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THE ROLE OF A PHYSICAL ANTHROPOLOGICAL FACTOR IN EPIDEMIOLOGY OF WILSON'S DISEASE

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РОЛЬ АНТРОПОЛОГІЧНОГО ЧИННИКА В ЕПІДЕМІОЛОГІЇ ХВОРОБИ ВІЛЬСОНА — КОНОВАЛОВА

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РОЛЬ АНТРОПОЛОГИЧЕСКОГО ФАКТОРА В ЭПИДЕМИОЛОГИИ БОЛЕЗНИ ВИЛЬСОНА — КОНОВАЛОВА

During recent decades researches of the role of a morphophysiological heterogeneity of human populations have been gaining a growing significance for issues of risk factors profiles, prevalence, formation, course, and outcomes of various psychoneurological pathologies. In the article results of an anthropomorhological examination of a population of patients with Wilson's disease are presented. The appropriate composition of this population was studied and peculiarities of its anthropological structure were revealed. On the base of the data obtained anthropological phenotypic complexes inherent to patients with Wilson's disease were determined. It was demonstrated an association between presence of this pathology and Mediterranean (61.29 % of patients) and, to a lesser extent, Atlantic-Baltic (16.13 %) anthropological phenotypic variants.

Key words: Wilson's disease, anthropological phenotypic variant, epidemiology

В останні десятиліття все більшого значення набуває вивчення ролі морфофізіологічної гетерогенності людських популяцій у профілі чинників ризику, поширеності, формування, перебігу та виходів різних психоневрологічних патологій. У статті подано результати антропоморфологічного дослідження популяції пацієнтів з хворобою Вільсона — Коновалова. Вивчено склад цієї популяції, виявлено особливості її антропологічної структури. На підставі отриманих даних визначено антропоморфологічні комплекси, що є властивими для пацієнтів з хворобою Вільсона — Коновалова, й показано зв'язок наявності цієї патології зі середземноморським (61,29 % пацієнтів) і, меншою мірою, атланто-балтійським (16,13 % пацієнтів) антропологічним типами.

Ключові слова: хвороба Вільсона — Коновалова, антропологічний тип, епідеміологія

В последние десятилетия всё большее значение приобретает изучение роли морфофизиологической гетерогенности человеческих популяций в профиле факторов риска, распространённости, формирования, течения и исходов различных психоневрологических патологий. В статье представлены результаты антропоморфологического исследования популяции пациентов с болезнью Вильсона — Коновалова. Изучен состав этой популяции, выявлены особенности её антропологической структуры. На основании полученных данных выделены антропоморфологические комплексы, характерные для пациентов с болезнью Вильсона — Коновалова, и показана связь наличия этой патологии со средиземноморским (61,29 % пациентов) и, в меньшей степени, атланто-балтийским (16,13 % пациентов) антропологическими типами.

Ключевые слова: болезнь Вильсона — Коновалова, антропологический тип, эпидемиология

One of important characteristics both mankind in general and its separate populations in particular is extreme morphophysiological heterogeneity. Mostly that is biological diversity stipulates wide human adaptive abilities and plasticity [1]. One of manifestations of abovementioned heterogeneity is anthropomorphological (phenotypic) diversity which is inherent more or less for every modern human population. Due to a number of reasons (destruction of traditionally closed societies and models of resettlement, a huge increasing of mobility of population including both short- and long-distance migrations, an inclusion of earlier absolutely uncharacteristic morphophysiological complexes into body of populations as results of establishment of marriage relations etc.) polytypicality of various populations is growing constantly and a factor of an individual morphophysiological diversity is getting more and more significance to understand mechanisms of formation, epidemiological peculiarities, course and outcomes of different pathologies.

In recent decades a number of studies, both generalizing and on local population level, confirmed an important role of ethnogenetic factors from the point of view of a risk degree, diagnosis, development, peculiarities of course and reaction to therapy, and outcomes of many psychoneurological pathologies [2—5]. Although the majority of such studies investigated mentioned parameters in representatives of so called large human races (i.e., Caucasoid, Mongoloid, Negroid, and Australoid), it was shown also that there were certain distinctions between smaller anthropomorphological divisions, in particular, inside Caucasoid and Mongoloid races as well as in so called anthropomorphologically transient [6—8]. That is why anthropomorphological researches become actual, especially for investigations of genetically stipulated diseases. One of such pathologies is Wilson's disease.

