Cognitive impairment in patients with a primary episode of bipolar affective disorder
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An increasing number of studies on cognitive impairment associated with bipolar disorder indicate the relevance of the topic in psychiatry. The aim of the study was to investigate the features of cognitive functioning of patients with primary episode of bipolar disorder, taking into account sex and clinical variant. According to the method of “Remembering the Ten Words”, 153 patients were examined: with prevalence of depressive symptoms (44 men and 75 women), with prevalence of manic symptoms (15 men and 8 women) and with simultaneous presence of depressive and manic symptoms or with rapid change of phases (6 men and 5 women). Statistical analysis was performed using the non-parametric Mann-Whitney test. It was found that in the depressive variant, the memorization curve was characterized by difficulties of fixing information and difficulty in holding it: 4.2±1.2 words, 4.6±1.4 words, 5.9±1.8 words, 5.8±1.4 words, 4.4±1.3 words, 2.6±1.4 words (in men - 4.2±1.4 words, 4.6±1.5 words, 6.1±1.9 words, 5.7±1.5 words, 4.4±1.3 words, 2.6±1.4 words; in women - 4.2±1.1 words, 4.5±1.4 words, 5.9±1.7 words, 5.8±1.3 words, 4.4±1.3 words, 2.5±1.3 words); at manic - rapid rise with subsequent decrease and the lowest reproduction rates in an hour: 4.7±1.3 words, 7.5±1.3 words, 7.2±1.3 words, 6.7±1.8 words, 4.7±1.0 words, 2.0±1.0 words (in men - 4.9±1.3 words, 7.3±1.3 words, 7.1±1.2 words, 6.3±1.7 words, 4.7±0.9 words, 1.9±0.9 words; in women - 4.3±1.4 words, 7.9±1.4 words, 7.5±1.5 words, 7.5±1.7 words, 4.6±1.3 words, 2.3±1.2 words); when mixed - combined fixation difficulties and low reproduction rates: 4.5±0.9 words, 5.1±1.3 words, 5.9±1.1 words, 5.6±0.8 words, 4.2±1.1 words, 2.4±0.9 words (in men - 4.5±0.8 words, 5.5±1.0 words, 5.8±1.0 words, 5.8±0.8 words, 4.5±1.0 words, 2.0±0.9 words; in women - 4.6±1.1 words, 4.6±1.5 words, 6.0±1.4 words, 5.4±0.9 words, 3.8±1.1 words, 2.8±0.8 words). Certain differences in cognitive impairment were found depending on the clinical version of the primary episode; however, the differences between men and women are insignificant. Further prospects are related to the improvement of methods for predicting and treating cognitive impairment in bipolar disorders.

Keywords: bipolar affective disorder, primary episode, cognitive functioning.

Introduction
Bipolar affective disorder (BAD) is one of the most pressing problems in modern psychiatric science and practice. BAD has significant medical and social significance due to its high prevalence, high level of concomitant somatic morbidity and mortality from comorbid pathology and accidents, as well as high suicidal activity [8, 10, 17, 20, 22]. Of particular importance for the quality treatment and rehabilitation of patients with BAD is timely diagnosis of the disease at the initial stages. Recent studies have shown that the nature of future bipolar disorder is largely determined by the features of its primary episode (PE), which determines the relevance of the study of primary manifestations of this pathology and improvement of prodromal identification tools [2, 10, 11, 27].
An important component of the complex of psychopathological changes in BAD is cognitive impairment, which are detected at the pre-nosological stage and are manifested both in the manic and depressive phase, and during intermission [5, 7, 9, 21]. Cognitive disorders in BAD are represented by a wide range of disorders, among which - violations of the formal characteristics of thinking and its content, executive functions, attention and memory [14, 18,
The analysis of disorders in the cognitive sphere of patients with different variants of PE BAD revealed some differences associated with the peculiarities of the clinical manifestations of the onset of the disease (Table 1). In the depressive variant, the memory curve was characterized by difficulties in recording information and the difficulty of its retention: the maximum number of memorized words was reached on the third or fourth presentation and was characterized by low quantitative values, then the memory curve gradually decreased, and due to one hour patients were able to reproduce an average of no more than three words. In general, 4.2±1.2 words were memorized at the first presentation, 4.6±1.4 words at the second, 5.9±1.8 words at the third, 5.8±1.4 words at the fourth, 4.4±1.3 words at the fifth, through one hour - 2.6±1.4 words (Fig. 1). Such features reflect the difficulty of recording information, slow mental processes and rapid fatigue, inherent in a depressed state.

