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MODERN CONCEPTIONS OF COGNITIVE DISORDERS IN CLINICAL DEPRESSION AND THE PARTICULARITIES OF DIAGNOSING THOSE DISORDERS

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Cognitive disorders are very often identified under unipolar depressive condition. Moreover, they tend to remain in place under remission. Despite the large number of attempts to characterize the cellular and pan-cerebral mechanisms underlying the formation of cognitive functions, as well as to identify the causes of cognitive disorders in clinical depression, the problem of those disorders is still far from being solved. This article presents a critical assessment of the existing ideas about cognitive disorders, highlights the difficulties researchers face, and discusses further possibilities of improving the cognitive functioning of patients suffering from depression.

Keywords: unipolar depression, cognitive disorders, antidepressants.

Statement of the problem. Currently, a point of view is gaining ever more currency that patients, suffering from unipolar depression, show various kinds of cognitive disorders, down to cognitive deficit [1].

Review of the recent investigations and printed media publications. The steady growth of interest in cognitive dysfunctions under unipolar depression, judging by an increasing number of publications, is due to several factors, among which the following can be noted: a growth, registered by epidemiological studies [2], in the incidence of depression within the population occurring primarily as a result of increasing proportion of non-psychotic forms [3]; the involvement of persistent cognitive disorders in socially maladaptive behaviour models and in difficulties of everyday activities for depressed patients [4], as well as in the worst response to antidepressant therapy, regardless of the severity of depressive symptoms [5]; a «renaissance» of information theory in psychiatry [6] attributable to the latest discoveries in systems biology [7], neurobiology [8] and neuropsychology [9], and purporting to link together the structural and functional changes under the affective pathology; finally, the prospects of new approaches to the treatment of depressive conditions by means of correcting cognitive disorders [10].

Separation of the earlier unresolved sections of the common problem. Accordingly, many attempts have been made to characterize the cellular and pan-cerebral mechanisms underlying the formation of cognitive functions, to determine the nature, as well as to identify the causes of cognitive disorders under depressive conditions, and to develop methods for their correction. Despite some progress in this area, the consensus on the theoretical and practical aspects of identifying and eliminating cognitive dysfunctions under depression has not yet been reached.

Statement of objective of the present article. Debatable remain issues regarding the validity or arbitrariness of the division of mental functions and disorders into emotional and cognitive ones, regarding the commonality or separateness of their neurobiological substrates, regarding the diffuseness or

partiality, regarding the specificity or non-specificity, as well as regarding the primary or secondary nature of cognitive disorders under depressive conditions. The main objective of this article is to critically evaluate the existing conceptions of cognitive disorders, as well as to discuss further possibilities of improving cognitive functioning of patients suffering from depressive conditions.

Description of the main material. Historically, mental processes are usually classified into one of three broad categories: cognitive (the way we understand the world); affective, or emotional (the way we perceive it); conative (the way we manage our behaviour). Thus, the cognitive processes can alter the course of the processing of emotions, while the changes of mood, in turn, can affect the cognitive functions [11]. Currently, the classification of the mental processes is rather of pedagogical value that in itself diminishes as the neuroscience, which is dominated by integrative approaches to the study of the psyche, develops [12].

Existing data on the organization of the brain show signs of both structural and functional specialization of individual areas (e. g. the cytoarchitectonic Brodmann areas) and the integrity of the brain as a dissipative self-organizing system. On the one hand, there are brain structures that are more associated with either affective (e. g. the amygdala) or cognitive (e. g. the hippocampus) processes. On the other hand, the higher mental functions are always the result of the integrative work of the entire brain. That work involves self-regulation and self-organization of serial and parallel interactions between the specialized modules [13].

Taking into account the fact that the problems of the neurobiological substantiation of the higher mental functions are far from the final solution, we can still say that the potential biological targets to impact the cognitive processes in patients with depression do exist.

The cognitive dysfunctions under depressive conditions have begun to be spoken about quite recently after the widespread introduction into the research practice of psychometric tests to assess memory, attention and speed of psychomotor response in patients with mental disorders. As for

the attention, its changes in a depressive episode were shown in many studies [14].

