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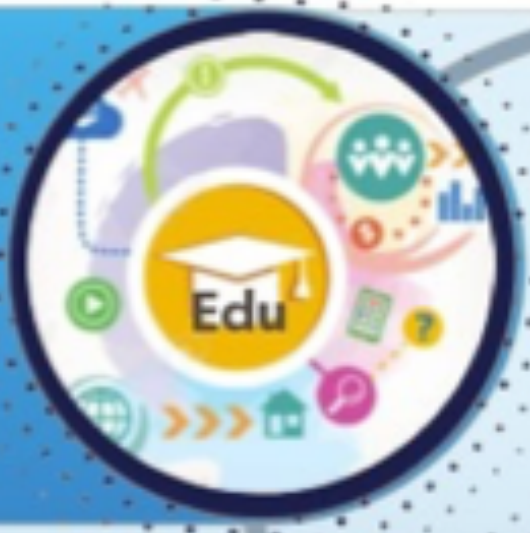

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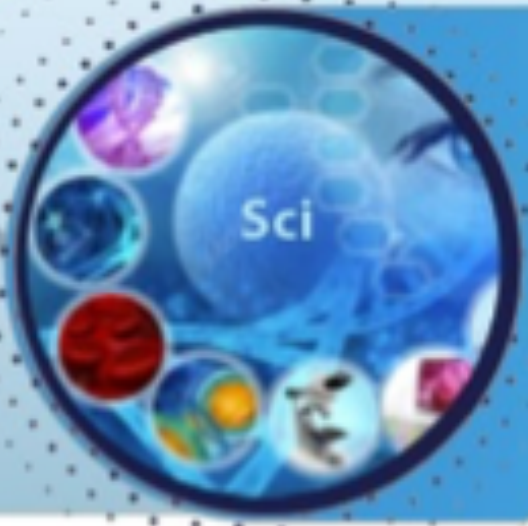

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Interhemispheric Asymmetry of the Brain in Parkinson's Disease

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ABSTRACT

Background. We found that in half of the cases, patients with Parkinson's disease are characterized mainly by the right individual profile of functional interhemispheric asymmetry, and in a third of patients there is a right asymmetry profile, mixed and left asymmetry profiles are much less common. We were able to show that the individual profile of functional interhemispheric asymmetry predetermines the clinical lateralization of motor manifestations in Parkinson's disease. At the same time, we also found that the combination of a certain individual functional profile of interhemispheric asymmetry with the clinical asymmetry of the disease determines the rate of progression of Parkinson's disease. The individual profile of functional interhemispheric asymmetry, the onset side of the disease, and the type of life experience do not affect anxiety-depressive disorders in patients with Parkinson's disease. Indicators of quality of life in patients with Parkinson's disease depend on the variant combination of an individual profile of functional interhemispheric asymmetry and clinical lateralization of the disease.

Conclusion. The relationship between the combination of the debut side of the disease and a certain individual profile with the localization of the generator of pathological activity according to the data of a computer electroencephalographic study in patients with Parkinson's disease has been established.

Keywords: Parkinson's disease, individual profile, diagnosis, and prognosis

INTRODUCTION

Parkinson's disease is one of the most common neurodegenerative diseases, the frequency of occurrence of which, according to different authors, ranges from 65.7 to 187 cases per 100 thousand people. Parkinson's disease is a chronic steady progressive disease leading to the gradual invalidation of patients [1, 2].

In recent years, much attention has been paid to motor asymmetry in Parkinson's disease and the one-sided debut of the disease. The asymmetry of symptoms in Parkinson's disease is so noticeable. That is a clinical sign of differential diagnosis of the disease from other neurodegenerative syndromes of parkinsonism. Despite the general recognition of asymmetry in the clinic of Parkinson's disease, there is little data explaining this feature [3, 4].

At the same time, the problem of functional interhemispheric asymmetry is one of the most relevant and complex in modern brain science [5, 6].

The question of the biological significance of the phenomenon of interhemispheric asymmetry in the functioning of the human brain and the provision of holistic

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neuropsychic activity in normal and pathological disorders remains important [7,8].

