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Application of screening techniques for early diagnosis of a risk of bipolar disorder in adolescents

Osipova N.N.[1], Bardenshteyn L.M.[1], Lyamets L.L.[2], Dmitrieva E.V.[2]

[1]A.I. Yevdokimov Moscow State University of Medicine and Dentistry
20/1, Delegatskaya Str., 127473, Moscow, Russian Federation

[2]Smolensk State Medical University
28, Krupskoy Str., 214019, Smolensk, Russian Federation

ABSTRACT

Aim. To assess the possibility of combined application of screening methods for early detection of risks of bipolar disorder in adolescents.

Materials and methods. The study included 139 adolescents aged 13–16 years. A clinical psychopathology assessment as well as screening methods were used. The screening methods included the Bipolar Spectrum Diagnostic Scale ((BSDS), R. Pies, 2005) and the Mood Disorder Questionnaire ((MDQ), R.M. Hirschfeld, 2000).

Results. The clinical psychopathology assessment was performed in accordance with criteria of ICD-10, Class V. No mental and behavioral disorders (F00-F99), including affective pathology, were identified. Following the MDQ screening, the risk of bipolar disorder was revealed in 63 individuals (45.3%; 95 % confidence interval (CI): (36.8–53.9). When the BSDS method was used, the risk of bipolar disorder was revealed in 16.2% of cases (CI: (11.9–28.3)). The combined use of the screening scales (MDQ and BSDS) confirmed their consistency in detecting values both not exceeding (48.7% of the cases) and exceeding the threshold rates (17.1% of the cases).

Conclusion. Early diagnosis of a risk of bipolar disorder in adolescents, along with a clinical psychopathology assessment, may include application of screening scales. Combined use of several screening methods is justified by polymorphism of initial hypomanic and depressive states, as well as by difficulties in subjective assessment of symptoms of bipolar disorder in adolescents.

Keywords: adolescents, bipolar disorder, hypomania, screening methods

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✉ *Osipova Natalia N.,* natinen@yandex.ru

Применение скрининговых методик для ранней диагностики риска биполярного аффективного расстройства у подростков

Осипова Н.Н.[1], Барденштейн Л.М.[1], Лямец Л.Л.[2], Дмитриева Е.В.[2]

[1]*Московский государственный медико-стоматологический университет (МГМСУ) им. А.И. Евдокимова Россия, 127473, г. Москва, ул. Делегатская, 20/1*

[2]*Смоленский государственный медицинский университет (СГМУ) Россия, 214019, г. Смоленск, ул. Крупской, 28*

РЕЗЮМЕ

Цель. Изучение возможности комплексного применения скрининговых методик в ранней диагностике риска биполярного расстройства (БР) у подростков.

Материалы и методы. В исследовании приняли участие 139 подростков в возрасте 13–16 лет. Были использованы клинико-психопатологический метод и скрининговые методы исследования: диагностическая шкала расстройств биполярного спектра (Bipolar Spectrum Diagnostic Scale, *BSDS*, R. Pies, 2005); вопросник расстройства настроения (Mood Disorder Questionnaire MDQ, R.M. Hirschfeld, 2000).

Результаты. При клинико-психопатологическом исследовании подростков в соответствии с критериями МКБ-10 (класс V: психические расстройства и расстройства поведения (F00-F99)) психические расстройства, в том числе аффективная патология, не выявлены. По результатам скрининговой методики MDQ показан риск БР у 63 респондентов (45,3%; 95-й доверительный интервал (ДИ): 36,8–53,9). С помощью методики BSDS риск БР отмечен у 16,2% респондентов (ДИ: 11,9–28,3). Совместное использование скрининговых шкал (MDQ и BSDS) продемонстрировало согласованность их работы по выявлению значений, как не превышающих пороговые (48,7% случаев), так и превышающих пороговые показатели (17,1% случаев).

Заключение. Ранняя диагностика риска БР у подростков наряду с клинико-психопатологическим методом может включать использование скрининговых шкал. Комплексное использование нескольких скрининговых методов обосновано проблемой полиморфизма начальных гипоманиакальных и депрессивных состояний, а также трудностями субъективной оценки симптомов биполярного аффективного расстройства подростками.