Wilson's disease (WD) of hepatocerebral dystrophy is a rare and severe chronic degenerative disease with genetically caused by an impairment of copper metabolism. This pathology is worldwide widespread and is pointed out among different national and ethnic groups. Frequency of a homozygote bearing of WD genes is 1 per 100,000 an average with irregular geographical and ethnic distribution [9, 10]. According to the unified all-European WD database, in European countries prevalence of this disease ranges from 1.2 to 1.8 cases per 100,000 [11]. According to other data, frequency of a homozygote bearing can reach 3.3 cases per 100,000 [12].

Taking into account a hereditary nature of WD and peculiarities of its prevalence, it was paid attention to an ethnogenetic component of epidemiology of this disease. For now, there are studies which demonstrated an existence of certain factors connecting with a locally abnormal increasing of WD prevalence. Thus, in Bashkortostan Republic (Russian Federation) during 20 years a level of WD prevalence have grown up from 0.62 to 0.83 per 100,000 [13], zones of concentration were detected in Central Kazakhstan where WD prevalence achieved to 15.5 per 100,0000 [14]. They explain these facts by improvement of diagnosis,

accumulation of patients in the population due to an enlargement of their lifespan, a mutagenic effect of heavy metals and small doses of radiation etc. It was supposed also that an increasing of incidence of this disease in several regions and ethnic groups might be associated with effect of inbreeding [15].

Despite of describing over 350 mutations of ATP7B gene at present, in the most of populations worldwide WD appears as result of a small number of mutations which are specific for these populations. Thus, in Europe, including Russia, the His1069Gln mutation (a replacement of Histidine by Glutamine in protein 1069 position) is presented in 37-63 % of cases of the disease [16]. During an integrated clinical and molecular-genetic examination of 60 patients with WD in Bashkortostan Republic the His1069Gln mutation was found out in 87.2 % of patients: in 17.6 % patients in the homozygote state and in 82.4 % of patients in the compound-heterozygote state. It is needed to pay a special attention to the fact that in Bashkortostan representation of the His1069Gln mutation in persons from different ethnic groups was varied. In particular, this mutation was revealed in 55.5 % of ethnic Russians, 38.9 % of ethnic Tatars, 44.4 % of ethnic Bashkirs, and 83.3 % of ethnic Chuvashs [13]. Also data concerning different types of WD course depended on phenotypic peculiarities of patients were published [14, 17].

However, despite of a close attention of researchers to investigations of genotypes and phenotypes in WD in various populations of the world, there is still no explanation for diversity of manifestations and severity of the course of this genetic pathology, as well as there no explanation for an expressed polymorphism inside families [18].

In this connection a factor of morphophysiological heterogeneity was paid attention by us. It is inherent for practically any contemporary population, as it was stated above. It should not be identified with ethnic or linguistic characteristics of these populations, as they are an expression of a sociocultural component, whereas a morphophysiological heterogeneity reflects a biological component of these populations, their ethnogenetic history. In each population there are several main anthropomorphological phenotypic variants (APhVs), every of these represents a human sample with similarity on a distinct stable historically conditioned complex of anthropomorphological features [19]. The composition and proportion of these APhVs can provide indirect but sufficiently reasonable data regarding a genetic history of their bearers, thus allowing us to determine groups of people sharing a common ancestry with a high probability. This is very important to study hereditary diseases, and WD particularly.

On the base of the Department of Neuroinfections and Multiple Sclerosis of the "Institute of Neurology, Psychiatry and Narcology of the National Academy of Medical Sciences of Ukraine" State Institution for this purpose an anthropomorphological examination was performed for 31 patients with Wilson's disease as the main group of the study. The control group included 44 persons without WD and other neurological pathologies from the general population. Diagnosis of Wilson disease was made or confirmed on the base of the conventional standard: blood serum ceruloplasmin < 20 mg/dL and an increasing of copper excretion with urine more than 100 mcg per day as well as a presence of Kayser-Fleischer rings.

The anthropomorphological examination included an anthropometric investigation of general body proportions, the main measures of a head and an anthroposcopic description of soft parts of a face, pigmentation of skin and iris, as well as shape, pigmentation, and degree of development of a hair-covering. Processing of data of the examination was based on a generalized anthropological classification worked out by E. N. Khrisanfova and I. V. Perevozchikov (1991) [20]. On the base of a morphological complex of features for each examined person a leading anthropological phenotypic variant (APhV) had been determined and also morphological complexes of other anthropological phenotypic variants were taken into account if they were present. For analysis of the data obtained a distribution of the examined persons according to APhV was based on a leading (dominant) APhV. Along with this, inside of each APhV group persons with an expressed mixed complex of anthropological characteristics, containing components of features of more than one phenotypic variant, were defined.