The results of previous studies on the relationship between functional interhemispheric (motor) and clinical asymmetries in patients with Parkinson's disease are quite contradictory. There is also a lot of data on the effect of clinical and interhemispheric asymmetries on the rate of progression of Parkinson's disease. All studies have not previously established the frequency of occurrence of different individual profiles of functional asymmetry in patients with Parkinson's disease and their relationship with the debut and rate of progression of the disease. Nevertheless, modern knowledge of this problem allows us to talk about the important role of interhemispheric asymmetry in the pathogenesis, symptom formation and course of Parkinson's disease [9,10].

In connection with the above, the purpose of our study was to establish an individual profile of functional interhemispheric asymmetry in patients with Parkinson's disease, to determine its relationship with the clinic of asymmetry and the effect on the neuropsychological, and neurophysiological characteristics of patients and the rate of progression of the disease.

MATERIAL AND METHODS

The results of a survey of 70 people with Parkinson's disease are presented. Among them, there were 28 men and 42 women. The median age of the patients was 65.3±9.2 years.

The duration of the disease was an average of 48 months. The control group included 15 people, among them 10 women (66.7%) and 5 men (33.3%), and the average age was 58.7±8.1 years.

The criteria for the inclusion of patients in the study: the presence of Parkinson's disease, stages of the disease from 1.5 to 3 according to Hen and Yar, MMSE from 27 to 30 points, a test of drawing hours more than 8 points, a signed form of informed consent to participation in the study.

Criteria for excluding patients from the study:

1) Availability of MRI data for acute cerebral circulation disorders, tumors, secondary parkinsonism, parkinsonism-plus and other neurodegenerative diseases.

2) Atherosclerotic lesion of the vessels of the head and neck by ultrasound transcranial Dopplerography, stenosis of more than 30%.

3) Moderate to severe cognitive impairment: less than 27 points on the MMSE scale, the test of drawing hours less than 9 points.

4) The presence of pronounced pathology on the part of the organs of hearing and vision.

5) Acute traumatic lesions of the nervous system, craniocerebral, cervical injuries and demyelinating diseases.

6) Diseases of the musculoskeletal system (rheumatoid arthritis, deforming osteoarthritis and others).

7) Mental illness, including severe and/or suicidal thoughts in the anamnesis, drug addiction, and alcoholism.

8) Serious concomitant somatic pathology: a) diseases of the cardiovascular system (coronary heart disease, arterial hypertension, congestive heart failure); b) acute inflammatory diseases of internal organs (hepatitis, acute cholecystitis, acute and chronic pyelonephritis); (c) Diabetes mellitus and other acute and chronic diseases that could potentially affect the patient during the study period; 9) any condition that may interfere with magnetic resonance imaging, including excess body weight, technically preventing the study; 10) family history of extrapyramidal pathology, that is, the presence of Parkinson's disease, Parkinson's syndrome in relatives - plus other diseases of the extrapyramidal system, including essential tremor.

At the time of the examination, 53 (75.7%) patients received levodopa drug therapy, and 17 (24.3%) patients took various non-Levodopa groups of drugs and their combinations under the supervision of a doctor in the Parkinson's care room.

Diagnosis of Parkinson's disease was carried out based on clinical and diagnostic criteria of the Brain Bank of the Parkinson's Disease Society of Great Britain. Clinical and neurological examination was carried out using the Hoehn & Yahr scale in the modification of O. Lindvall, the Schwab & England ADL scale of daily activity, and the UPDRS scale.

Standard criteria were used to assess the rate of progression of Parkinson's disease, which is nonlinear; To determine them, the collection of data more accurately on the history of the disease, the Hen and Yaru scales, UPDRS during the "off" period were used initially and two years after the initial examination. Thus, a rapid rate of progression (change of stages for 2 years or less, according to UPDRS more than 30 points in 2 years) occurred in 25 people with Parkinson's disease (35.7%), moderate (change of stages within 3-5 years, according to UPDRS from 29-12 points for 2 years) - in 37 (52.9%) patients, slow (change of stages for more than 5 years, according to UPDRS up to 12 points in 2 years) - in 8 (11.4%) patients.