In the manic variant, another type of memory curve was observed: with a rapid rise and achievement of the maximum on the second - third presentation, and its subsequent decrease; while the indicators of word reproduction after one hour in patients with a manic variant of PE BAR were the worst among all groups. The average value of memorization at the first presentation was 4.7±1.3 words, at the second presentation - 7.5±1.3 words, at the third presentation - 7.2±1.3 words, at the fourth presentation - 6.7±1.8 words, at the fifth presentation - 4.7±1.0 words, in one hour - 2.0±1.0 words.

Patients with a mixed variant of PE BAD also showed severe memory difficulties, and the curve differs from that found in the manic variant of PE BAD and is similar to that found in the depressive variant. At the first presentation, patients memorized an average of 4.5±0.9 words, at the second presentation - 5.1±1.3 words, at the third presentation - 5.9±1.1 words, at the fourth presentation - 5.6±0.8 words, at the fifth presentation - 4.2±1.1 words, after one hour - 2.4±0.9 words.

The analysis of the peculiarities of the test "Memorization of ten words" considering gender differences revealed that the profiles of men with depressed PE BAD are characterized by inertia in memorization and a small number of words that patients were able to remember (Fig. 2). The maximum number of words that could be memorized falls on the third presentation, while the average number of words in the first presentation in men was 4.2±1.4 words, in the second presentation - 4.6±1.5 words, in the third presentation phenomenon - 6.1±1.9 words, at the fourth presentation - 5.7±1.5 words, at the fifth presentation - 4.4±1.3 words, in one hour - 2.6±1.4 words.

In the manic variant of PE BAD, the memory profile in men is characterized by maximum values in the second or third presentations with a rapid decrease in the number of words as the test continues. Thus, the average number of words that the patient was able to remember, at the first presentation was 4.9±1.3 words, at the second presentation - 7.3±1.3 words, at the third presentation - 7.1±1.2 words, at the fourth presentation. phenomenon - 6.3±1.7 words, at
In the mixed version of PE BAD, the memorization profile is characterized by smoothing with a relatively low number of words memorized by patients and a slow decrease in time. Thus, the average number of words memorized by the patient at the first presentation was 4.5±0.8 words, at the second - 5.5±1.0 words, at the third - 5.8±1.0 words, at the fourth presentation - 5.8±1.8 words, at the fifth presentation - 4.4±1.1 words, and after one hour - 2.4±0.9 words.

In women, the memorization profile was slightly different from that of men (Fig. 3).

In the depressive variant of PE BAD, the memory curve is characterized by maximum values in the third and fourth presentation with approximately the same values in the first, second and fifth presentations. The average value of the indicator on the test was: at the first presentation 4.2±1.1 words, at the second presentation - 4.5±1.4 words, at the third presentation - 5.9±1.1 words, at the fourth presentation - 5.9±1.2 words, and at the fifth presentation - 4.4±1.0 words, and after one hour - 2.6±1.4 words.

In the manic variant of PE BAD, the memory curve is characterized by maximum values in the first and second presentation with approximately the same values in the third, fourth and fifth presentations. The average value of the indicator on the test was: at the first presentation 4.7±1.3 words, at the second presentation - 7.5±1.3 words, at the third presentation - 7.2±1.3 words, at the fourth presentation - 6.7±1.8 words, and at the fifth presentation - 4.7±1.0 words, and after one hour - 2.0±1.0 words.