Ключевые слова: подростки, биполярное аффективное расстройство, гипомания, скрининговые методы

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии финансирования при проведении исследования.

Соответствие принципам этики. Информированное согласие подписано родителями подростков по соответствующей форме. Исследование одобрено этическим комитетом СГМУ (протокол № 3 от 02.12.2018).

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INTRODUCTION

Bipolar disorder (BD) is a chronic, almost lifelong disease involving not only episodes of mood disorders (subdepression, depression, hypomania, mania, and mixed episodes), but also a wide range of comorbid disorders, decreased neurocognitive functions, and a significant decline in social functioning [1].

BD is one of the leading causes of disability in the population and is associated with high rates of premature mortality, both from suicide [2] and concomitant diseases [3, 4]. Among patients with BD, especially those with mixed episodes and psychotic disorders, the risk of suicidal behavior is one of the highest among all mental disorders, especially in adolescence [5].

BD is characterized by high prevalence in the general population (from 0.6 to 5.84%), and with account of subsyndromal manifestations, it reaches 12% [6]. The issue of studying BD manifesting in adolescence seems relevant in the light of the increase in the proportion of this pathology in puberty [7, 8].

An important aspect of this issue is a difficulty in diagnosis, largely associated with the atypical clinical presentation of subdepressive, depressive, hypomanic, manic, and mixed episodes debuting in adolescence, its polymorphism, and syndrome incompleteness due to the characteristics of the developing adolescent psyche [9]. This leads to the fact that a significant part (up to 70–80%) of adolescents suffering from BD do not receive timely adequate treatment or do not come to the attention of a psychotherapist or psychiatrist at all [10].

Depression is a frequent clinical manifestation of most mental illnesses at puberty, especially at their initial stage, which is probably due to the prevalence of the emotional and ideological response at this stage of ontogenesis [11, 12].

Hypomanic states often precede BD in adolescence [13]. A significant problem is differentiation between hyperthymic temperament, as an extreme variant of the norm, and hypomanic states in BD. In addition, adolescent behavioral features that determine developmental crisis during puberty (reaction of emancipation, opposition, grouping with peers, etc.) [12] are often associated with the onset of substance abuse, which may not exclude early symptoms of hypomania [13, 14].

Hypomania presents significant problems in the diagnosis of bipolar II disorder. Hypomanic states are difficult to recognize both by patients themselves and their relatives; most patients do not consider such states painful and, therefore, do not seek medical care [15]. This is especially true for adolescents, who may enjoy a state of heightened mood and elation. They can exacerbate this state by taking psychoactive substances followed by risky behavior [16].

Irritability, as one of the diagnostic criteria for mood disorders (hypomania, mania, subdepression, depression), is also quite common in the prepubertal and pubertal developmental periods. Irritability is often accompanied by various forms of aggressive behavior in adolescents and requires thorough differential diagnosis. In the study by F. Benazzi, H. Akiskal (2004), irritability was more often detected in bipolar II disorder. BD with irritability had an earlier onset, high comorbidity rates, as well as aggravated family history for BD [17].

Over the decades, international diagnostic systems have changed approaches to the diagnosis of hypomania, as one of the criteria for bipolar II disorder. This concerned both the duration of the hypomanic episode and the number of symptoms it should correspond to. The ICD-11 project includes changes concerning the diagnosis of a hypomanic episode [18–20].

J. Angst et al. (2020) conducted a comparative analysis of diagnostic criteria for BD using DSM-V (APA, 2013) and the ICD-11 project. They noted that, unlike DSM-IV-TR and ICD-10, in DSM-V and the ICD-11 project, among the main criteria for diagnosing a hypomanic episode, in addition to mood changes (euphoria, irritability), the emphasis is placed on increasing activity, a surge of strength, and a subjective feeling of vitality, which, according to the authors, is essential to describe a more complete and accurate clinical presentation of the disorder. In the DSM-V, the number of additional symptoms for the diagnosis of hypomania is limited to three or more for increased mood and to four or more for irritability. In the ICD-11 project, “a few” additional symptoms are necessary to make a diagnosis. The differences also concern the duration of the hypomanic episode: in DSM-V, symptoms must be present for at least 4 days, while there are no such restrictions in the ICD-11 project, and a period of “several days” is mentioned.