The neuropsychological study was conducted using the Mental Status Brief Scale (MMSE), the "clock drawing" test, the Spielberger scale to assess situational and personal anxiety and the Hamilton Depression Scale. The Levin Scale was used to identify autonomic disorders.

To assess social adaptation in 70 patients surveyed, the European Quality of Life Questionnaire (EuroQol), the Schwab and England scale, the Quality of Life Questionnaire of Patients with Parkinson's Disease (PDQ - 39) were used.

The individual profile of functional interhemispheric asymmetry was determined in all patients, according to a special protocol with the calculation of the coefficients of the right hand, right leg, right eye and right ear. According to the value of these coefficients, the asymmetry of the hands, feet, eyes and ears was revealed, and subsequently, the profile of each subject was determined. The individual profile of functional interhemispheric asymmetry was evaluated in dynamics in 70 patients with Parkinson's disease during the "inclusion" period, the values of the coefficients were calculated at the initial examination of patients with Parkinson's disease and repeated after 2 years.

The type of life experience was identified using a questionnaire including data on education, profession, place of work, sports, drawing, music, literature, and other activities related to creativity or not. If from childhood a person developed harmoniously and was engaged in singing, dancing, sports, drawing and other activities that require reliance on the image and imagination, then such a life experience is called right-brained. With the unilateral development of the individual or insufficient development of the functions of both hemispheres both in childhood and in later life, then such an experience is called left-hemisphere.

RESULTS

In all the patients examined, the onset of the disease was unilateral and manifested by awkwardness or trembling in the arm or leg. In 35 people (50%) there was an initial involvement of the right limbs, in 35 (50%) - the left, and during the disease, the symptoms were more pronounced on the side of the debut. There were significant differences between the age of onset, the duration of the disease, the distribution of the rate of progression, the forms, and stages of Parkinson's disease, the severity of Parkinsonian symptoms, average values of quality-of-life indicators in patients with right-sided and left-sided debut were not noted ($p>0.05$).

When analyzing the average values of the coefficients, reliable results were obtained that, regardless of the individual profile of the functional interhemispheric asymmetry in all groups, the right-hand coefficient prevailed in terms of value, then the right-foot coefficient was in the order of decreasing value, the right ear coefficient was next, and the right eye coefficient was the minimum in value. ($p<0.05$). From the data obtained, it follows that in patients with Parkinson's disease, as left-sided asymmetries accumulate, there is a decrease in both motor (coefficients of the right hand and right leg) and sensory (coefficient of the right eye and ear) functions, but to varying degrees. the coefficient of the right ear and the coefficient of the right eye, and the coefficient of the right eye - to a greater extent. The results obtained are consistent with several studies in which the leading role of the left hemisphere in the organization of the motor act was confirmed. Moreover, it is noted that most often in healthy people there is a left-hander hearing and vision, less often the legs, and finally, the least likely to be left-handed. According to the study, which determined the coefficients in patients with rheumatic diseases with cerebrovascular pathology of varying severity, the most common was mainly the right individual profile of functional interhemispheric asymmetry with the leading left ear or the leading left eye, the next was a mixed individual profile of functional interhemispheric asymmetry with a combination of the left eye and ear, less often their combination with the left leg was observed, and the profile of asymmetry with the left hand was not revealed.

Of the 70 patients with Parkinson's disease examined, 24 (34.3%) people had a right individual profile of functional interhemispheric asymmetry, 33 (47.1%) patients had a predominantly right individual profile of functional interhemispheric asymmetry, and 11 (15.7%) patients had a mixed individual profile of functional interhemispheric asymmetry, in 1 (1.4%) patient, the left was determined mainly and in another 1 (1.4%) patient - the left individual profile of functional interhemispheric asymmetry. In the control group, the right individual profile of functional interhemispheric asymmetry was determined in 4 (26.7%) people, mainly right - in 9 (60%) and mixed - in 2 (13.3%) of the examined. Thus, there are significant differences in the occurrence of right and mixed no individual profile of functional interhemispheric asymmetry was observed ($p>0.05$), but no individual profile of functional interhemispheric asymmetry was detected in any person in the control group. According to the literature, the right (38%) and predominantly right (43%) asymmetry profiles also prevailed in healthy subjects,

