and infertility ( $\chi^2$ =14.87, p<0.001) prevailed. It is necessary to point out that there is a significantly increased percentage of operative procedures on reproductive organs in persons with endometriosis, as well as high rate of artificial and spontaneous abortions. The commonest complications that occur during the gestation in the basic group include the pathology of fetoplacental complex – placental dysfunction ( $\chi^2$ =13.77, p<0.001), oligo- and polyhydramnios ( $\chi^2$ =4.49, p=0.03), foetal growth retardation and the threatened miscarriages. However, it should be stressed that the assessment of the functional state of the foetoplacental complex in 18-20 weeks of gestation revealed the early signs of compensatory changes of the foetus and placenta state in 14 (13.59 %) pregnant women of the basic group. The women of the basic group against the background of the high prenatal risk and the high rate of pregnancy complications were diagnosed to have the high frequency of foetal distress in labor ( $\chi^2$ =3.77, p=0.05), caesarean section ( $\chi^2$ =8.24, p=0.04) and during operative delivery ( $\chi^2$ =12.84, p<0.001). Conclusion. Thus, the results of scrutinizing the clinical signs of the pregnancy, labour and state of newborns demonstrated that pregnant women with endometriosis in their medical history are at high risk to develop the foetoplacental complex disorders, such as placental dysfunction, oligoand polyhydramnios, as well as foetal distress in labour and operative delivery.

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# A STUDY OF THE TIME-BASED CHARACTERISTICS OF PHENOMENOLOGY OF POST-STROKE FATIGUE OVER THE FIRST YEAR AFTER STROKE OCCURRENCE

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Post-stroke fatigue (PSF) is a common medical and social problem. Aim: to analyze time-based characteristics of PSF over the first year after stroke event. Material and methods. Patients were examined through definite time slots: during hospital staying (234 cases), in 1 month (203), in 3 months (176), in 6 months (156), in 9 months (139) and in 12 months (128 cases) after stroke. PSF was measured by fatigue assessment scale (FAS) and multidimensional fatigue inventory-20. (MIF-20) We conditionally divided all PSF cases into early PSF group (presented only within the 1<sup>st</sup> month after stroke), persistent PSF (presented within the 1<sup>st</sup> post-stroke month and later) and late PSF (appeared only in 3<sup>rd</sup> month observation or later). Results. Having analyzed all PSF cases according to FAS, we found out 15 PSF cases (16,0%) were assessed as early PSF, 51 (54,2%) assessed as persistent PSF and 28 (29,8%)— as late PSF. For all time-based types of PSF domains, according to MIF-20, the similar pattern of distribution was observed: early PSF domains — from 16,3% to 20,3%, persistent PSF domains — from 54,15 to 59,8%, late PSF domains — from 23,9% to 26,0%. All domains of early PSF, according to MIF-20, were statistically more intensive than all corresponding domains of persistent PSF and late PSF, whereas intensities of all persistent PSF domains and all late PSF domains were much or less similar. Conclusions. 1. About 20% of all PSF cases are early PSF, 25% are late PSF and slightly more than half of all cases is persistent PSF. 2. Proportions of all domains of early PSF, late PSF and persistent PSF are practically similar. 3. Significant differences between severities of early PSF and persistent PSF as well as late PSF can be as indirect evidences that all time-based PSF types are quite distinctive entities.

Key words: post-stroke fatigue, time characteristics, intensity.

The research described in this paper was performed within the framework of research plan of Neurological Department with Neurosurgery and Medical Genetics at Ukrainian Medical Stomatological Academy "Clinical and pathogenetic optimization of diagnosis, prognosis, treatment and prevention of complicated central nervous system's disorders and neurological impairments due to therapeutic pathologies" (state registration number 0116U004190).

