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FACTORS ASSOCIATED WITH POST-STROKE FATIGUE DIMENSIONS OVER THE SECOND YEAR AFTER ACUTE CEREBROVASCULAR EVENTS

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Introduction. Post-stroke fatigue (PSF) can be defined as a form of pathological fatigue, characterized by a continuous feeling of weariness, independent of physical exertion [1], and can develop early after stroke or in the chronic stroke phase [2]. PSF has a negative impact on daily functioning and rehabilitation, resulting in higher dependency and poor quality of life [3].

PSF has been associated with both biological and psychological factors, and is therefore hypothesized to be of multifactorial origin [4]. Moreover, PSF is a quite dynamic phenomenon that may occur in different post-stroke terms with variable subsequent clinical course [4]. On the other hand, PSF is understood as being multidimensional with mental, physical, motivational and other aspects [5].

For rational PSF managements it's significant to find possible relationships between certain PSF domain and definite factors. Previously we revealed factors that are statistically associated with certain PSF domains within the first year after acute cerebrovascular event (ACE) occurrence [6,7]. However, up to now almost nothing is known about risk factors for certain PSF aspects over second year after ACE.

The objectives of this study were to identify socio-demographic, cognitive, psychological, clinical and neuroimaging factors associated with general PSF and with certain PSF domains over the second year after ACE occurrence.

Object and methods. Initially we enrolled in the study 201 patients: 132 with ischemic strokes, 24 with hemorrhagic strokes and 45 with transient ischemic attacks. Patients were included in the study if they agreed to participate 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) [8], depressive and anxious disorders (Hospital Anxiety and Depression Scale scores more than 10 for both pathologies) [9], impaired speech function to participate (severe dysphasia or dysarthria), impaired language or written ability to complete the study questionnaire, severe functional disabilities (modified Rankin scale (mRS) scores ≥4).

Patients' characteristics had been evaluated consequently in certain time points: at 12, 15, 18, 21 and 24 months after ACE occurrence. 19, 21, 17 and 18 patients were dropped out due to different reasons during each next quarter of the second post-stroke year. So, at 15, 18, 21 and 24 months after ACE we had examined 182, 161, 144 and 126 patients, respectively.

PSF was measured by self-report multidimensional fatigue inventory-20 (MFI-20) questionnaire which covers general, physical, mental, activity-related and motivational fatigue dimensions. A cut-off of 12 out of 20 for every sub-scale has been suggested for use with people with stroke [10].

Socio-demographic factors such as age, gender, marital status (married/single), formal education level (higher/non-higher) were recorded.

Signs of anxiety and depression were assessed by the Hospital Anxiety and Depression Scale (anxiety and depression sub-scales using a cut-off of 4, which has been recommended for persons who have had a stroke) [11]. Apathy symptoms were assessed by the Starkstein apathy scale (a cut-off point 14 or more from the total score of the scale was used to dichotomize the patients into apathetic and non-apathetic) [12]. Cognitive impairments were evaluated by the Montreal cognitive assessment (cut-off scores less than 26) [13]. Sleepiness was measured using Epworth scale (scores 10 or more indicate excessive daytime sleepiness) [14]. The co-morbidities included arterial hypertension, ischemic heart disease, atrial fibrillation and diabetes mellitus.

For all stroke patients we recorded such clinical variables as post-stroke functional disability (according to mRS score). Additionally, for ischemic stroke patients we recorded some specific variables – stroke subtype (non-lacunar – lacunar, according to TOAST criteria [15]) and affected cerebral arterial region (carotid – vertebro-basilar).

Among enrolled patients 92 subjects underwent head magnetic resonance imaging with a 1,5-T system (Siemens MAGNETOM Avanto 1.5T) and 0,2-T system (Signa Profile HD GE 0.2T). For measurement of brain atrophy we used planimetrical indexes: bifrontal index (BFI), bicaudate index (BCI), maximum diameter of the third ventricle and cortical atrophy index (CAI) on T1 sequence [16]. White matter lesions derived from FLAIR imaging was graded on Fazekas scale on the basis of visual assessment both periventricular and subcortical areas [17].

Continuous variables were represented as mean (M) and standard deviation (SD), categorical data were represented by number (n) and percentage. Univariate logistic regression analysis was performed to analyze the odds ratio (OR) with 95% confidence intervals of factors associated with PSF. Variables having a p value less than 0,05 in the univariate analysis were selected and evaluated by multivariate logistic regression models. P

Table 1.