Cognitive disorders are very often reported under depressive conditions related to execution functions [15]. The deficit was revealed during the performance of tests on the inhibition of irrelevant stimuli [16], problem-solving and planning [17], mental flexibility [18], speech fluency and decision-making [19]. All in all, disorders of mental flexibility, among other cognitive dysfunctions, came to be the most common in patients with depressive conditions [20].

It is still unclear whether the cognitive deficit is a factor affecting all the key manifestations of depression, or whether it represents a separate case of dementia characterized by independent pathogenesis, prognosis and impact on the functional status of the patient. Several longitudinal studies have shown that there are patients with depressive conditions characterized by cognitive disorders, which manifest themselves in the domains of attention, verbal learning, memory and execution functions, and which persist after the ending of the affective phase [21].

Thus, evidence of a relationship between the cognitive and the emotional disorders under depressive conditions confirms, on the one hand, the dependence of the intensity of the cognitive dysfunction on the severity, the number of episodes and the duration of depressive conditions [22], and, on the other, reveals during the interictal period quite clear cognitive aberrations that were earlier considered typical for depressive episodes only [23].

In addition to unresolved scientific, theoretical and fundamental issues, a number of methodological problems significantly interfere with the systemic analysis of the emotional and cognitive relationship under depressive conditions.

The first set of problems concerns the object of the research, i.e. cognitive disorders. Despite the absence of any discrepancy between psychiatrists, psychologists, psycho-physiologists and other specialists interested in the correct understanding of the term «cognitive functions», the multi-dimensional and multi-component nature of this concept, which includes most of the totality of mental processes (perception, image recognition, attention, memory, imagination, speech, thinking, intellectual development, decision-making), implies an a priori impossibility of its simultaneous holistic study [24]. A single criterion that characterizes cognitive functioning as a whole remains uncertain. Many procedures and tests designed to assess individual elements of cognitive functioning sometimes make it difficult to compare the results of different studies. In this regard, integrative parameters of the cognitive sphere that fulfil an organizing (regulatory) role with respect to the behaviour and that are involved in the implementation of steps of a targeted behavioural act are of the greatest interest to the research.

The next set of problems involves research subjects, which are represented by the patients. Many factors other than mental disorder and its treatment affect cognitive functions of patients with depression. Those factors include age, educational level, hormonal status, comorbidity (physical and mental), and so on.

At the population level, the cognitive abilities of a human being are characterized by considerable variability, but at the individual one they have certain age dynamics. According to the concept suggested by R. B. Cattell (1971) [25], the intelligence can be divided into «mobile» one, i.e. the ability to think logically, to analyze and to solve problems, regardless of the previous experience, and «crystallized» one, i.e. the accumulated experience and the ability to use the acquired knowledge and skills.

A comparison of the cognitive development dynamics with the dynamics of depressive conditions shows that both processes have interpenetrating impact. At the same time, there is evidence both in favour of the increased risk of late-life depression under the growing shortage of execution functions, and vice versa: depression is often mentioned among the significant, potentially adverse factors for the development of dementia [26].

If in addition to age a risk factor or a comorbid condition in the form of an organic mental or physical illness is brought into the relationship between the cognitive functions and depression, the differential analysis of the causality of the cognitive disorders in question becomes even more difficult.

So, even within the same middle-aged group, the cognitive profile of patients with non-psychotic depressive conditions (with relatively stable intellectual and mnemonic abilities) can vary significantly, which was corroborated by a cluster analysis of memory characteristics and those of attention, neuro-dynamic coordination, execution functions, and autonomic tone.

It is evident that the clinical effects of drugs are primarily predetermined by their pharmacological action pattern. In this connection, we can assume that the negative impact of the thymoanaleptics on the cognitive functions will depend on their anticholinergic, antihistaminergic and antiadrenergic effects [27], as the cholinergic system is involved in functioning of the memory formation mechanisms while the histaminergic and the adrenergic ones are engaged in maintaining wakefulness.

The research conducted has shown that the effect of antidepressants of different classes on cognitive functions in patients with non-psychotic depressive conditions depends both on the differences in the mechanisms of pharmacological activity and the characteristics of the initial cognitive state of the patients.

There are two ways to influence the cognitive functions in a targeted manner. Firstly, it is possible to correct the pathological processes that cause cognitive deficit. Secondly, it is possible to use pro-cognitive mechanisms independent of the etiology that caused the deficit.

