CLINICAL AND NEUROPHYSIOLOGICAL CHARACTERISTICS OF POST-INSULAR COGNITIVE DISORDERS AND ISSUES OF THERAPY OPTIMIZATION

Yokutxon Madjidova
*Tashkent Pediatrics Medical Institute, 100125, Uzbekistan, Tashkent, Bogishamol 223,*, ndm2@mail.ru

Dilbar Xodjieva
*Bukhara State Medical Institute named after Abu Ali Ibn Sina 200101, Uzbekistan, Bukhara, Navoi Avenue 1*

D.K. Xaydarova
*Bukhara State Medical Institute named after Abu Ali Ibn Sina 200101, Uzbekistan, Bukhara, Navoi Avenue 1*

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Cover Page Footnote
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This article proposes the treatment of an acute period of ischemic stroke with Cellex, which improves speech, praxis and gnosia, which is confirmed by the results of neurophysiological studies. Thus, with mild dementia, disturbances in predominantly attention and regulatory functions were associated with clear impairments of memory, orientation, and visual-spatial function. Neuroimaging in most patients, along with focal post-stroke changes, revealed brain tissue atrophy, changes in white matter, and small focal lesions of the gray matter. It was established that a necessary condition for the verification of the syndrome of post-stroke cognitive impairment (CI), in addition to the volume and localization of the lesion, should be signs of impaired integrative mental activity of the brain, especially disruption of regulatory functions.

Key words: ischemic stroke; predictors; Cellex; Magnetic resonance imaging

Relevance

According to a meta-analysis, the development of dementia after a stroke is observed in 1 out of 10 patients, but among patients who have had a second stroke, every third is at risk of its development [1]. Moreover, it is believed that in 1 out of 10 patients, dementia preceded a stroke. According to various estimates, the frequency of dementia after a stroke is in the range from 7 to 42% and increases linearly from 1.7% (in population studies) to 3% (in hospital-based studies involving patients with recurrent stroke and dementia). A number of studies have shown that within 3 months after a stroke, at least 25% of patients suffer from cognitive impairment. A recent study also found that up to 83% of stroke patients 3 months ago show deterioration in at least one domain of cognitive functions, and in half, the deterioration affects at least 3 domains [2,3].

It is believed that in 75% of cases with post-stroke dementia, vascular dementia is detected, while in the remaining 25% of cases is Alzheimer's type dementia, dementia with Levy's corpuscle, etc. In relation to the vascular component, damage to small-caliber vessels is predominant. Nevertheless, the presence of small cortical infarction also plays a role in the pathogenesis of post-stroke dementia. A certain role in the etiopathogenetic mechanisms of the occurrence of post-stroke dementia is played by inflammation, leading to the death of neurons, as well as the activation of microglia and the accumulation of amyloid. Perhaps stroke becomes a trigger factor for pathophysiological processes that can trigger secondary neurodegeneration against the background of changes characteristic of the initial stages of Alzheimer's disease [4]. Currently, there are not many publications on improving diagnostic criteria and choosing the tactics of pathogenetic therapy for post-stroke cognitive disorders, therefore, we consider it relevant to conduct a study.

The objective aim: to conduct a comparative clinical and neurophysiological characteristic of post-stroke cognitive disorders and choose the optimal tactics of pathogenetic therapy.

Materials and methods

To achieve this goal, we examined 56 patients with a diagnosis of Acute Ischemic Stroke. The age of patients at the time of the examination ranged from 35 to 85 years (55.4 ± 10.2 years), among them 37 men (66%) and 19 women (34%). Clinical examination included an assessment of neurological deficit on the NIHSS scale and ranged from 0 to 16 points. Assessment of
cognitive status was carried out using a brief scale for assessing mental status (MMSE), a frontal test battery (FAB), a clock drawing test, a semantic speech activity test (CPA), and a 5-word memory test. Neurophysiological research methods included an MRI scan, which was performed on a Siemens device with a capacity of 1 Tesla. All patients underwent neurophysiological and clinical research methods. The main group included 29 patients who in the acute period were prescribed cellex at a dose of 0.1 mg (1 ml) subcutaneously for 10 days. The comparison group included 27 patients who underwent basic standard therapy. All patients were informed about the objectives of the upcoming study and gave written consent to participate in it.

Statistical processing was performed using the Statistica 8.0 application software package. Comparative analysis was performed using the Mann-Whitney test.

The results of the study
At the time of the examination, an assessment of the degree of neurological impairment according to the NISS stroke scale revealed that 16 patients (28.57%) had an atherothrombotic stroke, lacunar stroke was observed in 12 patients (21.43%), cardioembolic stroke was observed in 20 patients (35.71%), 8 (14.29%) - the cause of the stroke has not been established.