#### Introduction

Nowadays there is an accelerating growth of modern society diseases and their vascular complications, in particular stroke that can be explained to some extent by the consequences of urbanization and significant lifestyle changes [1]. For the last decade much attention of researchers has been paid to a variety of non-functional long-term complications of stroke. One of these, so called «silent» complications, is post-stroke fatigue (PSF). PSF is a common medical and social problem, which often affects post-stroke patients [2, 3]. It is well known that PSF negatively affects rehabilitation, recovery and survival rate after the cerebral event [4, 5].

For recent years PSF has being considered as evolutionary process. Five longitudinal studies de-

voted to PSF course in individual patients found that more than one third of patients had PSF at the initial assessment (usually within the first 3 months after stroke) [6-10]. Among patients with PSF at the initial assessment, about two thirds of them had PSF at a later stage of follow-up (usually over 1 year after stroke), and nearly one third of them had recovered by that time. Among patients without PSF at the initial assessment, PSF developed in 12% to 58% of them during the course of the followup [6-10]. These findings were grounds for the development of conceptual model for PSF, which reveals three patterns of temporal course of PSF after stroke, that is, early onset PSF, persistent PSF, and late onset PSF [11]. At the same time up to now there are no in-depth studies aimed to study the

temporal course and characteristics of early, persistent and late PSF. However for better understanding the nature of PSF management it is very important to determine time-related aspects of this pathological entity. The aim pf this study was to analyze time-based characteristics of PSF over the first year after stroke event.

#### Material and methods

The study included patients who had an acute stroke (ischemic or hemorrhagic), agreed to participate in the study and were able to provide informed consent. Exclusion criteria were major medical illness that could cause secondary fatigue (oncological, hematological diseases, cardiac, liver, kidney and respiratory insufficiency, progressive angina pectoris, acute myocardial infarction), alcohol abuse, consciousness impairments, insufficient cognitive ability (Mini-Mental State Examination scores less than 24) [12], depressive and anxious disorders (Hospital Anxiety and Depression Scale scores more than 10 for both pathologies) [13], impaired speech function to participate (severe dysphasia or dysarthria), impaired language or written ability to complete the study questionnaires, severe functional disabilities (modified Rankin scale scores ≥4).

Patients' characteristics were evaluated in definite time slots: during hospital staying (234 cases), in 1 month (203), in 3 months (176), in 6 months (156), in 9 months (139) and in 12 months (128

cases) after stroke.

PSF was measured by two self-report questionnaires: fatigue assessment scale (FAS) and multidimensional fatigue inventory-20 (MFI-20). FAS included 5 questions about mental components and 5 questions about the physical part of fatigue. The score ≥22 indicates fatigue presence [14]. MFI-20 is a 20-item multidimensional questionnaire, which covers global, physical, mental, motivational and activity-related fatigue domains. A cut-off of 12 out of 20 for every sub-scale has been suggested to apply fro people with stroke [15].

Distributions of continuous variables were checked by Shapiro-Wilk test. Parametric variables were represented as mean±standard deviation, non-parametric – as mediana (Me) and interquartile (25%-75%) range (Q1-Q3). Intensity of each PSF domain was measured at time of initial detection. For determination differences between severities of certain PSF domains Mann-Whitney U test was used. A *p*-value <0,05 was considered as statistically significant.

#### Results and discussion

Patients' age ranged from 43 to 79 years (63,3±8,4 years). Initially there were 112 (47,9%) males and 122 (52,1%) females. 201 (85,9%) patients had ischemic strokes, and 33 (14,1%) had hemorrhagic strokes in their histories.

Table 1 Numbers of PSF cases, according to FAS, over the first year after stroke event

Time slots after stroke evetn	Number of PSF cases	Increase compared with previous time slot, n (%)	Decrease compared with previous time slot, n (%)
stay in hospital	65	-	-
1 month	63	14 (33,3%)	8 (34,8%)
3 months	76	26 (61,9%)	7 (30,4%)
6 months	69	1 (2,4%)	3 (13,0%)
9 months	54	1 (2,4%)	4 (17,4%)
12 months	58	0	1 (4,4%)

The table 1 demonstrated that the significant dynamics of PSF (both increase and decrease) was observed within the first 3 months after stroke event. Increase in PSF number was especially noticeable within the period between 1<sup>st</sup> and 3<sup>rd</sup> months after stroke (that made up almost two third of all new PSF cases), while within the period between 3<sup>rd</sup> and 9<sup>th</sup> post-stroke months, only 2 new PSF cases were registered.