Among 31 patients who were included into the study, there were natives of 17 regions of Ukraine. The most number of patients were from Dnipropetrovs'k, Kharkiv, Lviv, and Mykolayiv Regions (4 persons for each), whereas Kherson and Khmel'nyts'kyi Regions were presented by 2 persons for each, and Chernihiv, Donets'k, Kirovohrad, Kyiv, Luhans'k, Odesa, Poltava, Rivne, Vinnytsia, Zakarpattia, and Zaporizhzhia Regions were presented by 1 person for each. Thus, in the main group there were representatives of all anthropological areas of the country, which had been defined on the base both morphological and hematological, dermatoglyphic, and odontological methods [21, 22]. This geographical representativeness allows us an additional reasons to compare the anthropomorphological structure of the studied group of patients with WD with a general population.

All the persons examined from both groups belonged anthropologically to a various phenotypic varieties of the large Caucasian race embracing the vast majority of the population of Ukraine. However, on the APhV level the investigated groups demonstrated sharp distinctions. Anthropomorphological characteristics of the main group and the control group are presented in Table 1 and Table 2 respectively.

When analyzing the abovementioned data, marked and statistically significant differences in the general anthropomorphological structure between patients with WD and the control group attract attention first of all. Thus, in the control group 6 of 9 anthropomorphological complexes being part of the large Caucasian race (Alpine (or Central European), Atlanto-Baltic, Baltic, Dinaric, Mediterranean, and Paleo-European) were represented. According to data previous anthropomorphological examinations of the rural population of Ukraine [21], these APhVs (with exclusion of Atlanto-Baltic one) are characteristic for the territory of Ukraine, including also an historical perspective, with a different percentage depending upon a region of the country.

In contrast to the control group, among patients with WD there were persons with only 5 of 9 APhVs. A relative representation of these APhVs was distinct sharply in comparison with the main group and some widely distributed in the general population APhVs (particularly, Alpine and Baltic) were absent completely.

Table 1

Anthropomorphological characteristics of patients with Wilson's disease according to data of the anthropomorphological examination

Anthropological phenotypic variant (APhV)	Number, including					
	Total		Leading APhV		Unclearly expressed APhV with predomination	
	N, pers.	% ± *m*%	*N*, pers.	% ± *m*%	*N*, pers.	% ± *m*%
Alpine	—	—	—	—	—	—
Armenoid	—	—	—	—	—	—
Atlanto-Baltic	5	16.13 ± 6.72	4	80.00 ± 20.00	1	20.00 ± 20.00
Baltic	—	—	—		—	
Dinaric	5	16.13 ± 6.72	2	40.00 ± 24.49	3	60.00 ± 24.49
Indo-Afghan	—	—	—	—	—	—
Mediterranean	19	61.29 ± 8.89	16	84.21 ± 8.59	3	15.79 ± 8.59
Paleo-European	1	3.23 ± 3.23	—	—	1	100.0
Uralic	1	3.23 ± 3.23	1	100.0	—	—
TOTAL	31	100.0	22	70.97 ± 8.29	9	29.03 ± 8.29

Table 2

Anthropomorphological characteristics of the control group according to data of the anthropomorphological examination

Anthropological phenotypic variant (APhV)	Number, including					
	Total		Leading APhV		Unclearly expressed APhV with predomination	
	N, pers.	% ± *m*%	*N*, pers.	% ± *m*%	*N*, pers.	% ± *m*%
Alpine	13	29.55 ± 6.96	12	92.31 ± 7.69	1	7.69 ± 7.69
Armenoid	—	—	—	—	—	—
Atlanto-Baltic	2	4.55 ± 3.18	2	100.0	—	—
Baltic	4	9.09 ± 4.38	3	75.00 ± 25.00	1	25.00 ± 25.00
Dinaric	6	13.64 ± 5.23	5	83.33 ± 16.67	1	16.67 ± 16.67
Indo-Afghan	—	—	—	—	—	—
Mediterranean	8	18.18 ± 5.88	7	87.50 ± 12.50	1	12.50 ± 12.50
Paleo-European	11	25.0 ± 6.60	11	100.0	—	—
Uralic	—	—	—	—	—	—
TOTAL	44	100.0	40	90.91 ± 4.38	4	9.09 ± 4.48

Persons with Mediterranean APhV predominated markedly in the group of patients with WD in comparison with the control group (61.29 % and 18.18 %, respectively; $p < 0.05$). These patients were originated from Lviv (3 persons), Mykolayiv (3 persons), Dnipropetrovs'k (2 persons), Kharkiv (2 persons), Donets'k, Khmel'nyts'kyi, Kirovohrad, Kyiv, Luhans'k, Odesa, Vinnytsia, Zakarpattia, and Zaporizhzhia (1 persons for each) regions. Thus, Mediterranean APhV was presented among patients with WD despite of a geographical factors, both in regions with a substantial prevalence of this APhV (e.g., Dnipropetrovs'k, Luhans'k, Mykolayiv, and Odesa Regions) and in regions where this APhV was rare (Khmel'nyts'kyi, Lviv, Zakarpattia Regions). It should be pointed out that in accordance with literature [21, 22] none of regions of Ukraine has so high part of population with Mediterranean APhV as it was registered in the group of patients with WD.