Table 1. Quantitative characteristics of indicators according to the test “Memorization of ten words” by A. R. Luria in the examined patients, considering gender and clinical variant of PE BAD.

| Presentation            | Indicator (M±σ / Me (Q25-Q75)) | p     |
|------------------------|---------------------------------|-------|
|                        | total men women                 |       |
| **Depressed version of PE BAD** |                                 |       |
| First presentation     | 4.2±1.2 / 4.0 (3.0-5.0) 4.2±1.4 / 4.0 (3.0-5.0) 4.2±1.1 / 4.0 (3.0-5.0) | >0.05 |
| Second presentation    | 4.6±1.4 / 4.0 (3.0-5.0) 4.6±1.5 / 4.0 (3.0-5.0) 4.5±1.4 / 4.0 (3.0-5.0) | >0.05 |
| Third presentation     | 5.9±1.8 / 6.0 (5.0-7.0) 6.1±1.9 / 6.0 (5.0-7.0) 5.9±1.7 / 6.0 (5.0-7.0) | >0.05 |
| Fourth presentation    | 5.8±1.4 / 6.0 (5.0-7.0) 5.7±1.5 / 6.0 (5.0-7.0) 5.8±1.3 / 6.0 (5.0-7.0) | >0.05 |
| Fifth presentation     | 4.4±1.3 / 4.0 (3.0-5.0) 4.4±1.3 / 4.0 (3.0-5.0) 4.4±1.3 / 4.0 (3.0-5.0) | >0.05 |
| After one hour         | 2.6±1.4 / 2.0 (2.0-3.0) 2.6±1.4 / 2.0 (2.0-3.0) 2.5±1.3 / 2.0 (1.0-4.0) | >0.05 |
| **Manic version of PE BAD** |                                 |       |
| First presentation     | 4.7±1.3 / 4.0 (4.0-6.0) 4.9±1.3 / 5.0 (4.0-6.0) 4.3±1.4 / 4.0 (3.0-5.0) | >0.05 |
| Second presentation    | 7.5±1.3 / 7.0 (6.0-9.0) 7.3±1.3 / 7.0 (6.0-8.0) 7.9±1.4 / 8.5 (6.5-9.0) | >0.05 |
| Third presentation     | 7.2±1.3 / 7.0 (6.0-8.0) 7.1±1.2 / 7.0 (6.0-8.0) 7.5±1.5 / 7.5 (6.5-9.0) | >0.05 |
| Fourth presentation    | 6.7±1.8 / 7.0 (5.0-8.0) 6.3±1.7 / 6.0 (5.0-8.0) 7.5±1.7 / 8.0 (6.0-9.0) | >0.05 |
| Fifth presentation     | 4.7±1.0 / 5.0 (4.0-6.0) 4.7±0.9 / 5.0 (4.0-5.0) 4.6±1.3 / 4.5 (3.5-6.0) | >0.05 |
| After one hour         | 2.0±1.0 / 2.0 (1.0-3.0) 1.9±0.9 / 2.0 (1.0-3.0) 2.3±1.2 / 3.0 (1.5-3.0) | >0.05 |
| **Mixed version of PE BAD** |                                 |       |
| First presentation     | 4.5±0.9 / 4.0 (4.0-5.0) 4.5±0.8 / 4.0 (4.0-5.0) 4.6±1.1 / 5.0 (4.0-5.0) | >0.05 |
| Second presentation    | 5.1±1.3 / 5.0 (4.0-6.0) 5.5±1.0 / 5.5 (5.0-6.0) 4.6±1.5 / 4.0 (4.0-5.0) | >0.05 |
| Third presentation     | 5.9±1.1 / 6.0 (5.0-7.0) 5.8±1.0 / 5.5 (5.0-7.0) 6.0±1.4 / 6.0 (6.0-6.0) | >0.05 |
| Fourth presentation    | 5.6±0.8 / 6.0 (5.0-6.0) 5.8±0.8 / 6.0 (5.0-6.0) 5.4±0.9 / 6.0 (5.0-6.0) | >0.05 |
| Fifth presentation     | 4.2±1.1 / 4.0 (3.0-5.0) 4.5±1.0 / 4.5 (4.0-5.0) 3.8±1.1 / 3.0 (3.0-5.0) | >0.05 |
| After one hour         | 2.4±0.9 / 2.0 (2.0-3.0) 2.0±0.9 / 2.0 (1.0-3.0) 2.8±0.8 / 3.0 (2.0-3.0) | >0.05 |

Fig. 1. Memorization curve according to the test "Memorization of ten words" by A. R. Luria in all examined patients.