Literature sources about longitudinal characteristics of PSF are quite limited and somewhat controversial. Sone studies reported that about two thirds of patients with PSF in a month after stroke (according to FAS) had become non-fatigued by the 6 month and most of them remained non-fatigued at the 12 month [6]. Accoording to other studies, PSF measured by Fatigue Severity Scale was found at admission, at the 6 month and in a year of post-stroke life in 37,7% of the patients and was

absent at all in 17,4% of the patients, whereas the remaining 44,9% of the patients had variable course of PSF during the first post-stroke year [7]. PSF, according to Fatigue Severity Scale, was found at the time of discharge from inpatient rehabilitation departments and also in 24 weeks later in 40,5% of the patients, whereas about a quarter of the patients reported no PSF at either measurement and rest of patients had PSF only at one observation [9]. Among the patients who reported PSF (due to Fatigue Assessment Instrument) at the 6 month of the follow up had a minor stroke, 77,3% still reported PSF at the 12 month of the follow-up and 11,6% were newly diagnosed cases, when patients reported about PSF later on [10].

Thus, according to our results, between 1<sup>st</sup> and 3<sup>rd</sup> months after stroke there was upsurge of PSF numbers. How to interpret this phenomenon? From the positions of the evolutionary concept of PSF by

Wu S. et al [11], it can be assumed that just in this time interval (exactly, between 1<sup>st</sup> and 3<sup>rd</sup> months after stroke event) some dramatical changes of PSF nature with corresponding clinical manifestations occur. Based on above mentioned time-based PSF characteristics and according to evolutionary concept of PSF, we conditionally divided all PSF cases into early PSF group (PSF found out only within the 1<sup>st</sup> month after stroke and disappeared at the 3<sup>rd</sup> month of the follow-up), persistent PSF (presented within the 1<sup>st</sup> post-stroke month and later) and late PSF (appeared only at 3<sup>rd</sup> month of follow-up or later).

Proceeding from the time-based concept of PSF, throughout all PSF diagnoses, according to FAS, 15 PSF cases (16,0%) were found as early PSF, 51 PSF cases (54,2%) were assessed as persistent PSF and 28 PSF cases (29,8%) – as late PSF.

Number of all PSF domains, according to MFI-20, at each post-stroke time slot was comparable to the amounts of PSF, according to FAS. Therefore, we consider it is unnecessary to present the data about number of each PSF domain within the observation period.

Table 2 Changes in number of PSF domains according to MFI-20, compared with previous time point over the first year after stroke event

	PSF domain									
Time point after stroke occurrence	Global		Physical		Mental		Activity-related		Motivational	
	+ N, (%)	- n, (%)	+ n, (%)	- n, (%)	+ n, (%)	- n, (%)	+ n, (%)	- n, (%)	+ n, (%)	- n, (%)
1 month	5 (38%)	9 (32%)	16 (39%)	9 (32%)	15 (38%)	8 (30%)	13 (37%)	7 (26%)	13 (41%)	8 (33%)
3 months	24 (60%)	8 (29%)	24 (59%)	9 (32%)	25 (62%)	9 (33%)	22 (63%)	8 (30%)	19 (59%)	7 (30%)
6 months	1 (2%)	4 (14%)	1 (2%)	3 (11%)	0	7 (26%)	0	8 (30%)	0	7 (30%)
9 months	0	4 (14%)	0	6 (21%)	0	0	0	2 (7%)	0	1 (3%)
12 months	0	3 (11%)	0	1 (4%)	0	3 (11%)	0	2 (7%)	0	1 (3%)