Characteristics of the baseline study sample

Characteristics			Value
age (years), M±SD			61,8±7,7
males, n (%)			95 (47,3%)
married, n (%)			134 (66,7%)
higher education, n (%)			65 (32,3%)
anxious signs, n (%)			54 (26,9%)
depressive signs, n (%)			70 (34,8%)
apathy symptoms, n (%)			53 (26,4%)
cognitive impairments, n (%)			91 (45,3%)
excessive daytime sleepiness, n (%)			58 (28,9%)
co-morbidities	arterial hypertension, n (%)		174 (86,6%)
	ischemic heart disease, n (%)		157 (78,1%)
	atrial fibrillation, n (%)		50 (24,9%)
	diabetes mellitus, n (%)		72 (35,8%)
stroke characteristics	mRS score	0	59 (37,8%)
		1	52 (33,3%)
		2	33 (21,2%)
		3	12 (7,7%)
ischemic stroke characteristics	subtype	non-lacunar	102 (77,3%)
		lacunar	30 (22,7%)
	affected cerebral arterial region	carotid	96 (72,7%)
		vertebrobasilar	36 (27,3%)
neuroimaging characteristics	brain atrophy indexes	BFI	0,34±0,04
		BCI	0,23±0,06
		third ventricle diameter, mm	8,3±2,0
		CAI	0,04±0,02
	Fazekas scale score, n (%)	1	11 (12%)
		2	21 (23%)
		3	25 (27%)
		4	24 (26%)
		5	11 (12%)

values less than 0,05 were considered significant. Statistical analyses were performed using SPSS 14.0 statistics software.

Results and discussion. As article is limited we present only significant results. First of all, in univariate logistic regression analysis most of the studied variables that are present in **table 1** (gender, marital status, education level, apathetic impairments, excessive daytime sleepiness, arterial hypertension, ischemic heart disease, atrial fibrillation, diabetes mellitus, ischemic stroke subtype, affected cerebral arterial region, all neuroimaging variables except Fazekas scale score) were not significantly associated with any PSF domain in any time point within second year after ACE. So, only depressive and anxious signs, cognitive impairments, mRS score, Fazekas scale score had statistical associations with increased risk of certain PSF domains during observation period.

As can be seen from **table 2,** general PSF (overall feelings of being tired) is predominantly associated with depressive signs and mRS score. Revealed associations between depressive signs and general PSF are consistent with a meta-analysis of psychological factors in relation to PSF [18]. This is especially true for later periods after stroke: according to Wu S. and co-authors so-called «late» PSF may be more attributable to psychological and behavioral factors [4]. Associations between general PSF and post-stroke functional condition due to mRS can be explained by the fact that PSF might be triggered by physical de-conditioning which sets up a vicious, self-perpetuating cycle of fatigue, avoidance of physical activity, further deconditioning and more fatigue [19].

As for physical PSF domain, it had statistical association only with mRS score and only at 12 months after ACE – OR 2,85 (1,85-4,38), p<0,01.

Table 3 shows that anxious signs, cognitive impairments and Fazekas scale score have statistical associations with increased risk of mental PSF. Mental fatigue, according to corresponding MFI-20 sub-scale, is mainly described as “loss of concentration” [10]. It is quite difficult to explain why anxious signs (but not depressive signs) are associated with mental PSF. Maybe, stroke survivors with higher anxiety levels are more susceptible to negative interpretation such feelings as “loss of concentration” and (or) cognitive function deficit. Associations between cognitive impairments and mental PSF may be partly explained by the coping hypothesis, which suggests that the brain needs to work harder to compensate for impairments to cognitive functions such as attention and processing speed, which in turn results in fatigue feeling [20]. Associations between leukoaraiosis extension due to Fazekas scale score and mental PSF may be partially explained via cognitive impairments (higher Fazekas scale scores were significantly correlated with the increased risk of long-term post-stroke cognitive impairments [21]).

Table 2.

Factors associated with general PSF domain from multivariate logistic regression models

Time point after ACE	Factors	OR
12 months	cognitive impairments	4,07 (1,98-8,35), p<0,01
	mRS score	2,96 (1,85-4,76), p<0,01
15 months	depressive signs	4,88 (2,25-10,59), p<0,01
18 months	depressive signs	3,37 (1,45-7,79), p<0,01
	mRS score	2,05 (1,23-3,40), p=0,01
21 months	depressive signs	4,84 (1,95-12,03), p<0,01
	mRS score	1,89 (1,11-3,22), p=0,02
24 months	depressive signs	7,26 (2,69-19,55), p<0,01

Due to **table 4,** motivational PSF is associated with anxious and depressive signs, as well as with Fazekas scale score. According to MFI-20, the essence of fatigue motivational component has close overlap with depressive signs [10], so it is likely that motivational PSF are more sensitive to psychological abnormalities then other fatigue domains. White matter hyperinten-

Table 3.