Fig. 2. Memorization curve according to the test "Memorization of ten words" by A. R. Luria in men.

- 4.7±0.9 words, after one hour - 1.9±0.9 words.

In the mixed version of PE BAD, the memory curve is characterized by maximum values in the third and fourth presentation with approximately the same values in the first, second and fifth presentations. The average value of the indicator on the test was: at the first presentation 4.2±1.1 words, at the second presentation - 4.5±1.4 words, at the
third presentation - 5.9±1.7 words, at the fourth presentation - 5.8±1.3 words, at the fifth presentation - 4.4±1.3 words, in one hour - 2.5±1.3 words.

In the manic variant, the memory curve in women is characterized by a rapid increase with a peak at the second presentation (although the quantitative characteristics of memory in this group of patients are relatively low) with approximately equal averages in the third and fourth presentations. In the future, the number of words decreases, and in an hour is almost no different from that found in the depressive variant. The average value of the test was: at the first presentation: 4.3±1.4 words, at the second presentation - 7.9±1.4 words, at the third presentation - 7.5±1.5 words, at the fourth presentation - 7.5±1.7 words, at the fifth presentation - 4.6±1.3 words, in one hour - 2.3±1.2 words.

The mixed variant of PE BAD is characterized by a specific memory curve with a relatively slow increase and low values, followed by a rapid decline: at the first presentation of 4.6±1.1 words, at the second presentation of 4.6±1.5 words, at the third presentation of 6.0±1.4 words, at the fourth presentation 5.4±0.9 words, at the fifth presentation 3.8±1.1 words, in one hour 2.8±0.8 words. Such features, in our opinion, reflect the heterogeneity of this group in clinical symptoms, as well as the instability of the emotional state with rapid phase change, inherent in the mixed version of PE BAD.

In general, differences in the rates between men and women in all presentations in all clinical variants of PE BAD were not statistically significant (p>0.05).

When comparing groups with different clinical variants, significant differences were found when comparing groups of patients with depressive and manic (p<0.01), and with manic and mixed (p<0.05) variants of PE BAD.

Discussion

On the raised problem today, it is known that cognitive dysfunction is considered as the main sign of bipolar disorder [26]. Neurocognitive deficit is not considered specific for bipolar disorder. Thus, it is known that up to 94% of patients with schizophrenia show neurocognitive deficits [25].

There is also evidence that in bipolar disorder cognitive decline (impaired attention, verbal learning and memory, impaired executive function), along with other neurobiochemical changes, is present in all phases of the disease, including premorbid stages before the disease [16], in the early stages of the disease [4], in the primary episode, does not depend on mood and condition [13], are detected during euthymia [6].

However, patients with bipolar disorder are characterized by variability in psychosocial functioning, which suggests the existence of several neurocognitive subtypes among them. According to Bora E. et al. (2016) neurocognitive variability may reflect the etiological heterogeneity of bipolar disorder, including potentially different subtypes associated with different genetic susceptibility factors [3]. One of them is characterized by normal cognitive functioning, the decrease in cognitive functions of which is influenced by the number of recurrent affective episodes [23]. However, the progress of the violation after repeated episodes remains unclear. Another subtype includes patients in whom the pattern of cognitive impairment is similar to that of schizophrenia and is characterized by low premorbid cognitive function before the onset of the disease, which may be associated with disorders of the nervous system. Obviously, such patients will have common genetic risk factors for schizophrenia.

Therefore, early detection of such patients, who will develop a neuroprogressive disorder, which is largely decisive for the social prognosis of the disease, labor and social maladaptation of patients, is an urgent problem of psychiatry [19].