A complete absence of persons with Alpine APhV (sometimes called also as Central European) among patients with WD became the second important peculiarity, which was revealed by this study. In the control group percentage of this APhV was 29.55 % and according to previous literature source this APhV is the most represented in the anthropomorphological structure of the rural Ukrainian population (up to 60 %) [21]. It should be emphasized, that among patients, who referred primarily to the "INPN of the NAMS of Ukraine" SI with diagnosis of Wilson's disease, there was 1 female patient belonging in accordance with the results of the anthropomorphological examination to the Alpine morphological complex. After a comprehensive clinical examination in the "INPN of the NAMS of Ukraine" SI this diagnosis had been recognized as fallacious and a diagnosis of iron deficiency anemia was made. Thus, it was confirmed indirectly that one of the most widespread in the general population APhVs, Alpine, is completely uncharacteristic for patients with WD.

Paleo-European APhV, which was well represented among persons from the control group, was also practically absent in the main group (25.00 % and 3.23 %, respectively; $p < 0.05$). On the territory of Ukraine this APhV is located predominantly in northern wood regions. The only patient with Paleo-European APhV was from Chernihiv Regions that corresponded to a picture observed for the general population.

In the group of patients with WD there was also a relatively high number of persons with Atlanto-Baltic APhV (16.13 % as compared with 4.55 % in the control group; $p < 0.05$): persons originated from Kharkiv, Kherson, Lviv, Poltava, and Rivne Regions, one for each region/ Such a sporadic geographical distribution is not surprising as Atlanto-Baltic APhV historically was practically not represented in the general population of any regions of Ukraine. In this connection a presence of 5 persons with Atlanto-Baltic APhV in the group of patients with WD compels a special our attention to this APhV from the point of view of WD epidemiology.

At the same time in the main group there were not patients with Baltic APhV in contrast to the control group, although in it percentage of such patients was relatively small (9.09 %). Generally, this anthropomorphological complex was not inherent for Ukrainian populations (approximately 5 %) [21], but by now its part in the population has been increased, mainly due to migrations of people during the last century.

Parts of persons with Dinaric anthropomorphological phenotypic variants appeared as similar in the main and control groups of the study (16.13 % and 13.64 %, respectively). Patients with this APhV were admitted form Dnipropetrovs'k (2 persons), Kharkiv, Khmel'nyts'kyi, and Mykolayiv Regions (1 for each region). According to literature data, Dinaric APhV in its different varieties was one of stable components of the anthropological structure of the general rural Ukrainian population and percentage of this APhV was 12—14 % that is well corresponded to data obtained in our work.

The anthropological structure of both investigated groups did not contained persons with such anthropomorphological complexes as Armenoid and Indo-Afghan ones. Uralic APhV did not practically present in the study (only 1 person; 3.23 % in the main group). Mentioned APhVs historically was not inherent to the general population of Ukraine and they were linked to some groups of other ethnogenetic origin.

That way, despite of a quite limited size of the examined sample of patients, on the base of the results obtained we are able to conclude preliminary as it follows.

The data from the study suggest that the population of patients with WD is characterized by a very high proportion of persons with Mediterranean APhV as compared with the general population. This allows us to suppose that there is an association between the WD bearing exactly with this anthropomorphological complex. This assumption is confirmed by the fact that Mediterranean complex of features in patients with WD is registered in all the regions and is not connected with a geographical area of a predominant prevalence of this APhV in Ukraine.

It could be said the same concerning Atlanto-Baltic APhV, proportion of which was a significantly higher in the group of patients with WD. Along with this, mentioned anthropomorphological complex entirely is rare in the general population. That strengthens the significance of obtained data in the perspective of epidemiology of WD.

Indices of proportion of persons with Dinaric APhV were very similar for the main and control groups. This finding might be an evidence of lack of both positive and negative associations between this anthropomorphological complex and prevalence of WD.