but mixed asymmetry profiles also occurred with a lower frequency. individual profile of functional interhemispheric asymmetry (13%) compared with Parkinson's patients we examined, and no left individual profile of functional interhemispheric asymmetry was detected. The results are consistent with studies indicating a greater frequency of occurrence of left-handed people among patients with mental and neurological diseases compared with healthy persons and do not contradict the data of known information, where it is noted that full left-handed is very rare, but absolute right-handed people are found only in 40% of the sample.

A significant difference in the age of onset, duration of Parkinson's disease, distribution of stages, forms, and rate of occupationalization of the disease in patients depending on the individual profile of functional interhemispheric asymmetry was not revealed ($p>0.05$).

When comparing the clinical and functional interhemispheric asymmetries, it was found that in patients with a right individual profile of functional interhemispheric asymmetry, the right-sided debut was significantly more common compared to the left-sided ($p<0.05$), in patients with a mixed individual profile of functional interhemispheric asymmetry, left-sided debut ($p<0.05$) was significantly more common. By the individual profile of functional interhemispheric asymmetry, the number of patients with right-sided and left-sided debuts of Parkinson's disease was comparable ($p>0.05$).

For patients with predominantly left and left individual profiles of functional interhemispheric asymmetry was the nature of left-sided clinical asymmetries. The findings are consistent with several previous studies. One of them revealed the tendency of the onset of clinical manifestations of Parkinson's disease from the dominant side in both right-handed and left-handed people. In another, it was found that the dominance of the hand is associated with the asymmetry of the clinic of the disease in such a way that left-handers tend to have more severe manifestations on the left side of the body. So, the motor symptoms of the disease significantly more often began and prevailed on the contralateral dominant hemisphere side.

When analyzing a group of patients with a right individual profile of functional interhemispheric asymmetry, it was determined that with the right-sided debut of Parkinson's disease, a rapid rate of progression of the disease prevailed in 9 (56.3%) patients, in contrast to patients with a right individual profile of interhemispheric asymmetry and left-sided debut, among which medium and slow rates prevailed, and a fast pace was not detected in any person. It was previously established that in right-handers with greater involvement in the pathological process of the left hemisphere (debut by right-sided movement disorders), generalization of Parkinson's disease occurs more often, and movement disorders are more severe.

There were no significant differences between the occurrence of stages and forms depending on the side of the debut of Parkinson's disease ($p>0.05$). The age of onset of the disease was comparable, and the duration of the disease with a left-sided debut was significantly higher than with a right-sided debut ($p<0.05$). The results obtained indicate a slower rate of progression of Parkinson's disease in patients with a right individual profile of functional interhemispheric asymmetry and a left-hand debut.

In several studies of right-handed people with Parkinson's disease using the motor potential method, it was found that in patients with a predominantly left-sided motor defect in the study of all components of motor potential, the predominant lesion of the dominant hemisphere of the disease progresses faster than in the case of damage to the subdominant hemisphere.

As a result of a study of patients with a predominantly right individual profile of functional interhemispheric asymmetry (33), it was found that with a right-sided debut (16), a rapid rate of progression was observed in 37.5% (6) of cases, and there was no slow pace in contrast to patients with left-sided onset (17), among which in 11.7% (2) cases a slow pace was determined, and in 23.6% (4) cases - a rapid rate of progression of the disease. The results obtained indicate the predominance of a more rapid course of the disease with a predominant lesion of the left hemisphere in patients with a predominantly right individual profile of functional interhemispheric asymmetry.

In the group of patients with a mixed individual profile of functional interhemispheric asymmetry, a significant difference in the age of onset of the disease depending on the side of the debut was not obtained ($p>0.05$), and the duration of the disease was significantly higher with a right-sided debut compared with a left-sided debut ($p<0.05$). Moreover, 5 (62.5%) patients with left-sided lateralization of symptoms noted a rapid rate of progression of Parkinson's disease and not was detected in any patient with a right-sided debut of the disease.