Table 3 Number and frequencie of time-based types of PSF domains over the first year after stroke event

PSF domain		Time-based type of PSF				
	Early	Persistent	Late			
global	17 (17,7%)	54 (56,3%)	25 (26,0%)			
physical	18 (17,8%)	58 (57,4%)	25 (24,8%)			
mental	17 (17,5%)	55 (56,7%)	25 (25,8%)			
activity-related	15 (16,3%)	55 (59,8%)	22 (23,9%)			
motivational	15 (20,3%)	40 (54,1%)	19 (25,6%)			

Table 2 shows that all PSF domains, according to MIF-20, have the similar dynamics of evolution as global PSF. There is an intense increase in the number of new PSF cases (no matter of PSF domain) within the first 3 post-stoke months with subsequent zero dynamics during the next 9 months. Also, just within the first 3 post-stroke months there is a significant reduction of PSF cases (likewise, no matter of PSF domain).

In the same manner, on the basis of time-based

pattern, we conditionally divided all PSF domains into three types – early PSF, persistent PSF and late PSF.

Table 3 demonstrates that for all time-based types of PSF domains the similar pattern of distribution is observed: about one-fifth of the patients were diagnosed to have early PSF, about a quarter of them had late PSF, and all the rest cases were assessed as persistent PSF.

Table 4 Intensities of time-based types of PSF domains over the first year after stroke occurrence

PSF domain		Time-based type of PSF			
	Early	Persistent	late		
global	15 (14; 16)* **	14 (13; 14)	14 (13; 14)		
physical	15 (14; 16)* **	14 (13; 14)	14 (13; 14)		
mental	15 (14; 16)* **	14 (13; 14)	14 (13; 14)		
activity-related	15 (15; 16)* **	14 (13; 14)	14 (13; 15)		
motivational	14 (14; 15)*	14 (13; 14)	14 (13; 15)		

<sup>\* -</sup> significant differences (p<0,05), according to Mann-Whitney U test, between early PSF and persistent PSF;

As it can be seen in the table 4, all domains of early PSF are statistically more intensive than corresponding domains of persistent PSF and late PSF (exception is motivational domain of late PSF).

Significant difference between severities of early PSF and late PSF can also be as indirect evidence that early PSF and late PSF are quite different entities, which have, probably, their own special etiopa-

<sup>\*\* -</sup> significant differences (p<0,05), according to Mann-Whitney U test, between early PSF and late PSF.

thogenetic peculiarities. Moreover, significant weakening of early PSF during its transition into persistent PSF can also be a confirmation that early PSF and persistent PSF are quite distinctive entities, each with its peculiar nature.

At the end of the paper, it is necessary to underscore that our findings are quite important for clinical practice because the understanding of PSF development peculiarities is the ground for adequate PSF management. For example, based on our results, PSF prevention must be dealt as early as possible after stroke but just within the first 3 months after stroke (precisely during this period occur majority of new PSF cases), whereas in 3 months after stroke event or later preventive measures should be nearly ineffective and clinicians should focus on PSF treatment issues.

#### **Conclusions**

- 1. According to time-based PSF concept, about 20% of all PSF cases are early PSF, 25% of the cases are late PSF and slightly more than half of all cases are persistent PSF.
- 2. Proportions of all domains of early PSF, late PSF and persistent PSF are practically similar.
- 3. Intensities of all domains of early PSF are significantly higher than intensities of the corresponding domains of persistent PSF and late PSF.

Future investigations in this field should be directed toward the identification of socio-demographic, personal, neurological, neuroimaging and other factors associated with early PSF, persistent PSF and late PSF as well as with certain domains of time-based PSF types. These findings could help to understand ethiopathogenetic peculiarities of time-based types of PSF.