Factors associated with mental PSF domain from multivariate logistic regression models

Time point after ACE	Factors	OR
12 months	anxious signs	2,66 (1,25-5,66), p=0,01
	cognitive impairments	3,31 (1,65-6,62), p<0,01
	Fazekas scale score	3,28 (2,02-5,31), p<0,01
15 months	anxious signs	3,94 (1,68-9,28), p<0,01
	cognitive impairments	4,16 (2,03-8,50), p<0,01
	Fazekas scale score	2,71 (1,76-4,19), p<0,01.
18 months	anxious signs	4,27 (1,67-10,98), p<0,01
	cognitive impairments	4,45 (2,03-9,77), p<0,01
	Fazekas scale score	2,60 (1,61-4,19), p<0,01
21 months	anxious signs	3,87 (1,49-10,07), p=0,01
	cognitive impairments	3,69 (1,62-8,36), p<0,01
	Fazekas scale score	2,54 (1,54-4,18), p<0,01
24 months	anxious signs	3,93 (1,51-10,19), p<0,01
	cognitive impairments	3,15 (1,34-7,41), p=0,01
	Fazekas scale score	2,54 (1,48-4,37), p<0,01

sities may significantly contribute to the development of post-stroke depressive signs and indirectly increase risk of motivational PSF [22].

Table 5 shows that only depressive signs and mRS score have significant associations with risk of activity-related PSF. Reduction in physical activity due to post-stroke functional limitation may increase the perception of the physical effort required to carry out daily tasks [19].

Summing up we can say that this is the first study to examine factors that could be related to certain PSF domains within the second year after ACE occurrence. The clinical implications of our study are that clinicians in routine practice should consider screening all stroke and transient ischemic attack patients for subclinical depressive, anxious and cognitive impairments, as modifiable factors, and deliver an intervention to reduce these symptoms.

Table 4.

Factors associated with motivational PSF domain from multivariate logistic regression models

Time point after ACE	Factors	OR
12 months	depressive signs	1,99 (1,06-3,77), p=0,03
	Fazekas scale score	1,82 (1,18-2,82), p=0,01.
15 months	depressive signs	2,56 (1,12-5,84), p=0,03
	Fazekas scale score	1,59 (1,07-2,37), p=0,02
18 months	depressive signs	2,90 (1,16-7,24), p=0,02
	Fazekas scale score	1,68 (1,10-2,58), p=0,02
21 months	anxious signs	3,81 (1,47-9,88), p=0,02
	Fazekas scale score	1,59 (1,02-2,48), p=0,04
24 months	anxious signs	3,34 (1,29-8,67), p=0,02
	Fazekas scale score	1,96 (1,08-3,55), p=0,03

Table 5.

Factors associated with activity-related PSF domain from multivariate logistic regression models

Time point after ACE	Factors	OR
12 months	depressive signs	2,74 (1,38-4,46), p<0,01
	mRS score	2,36 (1,54-3,61), p<0,01
15 months	depressive signs	2,42 (1,06-5,49), p=0,03
	cognitive impairments	2,13 (1,03-4,42), p=0,04
	mRS score	2,77 (1,69-4,54), p<0,01
18 months	mRS score	2,67 (1,59-4,49), p<0,01
21 months	mRS score	2,83 (1,63-4,93), p<0,01
24 months	mRS score	2,58 (1,40-4,75), p<0,01

Conclusions

1. Different PSF domains are associated with quite different set of factors over the second year after ACE occurrence.

2. The full set of contributing to PSF factors includes anxious and depressive signs, cognitive impairments, post-stroke disability (due to mRS score) and leukoaraiosis level (due to Fazekas scale score).

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ФАКТОРИ, АСОЦІЙОВАНІ З КОМПОНЕНТАМИ ПОСТІНСУЛЬТНОЇ ВТОМИ ПРОТЯГОМ ДРУГОГО РОКУ ПІСЛЯ РОЗВИТКУ ГОСТРИХ ПОРУШЕНЬ МОЗКОВОГО КРОВООБІГУ

Дельва І. І.