Thus, a slower progression was found in patients with a mixed individual profile of functional interhemispheric asymmetry in right-sided debut compared to left-sided. In patients with Parkinson's disease with a predominant-

ly left (1) and left (1) individual profile of functional interhemispheric asymmetry, medium and rapid rates of progression were observed, respectively.

When assessing the individual profile of functional interhemispheric asymmetry in the dynamics of 7 patients with Parkinson's disease, there were no significant differences between the values of the right hand, right leg, right eye and right ear obtained during the initial and repeated examination ($p>0.05$). Nevertheless, there was an appearance and increase in the smoothness of the individual profile of functional interhemispheric asymmetry due to a decrease in the values of the right leg and right hand.

This mainly concerned patients with a right and predominantly correct individual profile of functional interhemispheric asymmetry in combination with the right-sided debut of the disease, that is, in cases of predominant lesions of the dominant hemisphere with high lateralization of interhemispheric asymmetry and, accordingly, the predominant symptoms of Parkinson's disease on the side with the leading arm and leg. In contrast, an increase in the values of the coefficients of the right hand and right leg was noted in a patient with a left individual profile of functional interhemispheric asymmetry and a left-sided debut of Parkinson's disease. The findings are consistent with the evidence that motor asymmetry is unstable and may change during the adaptation period. At the same time, sensory asymmetry is a clearer and more permanent characteristic of the activity of central systems, which is preserved and fixed throughout life.

In 70 patients with Parkinson's disease, there was no reliable correlation between the individual profile of functional interhemispheric asymmetry and the stage of Parkinson's disease ($p>0.05$). Even though according to many works on lateralization, the side is most likely genetically based, studies in this area have not yielded a definite result, which suggests the influence of other factors on the choice of the dominant party.

The lack of a clear relationship between the severity of Parkinson's disease according to Hen and Yar and the individual profile of functional interhemispheric asymmetry is probably due to the presence of a prolonged (10-15 years) premotor stage of the disease, in which nigrostriatal structures are involved in the multifocal neurodegenerative processes, and there is already a change in functional interhemispheric asymmetry.

When determining the type of life experience among 70 patients with Parkinson's disease, 41 (58.6%) patients had a right-hemisphere type of life experience, and 29 (41.4%) had a left-hemisphere type of life experience. There are no significant differences in the predominance of the type of life experience in different individual profiles of functional interhemispheric asymmetry depending on the clinical asymmetry of Parkinson's disease ($p>0.05$). Reliable correlations of the type of life experience with the rate of progression of Parkinson's disease, the level of reactive and personal anxiety, the severity of depression, clinical manifestations and UPDRS-III, indicators of PDQ scales -39, EuroQol not detected ($p>0.05$).

When assessing reactive anxiety in 18 (26%) patients, a low level of anxiety was determined, in 45 (64%) patients' moderate anxiety was observed and in 7 (10%) - high reactive anxiety. The average score of the level of anxiety corresponded to the data of previous studies. There was no significant difference between the general indicators of reactive anxiety in different individual profiles of functional interhemispheric asymmetry ($p>0.05$). In the group of patients with a right individual profile of functional interhemispheric asymmetry, the level of reactive anxiety was significantly higher with a left-sided debut compared with a right-sided ($p<0.05$). It is known that the state of negative emotional stress is manifested by the activation of the parietal-temporal region of the right hemisphere. In the same area, the number of neurocytes is higher than in the contralateral part of the brain.

When determining personality anxiety in 1 (1%) of the patient, a low degree was detected, in 17 (25%) patients – a moderate degree and in 52 (74%) - high personal anxiety. Since the level of personality anxiety correlated with the severity of movement disorders according to UPDRS-III ($p<0.05$), the prevailing in our study of patients with a later stage of Parkinson's disease explains the higher percentage of severe degree of anxiety compared to previous work. There was no significant difference in the level of personality anxiety in different individual profiles of functional interhemispheric asymmetry in depending on the side of the debut of the disease ($p<0.05$).