Despite the conceptual attractiveness, approaches reasoned in a pathophysiological way have limitations of their own. This policy applies only to those categories of disorders or patient cohorts, for which the molecular substrates that condition the cognitive dysfunction development are apparent. In addition, it is unclear whether it is possible to influence the pathological cognitive processes that formed in the early stages of development, as the synaptic architecture and neuronal networks are laid down in childhood.

The existing strategies of the symptomatic therapy are apparently unable to correct profound disorders, but they can contribute to the activation of parallel compensatory pro-cognitive functions. Thus, there is no experimental evidence of the sixth-type serotonin receptors' or the third-type histamine ones' hyper-function under depressive conditions, but their antagonists demonstrate promising effects as regards the cognitive deficit correction, under depression included [28, 29]. The mechanisms that are not directly related to the progress of the illness are likely to have a wider range of applications. Finally, some of such drugs can not only improve cognitive function but can also affect other symptoms of the illness.

Another important issue is the specificity of the correction of cognitive functions, that is, how the drug affects different cognitive domains – all at the same time or individually. It is logical that the answer to that question is directly linked to the mechanism of action of each particular drug. The pathogenetic therapy is expected to radically improve if not all but many cognitive domains. Nowadays, certain ways of normalizing the activity of the individual cognitive domains are being developed that could be efficient for

various illnesses [30]. Although the appearance of psychopharmacological agents that improve all cognitive functions is unlikely, multimodal drugs that affect multiple mediator paths may have more optimum action pattern.

Conclusions of this study and future prospects.

Despite a series of theoretical and practical difficulties associated with the assessment of cognitive disorders under depressive conditions, studies that exist to date strongly suggest that cognitive symptoms are detected in a large number of patients with unipolar depression. The most characteristic of those are disorders of psychomotor ability, execution functions and short-term memory. The above symptoms are present already in the early stages of the illness and may even precede its onset. Some antidepressants, especially those with multimodal action, are capable of improving cognitive functions in patients with depressive conditions. Nevertheless, certain disorders are apparently quite persistent, and may stay in place even after the symptomatic remission is reached. As a result, cognitive symptoms substantially affect the functional recovery demanding the introduction of more sophisticated treatment methods aimed at overcoming the cognitive difficulties.

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СУЧАСНІ УЯВЛЕННЯ ПРО КОГНІТИВНІ РОЗЛАДИ ПРИ ДЕПРЕСИВНИХ СТАНАХ ТА ОСОБЛИВОСТІ ЇХ ДІАГНОСТИКИ

Анотація

Когнітивні розлади досить часто виявляються при уніполярному депресивному розладі. Більш того, вони мають тенденцію зберігатися в ремісії. Незважаючи на велику кількість спроб охарактеризувати клітинні і загально мозкові механізми, що лежать в основі формування когнітивних функцій, а також виявити причини когнітивних порушень при депресивних розладах, проблема когнітивних порушень все ще далека від свого рішення. У даній статті дається критична оцінка існуючих уявлень про когнітивних розлади, висвітлюються труднощі, що постають на шляху у дослідників, і обговорюються подальші можливості поліпшення когнітивного функціонування пацієнтів, які страждають депресивними розладами.

Ключові слова: уніполярная депресія, когнітивні розлади, антидепресанти.

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СОВРЕМЕННЫЕ ПРЕДСТАВЛЕНИЯ О КОГНИТИВНЫХ РАССТРОЙСТВАХ ПРИ ДЕПРЕССИВНЫХ СОСТОЯНИЯХ, А ТАКЖЕ ОСОБЕННОСТИ ИХ ДИАГНОСТИКИ

Аннотация

Когнитивные нарушения весьма часто выявляются при уніполярном депрессивном расстройстве. Более того, они имеют тенденцию сохраняться в ремиссии. Несмотря на большое число попыток охарактеризовать клеточные и общемозговые механизмы, лежащие в основе формирования когнитивных функций, а также выявить причины когнитивных нарушений при депрессивных расстройствах, проблема когнитивных нарушений все еще далека от своего решения. В данной статье дается критическая оценка существующих представлений о когнитивных нарушениях, освещаются трудности, встающие на пути у исследователей, и обсуждаются дальнейшие возможности улучшения когнитивного функционирования пациентов, страдающих депрессивными расстройствами.

Ключевые слова: уніполярная депрессия, когнитивные расстройства, антидепрессанты.