Резюме. Постінсультна втома (ПІВ) – часте ускладнення гострих порушень мозкового кровообігу (ГПМК). *Мета. Вивчити фактори, асоційовані з різними компонентами ПІВ протягом другого року після розвитку ГПМК. Об'єкт і методи. Пацієнти обстежувалися щоквартально: 201 на початку та 126 – в кінці другого року після ГПМК. Глобальна ПІВ, як і окремі її компоненти, діагностувалася за допомогою шкали багатовимірної оцінки втоми (MIF-20). Результати. В мультиваріантному логістичному аналізі не виявлено, що* глобальна ПІВ достовірно асоціюється з депресивними ознаками та показниками модифікованої шкали Ренкіна, психічна ПІВ – з тривожними розладами, когнітивними порушеннями та показниками візуальної шкали оцінки лейкоареозу Fazekas, мотиваційна ПІВ – з тривожними та депресивними розладами, з показниками шкали *Fazekas, ПІВ, що пов'язана з активністю – з депресивними розладами та показниками модифікованої шкали Ренкіна. Висновки. Протягом другого року після розвитку ГПМК окремі компоненти ПІВ асоціюються з досить різною сукупністю факторів.*

Ключові слова: *пізній постінсультний період, компоненти втоми, асоційовані фактори.*

ФАКТОРЫ, АССОЦИИРОВАННЫЕ С КОМПОНЕНТАМИ ПОСТИНСУЛЬТНОЙ УСТАЛОСТИ В ТЕЧЕНИИ ВТОРОГО ГОДА ПОСЛЕ РАЗВИТИЯ ОСТРЫХ НАРУШЕНИЙ МОЗГОВОГО КРОВООБРАЩЕНИЯ

Дельва И. И.

Резюме. Постинсультная усталость (ПИУ) – частое осложнение острых нарушений мозгового кровообращения (ОНМК). *Цель. Изучить факторы, ассоциированные с разными компонентами ПИУ на протяжение второго года после развития ПИУ. Объект и методы. Пациенты обследовались ежеквартально: 201 в начале и 126 – в конце второго года после ОНМК. Отдельные компоненты ПИУ, диагностировались с помощью шкалы многомерной оценки усталости (MIF-20). Результаты. В мультивариантном логистическом анализе выявлено, что* глобальная ПИУ достоверно ассоциируется с симптомами депрессии и показателями модифицированной шкалы Рэнкина, психическая ПИУ – с тревожными расстройствами, когнитивными нарушениями и показателями визуальной шкалы оценки лейкоареоза Fazekas, мотивационная ПИУ – с тревожными и депрессивными расстройствами, с показателями шкалы *Fazekas, ПИУ, связанная с активностью, – с депрессивными расстройствами и показателями модифицированной шкалы Рэнкина. Выводы. На протяжении второго года после развития ОНМК отдельные компоненты ПИУ ассоциируются с довольно разнообразной совокупностью факторов.*

Ключевые слова: *поздний постинсультный период, компоненты усталости, ассоциированные факторы.*

FACTORS ASSOCIATED WITH POST-STROKE FATIGUE DIMENSIONS OVER THE SECOND YEAR AFTER ACUTE CEREBROVASCULAR EVENTS

Delva I.

Abstract. Post-stroke fatigue (PSF) is a common and often debilitating sequel of both strokes and transient ischemic attacks. *Aim. Identify* factors that are associated with global PSF and certain PSF domains over the second year after acute cerebrovascular events (ACE) occurrence. *Object and methods. Patients were examined quarterly: 201 at the beginning and 126 patients – at the end of the second year after ACE. Global PSF and each PSF domain (physical, mental, motivational, activity-related) were measured by multidimensional fatigue inventory-20 scale (*a cut-off of 12 out of 20 for every sub-scale*). Results. In* univariate logistic regression analysis most of the studied variables (gender, marital status, education level, apathetic impairments, excessive daytime sleepiness, arterial hypertension, ischemic heart disease, atrial fibrillation, diabetes mellitus, ischemic stroke subtype, affected cerebral arterial region, neuroimaging indexes of cerebral atrophy) were not significantly associated with global PSF as well as with any PSF component. *Univariate and multivariate logistic regression analysis showed that during the second year after ACE occurrence global PSF was statistically significantly associated with depressive sings and modified Rankin scale score, mental PSF – with anxious signs, cognitive impairments and leukoaraiosis extension due to Fazekas scale score, motivational PSF – with anxious signs, depressive signs and Fazekas scale score, activity-related PSF – with depressive signs and modified Rankin scale score. Conclusions. 1. Different* PSF domains were associated with quite different set of factors over the second year after ACE occurrence. 2. The full set of contributing to PSF factors included anxious and depressive signs, cognitive impairments, post-stroke disability (due to modified Rankin scale score) and leukoaraiosis level (due to Fazekas scale score).

Key words: late post-stroke period, fatigue dimensions, associated factors.

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