In contrast to the APhVs described above, in the group of patients with WD there were no persons with Alpine and Baltic anthropomorphological complexes and persons with Paleo-European APhV were practically absent. Taking into account a very high proportion of these anthropomorphological complexes for the general population (in some regions of the country a vast majority of population belongs to them), abovementioned results indicate a small prevalence of WD among people with these APhVs.

An absence of persons with Armenoid, Indo-Afghan, and Uralic complexes of features both in the control group and among patients with WD might be explained, first of all, by an extremely low proportion of these APhVs in the general population connected with the historically formed anthropological structure of population of Ukraine.

Generalizing the data obtained, it should be emphasized an aspect discussed below. All the anthropomorphological complexes can be conventionally divided to 2 groups: dolicho- and brachymorphic ones [23]. As regards APhVs registered in this study, Atlanto-Baltic, Dinaric, Indo-Afghan and Mediterranean APhVs are dolichomorphic, whereas Alpine, Armenoid, Baltic, Paleo-European and Uralic APhVs are brachymorphic. After summarizing of total number of persons with dolichomorphic APhVs and brachymorphic APhVs in the main and control groups we can see that in the group of patients with WD there were 29 persons with dolichomorphic APhVs (93.55 ± 4.28 %) and only 2 persons with brachymorphic APhVs (6.45 ± 4.28 %). Appropriately, in the control group 16 persons with dolichomorphic APhVs (36.36 ± 7.33; $p < 0.05$) and 28 persons with brachymorphic APhVs (63.64 ± 7.33; $p < 0.05$) were registered. Thus, we could conclude that in the examined population Wilson's disease is significantly associated with the dolichomorphic group of APhVs, which probably have an ancient common origin.

The results of this study suggest an importance of anthropomorphological factor for investigations of epidemiology, mechanisms, and risk factors of Wilson's disease and indicate a necessity of conduction of further researches in this area.

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THE DYNAMICS OF HEMODYNAMIC INDEXES IN PATIENTS WITH CONSEQUENCES OF MILD TRAUMATIC BRAIN INJURY

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ДИНАМІКА ГЕМОДИНАМІЧНИХ ПОКАЗНИКІВ У ПАЦІЄНТІВ З НАСЛІДКАМИ ЛЕГКОЇ ЧЕРЕПНО-МОЗКОВОЇ ТРАВМИ

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ДИНАМИКА ГЕМОДИНАМИЧЕСКИХ ПОКАЗАТЕЛЕЙ У ПАЦИЕНТОВ С ПОСЛЕДСТВИЯМИ ЛЕГКОЙ ЧЕРЕПНО-МОЗГОВОЙ ТРАВМЫ

We examined 59 patients with consequences of mild traumatic brain injuries. The patients were examined by using the method of Doppler ultrasonography of the extracranial brain vessels of the carotid arterial system with the application of hypercapnic and hypocapnic test. During our investigation we detected changes of reactivity of vessels towards the decrease of indicators of linear velocity of blood flow (LVF) under the tests. A paradoxical vascular response was marked in all the patients under the hyper- and hypocapnic load; a test-induced delayed vessels reaction was marked in 37 out of 59 patients.

Key words: consequences of mild traumatic brain injury, cerebral autoregulation, reactivity of vessels.

Під нашим спостереженням перебували 59 пацієнтів з наслідками легкої черепно-мозкової травми. Всім пацієнтам проведено доплерографічне дослідження судин головного мозку екстракраніального сегмента артерій каротидного басейну з застосуванням гіперкапнічного та гіпокапнічного тестів. У ході нашого дослідження було виявлено порушення реактивності судин у вигляді зниження лінійної швидкості кровотоку на тлі проведення проб. У всіх пацієнтів була виявлена парадоксальна реакція судин у відповідь на гіпер- і/або гіпокапнію, а також у 37 пацієнтів з 59 спостерігалася відстрочена реакція судин у відповідь на проведені проби.

Ключові слова: наслідки легкої черепно-мозкової травми, реактивність судин.

Под нашим наблюдением находились 59 пациентов с последствиями легкой черепно-мозговой травмы. Всем пациентам проведено допплерографическое исследование сосудов головного мозга экстракраниального сегмента артерий каротидного бассейна с применением гиперкапнического и гипокапнического тестов. В ходе нашего исследования было выявлено нарушение реактивности сосудов в сторону снижения линейной скорости кровотока на фоне проведения проб. У всех пациентов была выявлена парадоксальная реакция сосудов в ответ на гипер- и/или гипокапнию, а также у 37 пациентов из 59 наблюдалась отсроченная реакция сосудов в ответ на проводимые пробы.

Ключевые слова: последствия легкой черепно-мозговой травмы, реактивность сосудов.