#### Literature

- Kaydashev IP. Izmeneniye obraza zhizni, narusheniye energeticheskogo metabolizma i sistemnoye vospaleniye kak faktory razvitiya bolezney tsivilizatsii [Change in lifestyle, violation of energy metabolism and systemic inflammation as factors in the development of the diseases of civilization]. Ukrains kiy Medichniy Chasopis. 2013; 5(97):103-8. (Russian).
- Delva I, Lytvynenko N, Delva M. Post-stroke fatigue and its dimensions within first 3 months after stroke. J. Wiadomosci Lekarskie. 2017; 1: 43-7.
- Delva I, Lytvynenko N, Delva M. Factors associated with poststroke fatigue within the first 3 month after stroke. J. Georgian Medical News. 2017; 6(267): 38-42.
- Glader E, Stegmayr B, Asplund K. Poststroke fatigue: a 2-year follow up study of stroke patients in Sweden. J. Stroke. 2002; 33:1327–1333.
- Van de Port I, Kwakkel G, Schepers V. Is fatigue an independent factor associated with activities of daily living, instrumental activities of daily living and health-related quality of life in chronic stroke? J. Cerebrovascular Diseases. 2007; 23:40–5.
- Duncan F, Greig C, Lewis S. Clinically significant fatigue after stroke: A longitudinal cohort study. Journal of Psychosomatic Research. 2014; 77:368–73. Doi: 10.1016/j.jpsychores.2014.06.013.
- Schepers V, Visser-Meily A, Ketelaar M. Poststroke fatigue: course and its relation to personal and stroke-related factors. J. Archives of Physical Medicine and Rehabilitation. 2006; 87:184–8. Doi: 10.1016/j.apmr.2005.10.005.
- Snaphaan L, Van der Werf S, De Leeuw F. Time course and risk factors of post-stroke fatigue: a prospective cohort study. European Journal of Neurology. 2011; 18: 611–7.
- Van Eijsden H, Van de Port I, Visser-Meily J. Poststroke fatigue: who is at risk for an increase in fatigue? J. Stroke Research and Treatment. 2012: 863978. Doi: 10.1155/2012/863978.
- Radman N, Staub F, Aboulafia-Brakha T. Poststroke fatigue following minor infarcts: a prospective study. J. Neurology. 2012; 79:1422–7. Doi: 10.1212/WNL.0b013e31826d5f3a.
- Wu S, Mead G, Macleod M. Model of understanding fatigue after stroke. J.Stroke. 2015; 46 (3): 893–8. DOI: 10.1161/STROKEAHA.114.006647.
- Folstein M, Folstein S, McHugh P. Mini-mental state: A practical method for grading the cognitive state of patients for the clinician. Journal of Psychiatric Research. 1975; 12:189-98.
- Zigmond A, Snaith R. The hospital anxiety and depression scale. J. Acta Psychiatrica Scandinavica. 1983; 67(6):361-70.
- Michielsen H, De Vries J, Van Heck G. Psychometric qualities of a brief self-rated fatigue measure: The Fatigue Assessment Scale. Journal of Psychosomatic Research. 2003; 54(4): 345-52.
- Smets E, Garssen B, Bonke B. The multidimensional fatigue inventory (MFI) psychometric qualities of an instrument to assess fatigue. Journal of Psychosomatic Research. 1995; 39:P. 315–25.

### Реферат

ЧАСОВІ ХАРАКТЕРИСТИКИ ФЕНОМЕНУ ПОСТІНСУЛЬТНОЇ ВТОМИ ПРОТЯГОМ ПЕРШОГО РОКУ ПІСЛЯ РОЗВИТКУ ІНСУЛЬТІВ

Дельва I.I.

Ключові слова: постінсультна втома, часові характеристики, інтенсивність.

