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Pathological Fatigue in Patients with Ischemic Stroke on the Background of Metabolic Syndrome

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Abstract

The objective of the research was to study the post-stroke pathological fatigue and anxiety and depressive disorders and to identify strategic brain areas of psycho-emotional disorders according to MRI in patients with ischemic stroke on the background of MS.

Materials and methods. The main group consisted of 30 patients (16 women and 14 men) at the age of 44 to 81 (the average age was 66 ± 4.2 years) being in the early rehabilitation period of ischemic stroke on the background of MS (atherothrombotic stroke – 13 patients, lacunar stroke – 15 patients, cardioembolic stroke – 2 patients). The control group consisted of 16 patients in the early rehabilitation period of ischemic stroke (atherothrombotic stroke – 6 patients, lacunar stroke – 10 patients) at the age of 54 to 76 (the average age was 63 ± 3.8 years) without MS. Volumetric investigation was performed on MRI scanner Toshiba Vantage Titan 1.5. Workstation for images post processing: Vitrea. Total volume of cerebral hemispheres, volume of white matter and gray (cortex) matter separately as well as corpus callosum area in cm^2 was determined. Neurological patients' condition was determined according to National Institute of Health Stroke Scale (NIHSS). HADS, FAS questionnaires were completed.

Results and discussion. According to FAS questionnaire median of fatigue severity constituted $Me=32.2(Q1=16.5; Q3=51.5)$ in the main group and $Me=26.25(Q1=14.5; Q3=48.5)$ in the control group before the treatment. The distribution of depression in the main and control groups was about the same. According to FAS pathological fatigue was diagnosed in the vast majority of patients of the main group (90%), and depression according to HADS was detected only in 21%. This indicates that depression and pathological fatigue have different pathogenetic substrate. According to NIHSS, positive dynamics was observed in the main and control groups after the treatment. Significant correlation dependence of pathological fatigue severity according to FAS and stroke severity according to NIHSS was not defined. The significant difference of volumes of white matter and cortex ($P < 0.05$) between the indices of the main and control groups was determined decreasing in the main group. A significant decrease ($p < 0.05$) in the corpus callosum area was observed in patients with cerebrovascular diseases on the background of MS in comparison with the patients without MS.

Conclusions. MS probably contributes to the development of atrophic processes in patients with cerebrovascular pathology. The combination of hypertension, insulin resistance, dyslipidemia, and so on, accelerates atrophic processes more than each of these components separately, which were determined in patients without MS.

Keywords: ischemic stroke, fatigue, metabolic syndrome.

Introduction

Treatment of patients with past ischemic stroke principally involves the restoration of lost limb functions, lessons with speech therapist concerning aphasia, secondary stroke prevention and comorbidities treatment. Such conditions as fatigue, asthenia, anxiety, and depression are sometimes left unnoticed by doctors and scientists. The literature provides descriptions of pathological fatigue in case of somatic, neurological and psychiatric diseases. Pathological fatigue after stroke is a common but yet understudied phenomenon^[1, 6]. As opposed to physiologic fatigue, it occurs even after minor exertion, remains for a long time, does not decrease after rest, and is usually a manifestation of a disease. According to the literature data, pathological fatigue develops in 36-77% of patients after stroke and is one of the most common consequences of cerebral apoplexy. The incidence of pathological fatigue is believed to increase with time during the first year and then it decreases but remains at a high level for a long time^[3, 4]. There are still no reliable data on the pathogenesis of pathological fatigue after stroke. Some authors associate its development with the damage to ascending reticular formation, others associate it with the damage to frontal-subcortical connections^[9]. Neuroimmune, neuroendocrinal and psychological factors are of significant importance^[9]. Account must be taken of the fact that pathological fatigue may be an adverse reaction to some

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drugs such as beta-blocking agents, tricyclic antidepressants, neuromuscular blocking agents, anticonvulsants and others [1, 5, 6, 7]. Observational results concerning the emergence of post-stroke fatigue are rather contradictory. Some authors believe fatigue after stroke to occur in older people and women more often [3, 8, 10, 11]. Other studies refute these data. Previously stated publications on the development of increased fatigue after stroke in unemployed people and single patients have not confirmed the dependence on marital and employment status [3, 10, 12, 13, 14, 15]. A number of publications have shown a connection between pathological fatigue and depression [16, 17, 18, 15, 19]. One study showed that patients with diabetes mellitus after stroke suffered from pathological fatigue more often [3]. At the same time, some authors did not find a connection between diabetes mellitus and pathological fatigue. Daily hypertension and hypotension were associated with the development of fatigue [3]. However, previous hypertension was not the predictor of its development. Further investigations showed the development of fatigue to be primarily associated with cerebral affection, the presence of focus but not with vascular risk factors and hospitalization stress [3]. Literature sources present very few publications on pathological fatigue in case of ischemic stroke in patients with metabolic syndrome (MS). The presence of ischemic stroke risk factors (overweight, arterial hypertension, insulin resistance, dyslipidemia) providing the development of severe and sometimes recurrent stroke is probable to promote pathological fatigue in patients with MS more often than in patients without MS.