In our study, we found patterns of cognitive impairment in PE BAD. The data obtained by us are consistent with the results of studies by a number of authors [5, 9], who emphasize the pronounced cognitive impairment in patients with BAD, mainly in the form of a deficit of executive function, attention and memory. Our data fit into the context of modern ideas about cognitive impairment as one of the earliest manifestations of BAD, which occur both at the nosological [15, 28] and at the prenosological stage [29]. At the same time, our selection of individual clinical variants of PE BAD (depressive, manic and mixed) allowed to establish certain differences in cognitive dysfunction depending on the clinical variant of PE, which should be considered when assessing the cognitive functions of patients with PE BAD.

Prospects for further research are related to the development of comprehensive programs for early prediction of cognitive impairment in BAD, and the development of therapeutic and diagnostic measures to correct cognitive disorders, which will reduce the risk of recurrence, prevent complications and improve patients’ quality of life.

Conclusions

1. The primary episode of BAD is characterized by severe cognitive impairment.
2. Significant in determining the characteristics of cognitive impairment is the clinical variant of the primary episode.
episode: depressive, manic or mixed.

3. In the depressive variant there are difficulties in recording information and the difficulty of its retention, in the manic - instability of attention with rapid displacement of information from memory, and in the mixed - a combined violation of memorization of information.

4. Gender differences in cognitive impairment in the primary episode of BAD are not expressed.

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ПОРУШЕННЯ КОГНІТИВНОГО ФУНКЦІОНАВАННЯ У ХВОРІХ З ПЕРВИЧНИМ ЕПІЗОДОМ БІПОЯРНОГО АФФЕКТИВНОГО РОЗЛАДУ

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Все зростає число досліджень, щодо когнітивних порушень, пов'язаних з біполярним афективним розладом, свідчить про актуальність цієї теми в психіатрії. Метою дослідження було дослідити особливості когнітивного функціонування хворих з первичним епізодом біполярного афективного розладу з врахуванням статі та клінічного варіанта. За методикою "Запам'ятовування десяти слів" обстежено 153 хворих: з переважанням депресивної симптоматики (44 чоловіків та 59 жінок) та з одночасною наявністю депресивної та маніакальної симптоматики (15 чоловіків і 8 жінок). Статистичний аналіз проведено з використанням непараметричного тесту Манна-Уїтні. Встановлено, що при депресивному варіанті крива запам'ятовування характеризувалася трудністю фіксації інформації і її утримування: 4,2±1,2 слів, 4,6±1,4 слів, 5,9±1,8 слів, 5,8±1,4 слів, 4,4±1,3 слів, 2,6±1,4 слів (у чоловіків 4,2±1,4 слів, 4,6±1,5 слів, 6,1±1,9 слів, 5,7±1,5 слів, 4,4±1,3 слів, 2,6±1,4 слів; у жінок 4,2±1,1 слів, 4,5±1,4 слів, 5,9±1,7 слів, 5,8±1,3 слів, 4,4±1,3 слів, 2,5±1,3 слів); при маніакально-швидким підійомом з подальшим зниженням і найвищими показниками відтворення через грудну: 4,7±1,3 слів, 7,5±1,3 слів, 7,2±1,3 слів, 6,7±1,8 слів, 4,7±1,0 слів, 2,0±1,0 слів (у чоловіків - 4,9±1,3 слів, 7,3±1,3 слів, 7,1±1,2 слів, 6,3±1,7 слів, 4,7±0,9 слів, 1,9±0,9 слів; у жінок - 4,3±1,4 слів, 7,9±1,4 слів, 7,5±1,5 слів, 7,5±1,7 слів, 4,6±1,3 слів, 2,3±1,2 слів); при змішаному - поєднаними трудностями фіксації та низькими показниками відтворення: 4,5±0,9 слів, 5,1±1,3 слів, 5,9±1,1 слів, 5,6±0,8 слів, 4,2±1,1 слів, 2,4±0,8 слів (у чоловіків - 4,5±0,8 слів, 5,5±1,0 слів, 5,8±1,0 слів, 5,8±0,8 слів, 4,5±1,0 слів, 2,0±0,9 слів; у жінок - 4,6±1,1 слів, 4,6±1,5 слів, 6,0±1,4 слів, 5,4±0,9 слів, 3,8±1,1 слів, 2,8±0,8 слів). Виявлено незначні відмінності у когнітивних порушеннях залежно від клінічного варіанту первинного епізоду: при цьому розбіжності між чоловіками та жінками незначні. Подальші перспективи пов'язані з використанням методів прогнозування і лікування когнітивних порушень при біполярному афективному розладі.