Постінсультна втома є розповсюдженою медико-соціальною проблемою. Мета: вивчити часові характеристики виникнення та перебігу постінсультної втоми протягом першого року після розвитку інсультів. Матеріал та методи. Обстеження пацієнтів проводилося у певні часові точки: під час перебування в стаціонарі (234 випадки), через 1 (203), 3 (176), 6 (156), 9 (139) та 12 (128) місяців після інсульту. Постінсультну втому вимірювали за допомогою шкали оцінки втоми, а окремі компоненти постінсультної втоми – за допомогою багатомірної шкали оцінки втоми. Усі випадки постінсультної втоми були умовно поділені на ранню постінсультну втому (присутня тільки протягом 1-го місяця після інсульту), персистуючу постінсультну втому (існує протягом 1-го місяця після інсульту з подальшим персистуванням), пізню постінсультну втому (виникає не раніше, ніж через 3 місяця після інсульту). Результати. Серед усіх спостережень постінсультної втоми, згідно шкали оцінки втоми, у 15 випадках (16,0%) фіксувалася рання ПІВ, у 51 (54,2%) - персистуюча постінсультна втома та у 28 (29,8%) - пізня постінсультна втома. Майже подібний розподіл спостерігався і відносно окремих компонентів постінсультної втоми (глобального, фізичного, психічного, мотиваційного, пов'язаного з діяльністю). Усі компоненти ранньої постінсультної втоми були достовірно більш вираженими, ніж відповідні компоненти персистуючої та пізньої постінсультної втоми. Висновки. 1. Біля 20% усіх випадків постінсультної втоми складає рання постінсультна втома, 25% - пізня постінсультна втома та трохи більше 50% – персистуюча постінсультна втома. 2. Більша інтенсивність ранньої постінсультної втоми, в порівнянні з пізньою та персистуючою постінсультною втому може бути непрямим доказом етіопатогенетичної відмінності різних типів постінсультної втоми.

## Реферат

ВРЕМЕННЫЕ ХАРАКТЕРИСТИКИ ФЕНОМЕНА ПОСТИНСУЛЬТНОЙ УСТАЛОСТИ НА ПРОТЯЖЕНИИ ПЕРВОГО ГОДА ПОСЛЕ РАЗВИТИЯ ИНСУЛЬТОВ

Дельва И.И.

Ключевые слова: постинсультная усталость, временные характеристики, интенсивность.

Постинсультная усталость – распространенная медико-социальная проблема. Цель: изучить временные характеристики возникновения и течения постинсультной усталости на протяжении первого года после развития инсультов. Материал и методы. Обследование пациентов проводилось в определенные временные точки: во время пребывания в стационаре (234 случая), через 1 (203), 3 (176), 6 (156), 9 (139) та 12 (128) месяцев после инсульта. Постинсультную усталость диагностировали с помощью шкалы оценки усталости, а отдельные компоненты постинсультной усталости – с помощью многомерной шкалы оценки усталости. Все случаи постинсультной усталости были условно поделены на раннюю постинсультную усталость (присутствует только на протяжении 1-го месяца после инсульта), персистирующую постинсультную усталость (диагностируется на протяжении 1-го месяца после инсульта и в дальнейших наблюдениях), позднюю постинсультную усталость (возникает не ранее, чем через 3 месяца после инсульта). Результаты. Среди всех наблюдений постинсультной усталости, согласно шкале оценки усталости, в 15 случаях (16,0%) фиксировалась ранняя постинсультная усталость, в 51 (54,2%) – персистирующая постинсультная усталость и в 28 (29,8%) – поздняя постинсультная усталость. Практически подобное распределение наблюдалось и относительно отдельных компонентов постинсультной усталости (глобального, физического, психического, мотивационного, связанного с деятельностью). Все компоненты ранней постинсультной усталости имели достоверно большую выраженность по сравнению с соответствующими компонентами персистирующей постинсультной усталости и поздней постинсультной усталости. Выводы. 1. Около 20% всех случаев постинсультной усталости составляет ранняя постинсультная усталость, 25% - поздняя постинсультная усталость и чуть более 50% – персистирующая постинсультная усталость. 2. Большая выраженность ранней постинсультной усталости, по сравнению с поздней и персистирующей постинсультной усталости может являться непрямым доказательством этиопатогенетического различия разных типов постинсультной усталости.