Patient age and cognitive impairment

![Fig. 1. Age of patients with various types of cognitive impairment.](image)

Patients with isolated mnestic deficiency were slightly younger than patients with neurodynamically-regulatory CN and were age-appropriate for patients with isolated decreased attention or R.F. Further, the trend was restored, i.e., patients with mixed neurodynamically-mnestic or regulatory-mnestic KN were older, and the greatest age was observed in the subjects with combined PIKN. Patients treated with neurotrophic therapy had a higher global cognitive status, as well as better neurodynamic, regulatory, and visual-spatial functions compared to control.

When analyzing the state of individual cognitive spheres, it was shown that 87% of patients in the acute period of AI have multifunctional KN. Most patients showed involvement of attention, RF, speech and memory. More than 1/3 of patients had multifunctional non-anamnestic K.N. Monofunctional non-anamnestic CNs occurred in 2–5.5%. Isolated mnestic deficiency was observed in 2% of patients. The frequency of multifunctional CNs revealed by us approximately corresponds to that in the early recovery period of AI according to S.J. Cho et al.
[6], although the frequency of single domain forms in our group was lower. While analyzing the ratio of fronto-subcortical and hippocampal types of CN, it was shown that the largest share in the structure of PICN was made up of neurodynamic and regulatory disorders. A predominant decrease in memory was observed in every 10 patients, and a combined deficit was observed in 1/3 of patients, which corresponds to data on the incidence of PICN in the first weeks of the disease (13-50%) [8]. The neuropsychological heterogeneity of PICN revealed in the study, which was also shown in our previous works [9, 10], may indicate different pathogenetic and structural basis of the described options, which is confirmed by the results of the study by W. Liu et al. [eleven]. The authors found that patients after a stroke or transient ischemic attack with Alzheimer’s type of beta-amyloid deposition according to positron emission tomography (mixed vascular CN with a decrease in memory, ZPF and RF), there was a faster and more pronounced decrease in cognitive functions during 3 years of follow-up compared with patients with a “clean” PICN variant [10]. The neuropsychological structure of CN depended on the age of the patients. So, in most elderly patients, CN was detected with a predominance of a mixed variant. In a group of young and middle-aged patients with CN, three out of four patients were dominated by an isolated decrease in the rate or regulation of cognitive activity. Combined K.N. diagnosed in every 4th patient. A general tendency towards an increase in the age of patients with the acquisition of CN of a mixed nature was revealed.

This phenomenon is associated with various pathological processes, such as amyloidosis and neurodegeneration, which are age-associated and underlie clinical manifestations. So, recently it was shown that in patients with an early onset of subcortical CN, there is a more pronounced lesion of the frontal neuronal network and regulatory dysfunction, while in patients with CN debut after 65 years, a greater amyloid deposition was revealed, as well as cortical and hippocampal atrophy [9]. In the context of the results of our study, it is also interesting that in Alzheimer's disease there are age-related differences in cerebral pathology. Thus, it was found that the rate of development of amyloidosis in the absence of background neurodegeneration is greatest at the age of 60–75 years, while neurodegeneration without previous amyloidosis is most active after 70 years [7]. When analyzing the effectiveness of the drug cellex in the acute period of AI, it was noted that its administration is associated with a higher global cognitive status, as well as the state of neurodynamic, regulatory, and visual-spatial functions, i.e., has the greatest influence on the vascular component of post-insulin cognitive impairment (PICN), which is consistent with the results of previous studies [5].

Fig. 2. MRI image of a 55-year-old patient with a diagnosis of “acute period of ischemic stroke”
If before the study, the severity of diffuse lesions of white matter was high, which is an important predictor of the development of PICN. It is known, one of the predictors of post-stroke cognitive impairment is changes in white matter in the form of foci of hyperintensity in T2 or FLAIR modes. If before the study in the main and control groups, almost all patients had cerebral atrophy, then after treatment with cellex in the main group, 87% of patients after 10 days showed a decrease in the area of atrophy both in the temporal lobe and in the hippocampus. These neurophysiological studies are confirmed by clinical data. So, in the group of patients taking cellex, there is an improvement in memory, speech, and speed of thinking in elderly patients. Two-year observation of patients showed that in patients of the control group, atrophy of the medial sections of the temporal lobes of the brain increases, which can be characterized as the development of a stroke.
According to a two-year observation, in patients of the control group there is a more extensive vascular pathology of the brain, low compliance. Moreover, this is expressed in the deterioration of self-service, household activity. Also, speech, praxis, gnosis become unsatisfactory.

**Conclusions:** According to the results of a two-year observation of patients in the main and control groups, significant differences were expressed. So in the main group, the improvement of clinical and psychological methods is also proved by neurophysiological methods (MRI) in the form of reducing atrophy in the hippocampus and temporal lobe of the brain.

**Practical recommendations.** According to the results of our studies, it is recommended to include the drug Cellex in the treatment of the acute period of ischemic stroke to reduce the prevalence of atrophy and restore cognitive functions.

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