The objective of the research was to study the post-stroke pathological fatigue and anxiety and depressive disorders and to identify strategic brain areas of psycho-emotional disorders according to MRI in patients with ischemic stroke on the background of MS and to compare it with data of patients without MS.

Materials and methods. The research involved 30 patients (16 women and 14 men) at the age of 44 to 81 (the average age was 66±4.2 years) being in the early rehabilitation period of ischemic stroke on the background of MS (atherothrombotic stroke – 13 patients, lacunar stroke – 15 patients, cardioembolic stroke – 2 patients). They constituted the main group. The control group consisted of 16 patients in the early rehabilitation period of ischemic stroke (atherothrombotic stroke – 6 patients, lacunar stroke – 10 patients) at the age of 54 to 76 (the average age was 63±3.8 years) not having enough components to determine MS.

All patients underwent volumetric investigation on MRI scanner Toshiba Vantage Titan 1.5. Workstation for images post processing: Vitrea. The following MR sequences were used: T1-weighted image, T2-weighted image, Isotropic, Flair, DWI, T2*, FSBB. Total volume of cerebral hemispheres, volume of white matter and gray matter (cortex) separately, and corpus callosum area in cm² was determined.

General and neurological patients' condition was determined according to National Institute of Health Stroke Scale (NIHSS).

Patients completed additionally questionnaires "Hospital Anxiety and Depression Scale" (HADS). Quantitative assessment of post-stroke fatigue was performed according to Fatigue Assessment Scale (FAS).

Results statistical processing was conducted by means of modern methods of mathematical analysis using statistical

software "Statistica-6" and "Exel 2003". Descriptive statistics was used. Quantitative values having non-normal distribution were presented as median and interquartile range (25%-75%). Analyzing statistical sampling not submitted to the laws of Gaussian distribution, non-parametric Mann-Whitney U test was used. Correlation analysis was performed according to Spearman.

Results and discussion

According to FAS questionnaire median of fatigue severity constituted Me=32.2(Q1=16.5; Q3=51.5) in the main group and Me =26.25(Q1=14.5; Q3=48.5) in the control group before the treatment. It stands to mention that the score according to fatigue scale was higher than / or 22 points in the vast majority of patients of the main group (27 patients, 90%). This indicated clinical significance of fatigue in patients. Indices of women and men in both groups were identified separately taken as a whole. They constituted 25.5(Q1=16.5; Q3=51.5) in men and 31.25(Q1=16.5; Q3=51.25) in women. The difference between these indices was statistically significant (p<0.05). Thus, in quantitative terms pathological fatigue was higher in women among our patients. None of the patients had signs of other diseases except for ischemic stroke which could lead to pathological fatigue. A survey according to Hospital Anxiety and Depression Scale was conducted to patients having signs of pathological fatigue (main group – 27 people, control group – 15 people). The results are presented in Table 1.

Table 1: The disposition of patients of the main and control groups according to Hospital Anxiety and Depression Scale

Scores	Main group (n=27) abs., %	Control group (n=15) abs., %
≥15 severe depression	2 (7.4%)	1 (6.6%)
11-14-moderate depression	4 (14.8%)	2 (13.3%)
8-10- mild depression	13 (48.15%)	7 (46.6%)
≤7 absent depression	8 (29.6%)	5 (33.3%)

According to the data presented in Table 1, the distribution of depression in the main and control groups was about the same. Taking into account pathological fatigue in the vast majority of patients of the main group on the one hand and clinically significant depression according to HADS only in 21% of patients on the other hand, we may suggest that depression and pathological fatigue have different pathogenetic substrate. Statistically significant correlation dependence of pathological fatigue and depression was not defined.

According to NIHSS, neurologic deficit constituted Me = 5 [3, 7, 5] points in the main group. The average total neurologic deficit constituted 4 [2, 6, 7, 5] points in the control group. Thus, minor stroke was defined in the patients participating in the research. Table 2 represents the dynamics of neurological changes according to NIHSS before and after the treatment.

Table 2: Dynamics of indices according to NIHSS

	Main group (n=30)		Control group (n=16)	
	Before the treatment	After the treatment	Before the treatment	After the treatment
Me [Q1; Q3]	5 [3;7,5].	2[1,5;3,0] *	4 [2;6,75]	3,25[1,5;4,5]

*P<0.05 – in comparison with the index before the treatment

Based on the data presented in Table 2, the positive dynamics according to NIHSS was observed in the main and control groups after the treatment. Significant correlation dependence of pathological fatigue severity according to FAS and stroke severity according to NIHSS was not defined.

