE ($R = -0.34$, $p < 0.001$) and NPE ($R = -0.30$, $p < 0.01$) and positively with CC ($R = 0.30$, $p < 0.01$) and CON ($R = 0.37$, $p < 0.001$). Whereas age of the patients correlated positively with PE ($R = 0.24$, $p < 0.05$) and NPE ($R = 0.27$, $p < 0.01$) and negatively correlated with CC ($R = -0.22$, $p < 0.05$) and CON ($R = -0.30$, $p < 0.01$).

Table 4. r-Spearman correlations between the results in Wisconsin Card Sorting Test and Rey Auditory Verbal Learning Test and the age and years of education in the studied group

	Years of education	Age
	R	R
WCST-PE	-0.34	0.24
WCST-NPE	-0.30	0.27
WCST-CC	0.30	-0.22
WCST-CON	0.37	-0.30
RAVLT-A1	0.31	
RAVLT-A2	0.37	
RAVLT-A3	0.37	
RAVLT-A4	0.29	
RAVLT-B1	0.27	
RAVLT-A6	0.27	
RAVLT-A7		-0.25

A positive correlation between learning time and trials on Rey Auditory Verbal Learning Test was found (except trial A5 and A7). In the case of age only A7 trial correlated negatively with this variable.

Discussion of results

The obtained results have confirmed that subjects with IHD exhibit significant cognitive impairment of working memory and executive functions related to the activity of the prefrontal cortex and hippocampus as well as immediate and delayed memory dysfunction, which are not found in the control group. In patients more rigid thinking, attention disorders that cause random and chaotic reactions, less effective thinking, problems to the use new information and adapt to the changing environment conditions were visible.

Impaired executive function and working memory are particularly dangerous in this group of patients, because they can cause problems with understanding, assimilating and recalling information, and may be largely responsible for the failure to comply with medical recommendations, re-coronary episodes and hospitalizations. A tool to measure cognitive functioning used in this study was Rey Auditory Verbal Learning Test (RAVLT). The study group received significantly lower scores in the scales of the Test, especially when analyzing the first presentation of the material, recalling after distraction and long-term memory.

Lower test scores in Rey's test indicate dysfunction of short-term delayed memory, slower auditory learning process, as well as greater susceptibility to distraction in the study group.

In our work, significant for the cognitive functioning of patients turned out to be their professional status. In the literature, there is no data on RAVLT testing among people working and not working. It can be assumed that professional work has an important therapeutic function in both the psychological and somatic spheres of the patient. The necessity to perform professional duties requires a certain level of cognitive performance, which is further developed by the tasks that the employee is to perform. Perhaps patients with cognitive impairments less often return to work, thus exposing themselves to a lower cognitive activity and deepening of these disorders.

In the analyzed group there were significant correlations between the number of years of education and neuropsychological tests results.

Time of education negatively correlated with the percentage of WCST perseverative errors ($R = -0.34$, $p < 0.001$) and non-perseverative ones ($R = -0.30$, $p < 0.01$), and positively with the number of categories completed ($R = 0.30$, $p < 0.01$) and the percentage of conceptual level responses ($R = 0.37$, $p < 0.001$). These results are consistent with literature data. In studies by Boone et al [18] level of education moderately correlated with performance in the WCST test. People with higher education generally achieved better results. Learning time in the study group correlated positively with all trials of RAVLT.

As regards this method, the data from the literature are varied, some point to the better performance of the test by persons with a higher level of education [19], others suggest that the level of education does not affect the outcome of the test, highlighting only the relationship of the RAVLT test results with general intelligence quotient IQ [20].

According to Strauss et al [21] age is variable highly affecting the WCST test results. They grow with age to about 19 years of age. From 20 to 50 years are maintained at a constant level, and after 60 years of age some test dimensions are reduced. In this study, age was positively correlated with the percentage of perseverative errors ($R = 0.24$, $p < 0.05$) and non-perseverative ones ($R = 0.27$, $p < 0.01$), and negatively with the number of categories completed ($R = -0.22$, $p < 0.05$) and the percentage of responses consistent with the concept of logic ($R = -0.30$, $p < 0.01$). In the case of RAVLT test negative correlation was found between trial A7 (delayed recalling) with age, indicating the deterioration of delayed recall over the years, as confirmed by the literature data [21].

The analysis showed no statistical differences in the severity of cognitive dysfunction, depending on the gender of respondents, also the severity of IHD turned out not to be a significant factor for the cognitive functioning of patients.

Conclusions

Impaired working-memory and executive functions as well as short-term and delayed verbal memory are a problem common among patients with IHD. Cognitive dysfunction can cause a decrease in quality of life, problems in social functioning and professional work and contribute to non-compliance with medical recommendations in this group of patients. It seems necessary to take into account screening tests of cog-

nitive function in patients with ischemic heart disease, as well as the implementation of the neurorehabilitation programs.

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