In the study of depressive disorders in 28 (40%) patients, mild depression was determined, in 15 (21%) - moderate severity and 3 (4%) - severe degree. Similar results in the analysis of emotionally effective disorders in patients with Parkinson's disease were obtained in previous works. Significant differences in the level of depression depending on the side of the debut of Parkinson's disease in patients with different individual profiles of functional interhemispheric asymmetry were not found ($p<0.05$).

The average assessment of autonomic disorders in 70 patients with Parkinson's disease was 7.4±3.1 points. Autonomic disorders were most often represented by dysfunction of the gastrointestinal tract (68%) and genitourinary system (39%), dysfunction of the cardiovascular system was noted in 6% of patients at stage 3 of the disease. There were no significant differences in the level of autonomic disorders in patients depending on the side of the debut of Parkinson's disease with different individual profiles. functional interhemispheric asymmetry ($p>0.05$).

As a result of the study of the influence of clinical asymmetry of the disease in combination with various individual profiles of functional interhemispheric asymmetry on the quality of life of patients with Parkinson's disease, it was found that the overall health status indices were significantly higher in patients with a right and mainly right individual profile of functional interhemispheric asymmetry with a right-sided debut compared with a left-sided debut ($p<0.05$).

Thus, with the predominant involvement of the dominant hemisphere in the process, the worst indicators of the quality of life were observed.

DISCUSSION

Quality of life indicators was significantly higher in patients with a right individual profile with a left-sided debut compared with a right-sided debut ($p<0.05$) and in patients with a mixed profile with a right-sided debut compared with a left-sided debut, that is, with a predominant lesion of the subdominant hemisphere. This is probably because patients with Parkinson's disease find it more difficult to adapt to the symptoms of the disease when they predominate on the side of the leading limbs [9] .

In all 32 patients examined by the electroencephalographic method, changes in bioelectrical activity were detected. At the same time, in 27 (84.3%) patients with Parkinson's disease, slow-wave activity was observed significantly more often than in the control group in the form of generalized bilaterally synchronous flashes ($p<0.0001$). Our results on the increase in power in the slow-wave part of the spectrum and in the range of slow-motion alpha rhythm coincide with the results of a study to study the functional state of the brain in patients with early stages of Parkinson's disease. It is necessary. Note that 21 (77.8%) patients had a clear sidelinerization of pathological slow-wave activity with no activation response, which was not observed in any person in the control group. This group of patients was studied using the method of three-dimensional localization, while significant repeated fragments of electroencephalography were taken, which do not change with functional tests. In all patients (21), the generator of pathological activity was recorded predominantly in the thalamostrionigral structures [15].

CONCLUSION

Thus, it was found that in half of the cases of patients with Parkinson's disease, there is a right individual profile of functional interhemispheric asymmetry (47.2%), in a third of patients - mainly the right asymmetry profile (34%) and much less often - mixed (15.7%) and left asymmetry profiles (1.4%). The right-sided debut of Parkinson's disease is characteristic of persons with a right individual profile of functional interhemispheric asymmetry, and the left-sided debut is characteristic of persons with mixed and left profiles. The rapid rate of progression of Parkinson's disease is more often observed with a combination of the right profile of functional interhemispheric asymmetry and the right-sided debut of the disease. Parkinson's disease in patients with a right asymmetry profile and a left-sided debut, as well as in patients with a mixed asymmetry profile and a right-sided debut is prone to slow progression.

It was revealed that the individual profile of functional interhemispheric asymmetry in dynamics changes due to motor function (right leg and right hand) in cases of damage to the dominant hemisphere with high lateralization of interhemispheric asymmetry and, accordingly, the predominance of symptoms of Parkinson's disease on the side with the leading arm and leg. Quality of life indicators is lower in patients with Parkinson's disease with a predominant lesion of the dominant hemisphere. The worst indicators of quality of life are observed in patients with right and mainly right individual profiles of functional interhemispheric asymmetry and right-sided clinical lateralization.

Ethics approval and consent to participate - All patients gave written informed consent to participate in the study.

Consent for publication - The study is valid, and recognition by the organization is not required. The author agrees to open the publication

Availability of data and material - Available

Competing interests - No

Financing – Self

Competing interests - No

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