Ключові слова: біполярний афективний розлад, первинний епізод, когнітивне функціонування.

НАРУШЕННЯ КОГНІТИВНОГО ФУНКЦІОНАРИВАННЯ У БОЛЬНЫХ С ПЕРВИЧНЫМ ЭПИЗОДОМ БИПОЯРНОГО АФФЕКТИВНОГО РАССТРОЙСТВА

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Все возрастающее количество исследований относительно когнитивных нарушений, связанных с биполярным аффективным расстройством, свидетельствует об актуальности поднятой темы в психиатрии. Целью исследования было изучение особенностей когнитивного функционирования больных с первичным эпизодом биполярного расстройства с учетом пола и клинического варианта. По методике "Запоминание десяти слов" обследовано 153 больных: с преобладанием депрессивной симптоматики (44 мужчин и 75 женщин), с преобладанием маниакальной симптоматики (15 человек и 8 женщин) и с одновременным наличием депрессивной и маниакальной симптоматики (6 мужчин и 5 женщин). Статистический анализ проведен с использованием непараметрического теста Манна-Уитни. Установлено, что при депрессивном варианте крива запоминания характеризовалась трудностями фиксации информации и тяжестью ее удержания: 4,2±1,2 слов, 4,6±1,4 слова, 5,9±1,8 слов, 5,8±1,4 слов, 4,4±1,3 слова, 2,6±1,4 слова (у мужчин 4,2±1,4 слова, 4,6±1,5 слова, 6,1±1,9 слов, 5,7±1,5 слова, 4,4±1,3 слова, 2,6±1,4 слова; у женщин - 4,2±1,1 слова, 4,5±1,4 слова, 5,9±1,7 слова, 5,8±1,3 слова, 4,4±1,3 слова, 2,5±1,3 слова); при маниакально-быстрым подъемом с последующим снижением и низкими показателями воспроизведения через час: 4,7±1,3 слова, 7,5±1,3 слова, 7,2±1,3 слова, 6,7±1,8 слова, 4,7±1,0 слова, 2,0±0,9 слова (у мужчин 4,9±1,3 слова, 7,3±1,3 слова, 7,1±1,2 слова, 6,3±1,7 слова, 4,7±0,9 слова, 1,9±0,9 слова; у женщин - 4,3±1,4 слова, 7,9±1,4 слова, 7,5±1,5 слова, 7,5±1,7 слова, 4,6±1,3 слова, 2,3±1,2 слова); при смешанном - сочетанными трудностями фиксации и низкими показателями воспроизведения: 4,5±0,9 слова, 5,1±1,3 слова, 5,9±1,1 слова, 5,6±0,8 слова, 4,2±1,1 слова, 2,4±0,9 слова (у мужчин - 4,5±0,8 слова, 5,5±1,0 слова, 5,8±1,0 слова, 5,8±1,0 слова, 4,5±1,0 слова, 2,0±0,9 слова; у женщин - 4,6±1,1 слова, 4,6±1,5 слова, 6,0±1,4 слова, 5,4±0,9 слова, 3,8±1,1 слова, 2,9±0,8 слова). Выявлены определенные различия в когнитивных нарушениях в зависимости от клинического варианта первичного эпизода; при этом различия между мужчинами и женщинами незначимы. Дальнейшие перспективы связаны с совершенствованием методов прогнозирования и лечения когнитивных нарушений при биполярном аффективном расстройстве.

Ключевые слова: биполярное аффективное расстройство, первичный эпизод, когнитивное функционирование.