Results of volumetric investigations

The volume of cerebral structures in 30 patients with MS (the main group) and 16 patients without MS (the control group) was compared.

The volumes of white and gray (cortex) matters of the cerebral hemispheres are presented in Table 3.

Table 3: Volume of white and gray (cortex) matters of the cerebral hemispheres (cm³)

Measurement area	Main group MC (n=30) Me (Q1,Q3)	Control group (n=16) Me (Q1,Q3)	P
Volume of gray (cortex) matter of the cerebral hemispheres (cm ³)	368.6 [140;422] * cm ³	630 [520;740] cm ³	0.05
Volume of white matter of the cerebral hemispheres (cm ³)	533.3 [140;422] *	672.5[635;720]	0.05

* P <0.05

According to the data presented in Table 3, the significant difference of volumes of white matter and cortex (P <0.05) between the indices of the main and control groups was determined decreasing in the main group.

Defining the volumes and measuring the indices of certain brain structures, the decrease in the size of the corpus callosum area was observed in some patients.

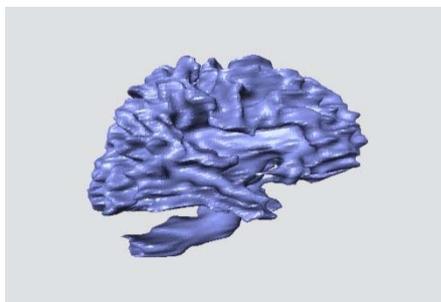


Fig 1: Determination of the total volume of the white matter (control group, patient D., age 51)

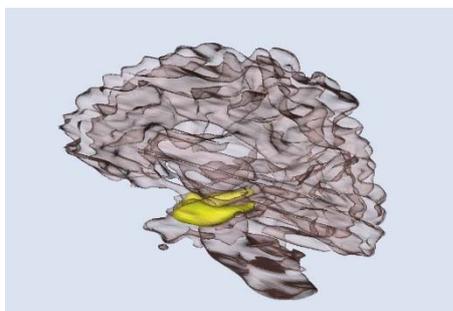


Fig 2: Determination of the cerebral cortex volume, hippocampi are in yellow color (control group, patient D., age 51)

Table 4: Corpus callosum area in the studied group

	Main group (patients with MS) (n=30)					Control group (patients without MS) (n=16)				
	Min	Max	Me	Q1	Q3	Min	Max	Me	Q1	Q3
Corpus callosum area (cm ²)	630	707	656.6*	645	685	689	780	734.5	720	760

*p < 0.05 in comparison with the second group

Analyzing the data presented in Table 4, it may be affirmed that a significant decrease (p<0.05) in the corpus callosum area was observed in patients with cerebrovascular diseases on the background of MS in comparison with the patients without MS.

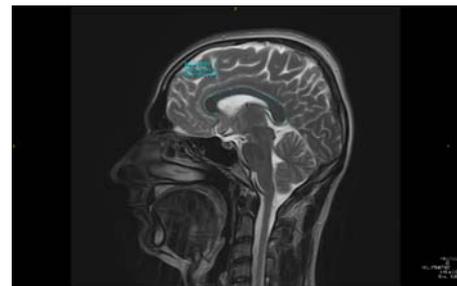


Fig 3: Determination of corpus callosum area

The decrease in corpus callosum area may be assumed to reflect the damage to association fibers passing through it and are important in providing integrative brain activity. This damage results in cognitive and psycho-emotional disorders. Violation of interhemispheric interaction and, therefore, a violation of two cerebral hemispheres coordinated work occur.

Conclusions

1. Pathological fatigue diagnosed in 90% of patients participating in the research must be taken into account during the treatment of patients in early rehabilitation period of acute ischemic stroke on the background of MS.
2. The degree of cortex and white matter atrophy was determined significantly higher in the patients with acute ischemic stroke on the background of the MS in comparison with patients without MS.
3. Significant decrease in the corpus callosum area (p <0.05) was detected in patients with MS. It could be associated with cognitive and emotional disorders.
4. MS probably contributes to the development of atrophic processes in patients with cerebrovascular pathology. The combination of hypertension, insulin resistance, dyslipidemia, and so on, accelerates atrophic processes more than each of these components separately, which were determined in patients without MS.

The results obtained in the research require further study. Sizes of other strategic brain structures in patients with ischemic stroke with and without metabolic syndrome are advisable to be defined. Possible connection of indices with cognitive function, post-stroke pathological fatigue and depression is advisable to be established.

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