J. Angst et al. (2020) note that the diagnostic criteria for a hypomanic episode in the ICD-11 project enable to detect it twice more often than in DSM-V. The issues requiring further study are social and psychological consequences of hypomania which are not always subjectively undesirable for the patient (increased efficiency, acceleration of associative processes, reduced duration of night sleep, increased creative abilities). The authors point out that for a more accurate diagnosis, it is necessary to take into account episodes of seeking outpatient medical care, which may be associated to a greater extent with the negative consequences of a hypomanic episode and will maximize objectification of the patient’s mental state [21].

Researchers indicate that the average age at the onset of BD varies from 20 to 30 years. Some authors note two peaks of BD debut: 15–24 years and 45–54 years. There are also indications of an earlier (up to 12 years) onset of the disease, associated, among other things, with the impact of a traumatic event [22]. Certain BD symptoms in the form of cyclothymic mood swings can be detected in adolescence and are characterized by a risk of progression to BD [23, 24].

Researchers are also discussing the diagnosis of prepubertal bipolar disorder (PPBD) [25]. However, clinical manifestations of the main BD symptoms in childhood differ significantly from those in adults, and in some cases are not similar. Mixed episodes that are difficult to diagnose and are common in adults, can also occur in childhood and adolescence, which further complicates early diagnosis of affective pathology in these age periods [26].

At the onset of BD in childhood, the disease is characterized not only by a more unfavorable course compared with the debut in adults (more episodes, substance use and disability), but also by a longer delay in the initiation of treatment. J.S. Kroon et al. (2013) found that the first episode of BD that occurred at the age of 15–24 years subsequently contributed to a more severe course of the disease in patients aged 45–54 years [27].

BD in adolescents is often complicated by comorbid mental and somatic disorders that significantly increase the risk of suicidal behavior. This primarily concerns substance abuse. According to M.H. Swahn et al. (2007), early initiation of alcohol consumption (especially at the prepubertal age) statistically significantly increases the risk of suicidal thoughts and can provoke suicidal attempts in both boys and girls [28].

Researchers attribute great importance to identifying prodromal symptoms that precede the onset of the disease. According to the study by G.A. Fava et al. (2007), the majority of patients had such symptoms as difficulty with falling asleep, irritability, and anxiety before the onset of clinically defined syndromes [29]. A.R. Van Meter et al. (2016) noted that more than half of the respondents had a symptom of a significant increase in energy before the onset of a manic episode [30]. There is evidence that behavioral disorders, aggressiveness, and impulsivity in adolescence also precede BD [31].

Along with the main clinical and psychopathological method, screening tools are widely used for the diagnosis of BD, especially for timely detection of hypomanic episodes. These include the Mood Disorder Questionnaire (MDQ) developed in 2000 by a team led by R.M.A. Hirschfeld [32], the Bipolar Spectrum Diagnostic Scale (BSDS) developed by R. Pies and improved by a group of researchers led by S.N. Ghaemi in 2005 [33], and the 32-item Hypomania Checklist (HCL-32) [34] proposed by J. Angst et al. in 2005 and validated in Russia by S.N. Mosolov et al. [35]. These screening methods are used in both clinical and non-clinical populations.

Thus, studies on hypomania in a non-clinical adolescent population using HCL-32 showed the relationship of hypomania with sleep disorders and personality traits, which confirms the validity of using this screening method as a tool for identifying adolescents at risk of developing BD [36]. A. Päären et al. (2012), studying adolescents (n = 2,300) with a positive screening result for hypomania, upon re-examination after 15 years, revealed hypomanic episodes in 3–6% of cases [37].

According to many researchers, the use of screening techniques in non-clinical populations to identify the risk of BD causes many difficulties, since the sensitivity and specificity parameters vary widely. A subjective assessment of the emotional state (hypomania) in adolescents is also complicated. In addition, the debut of BD is characterized by a high degree of polymorphism, which poses additional challenges for the diagnosis of the disease at early stages [38].

MATERIALS AND METHODS

The aim of the study was to investigate diagnostic capabilities of combined use of the Mood Disorder Questionnaire (MDQ) and the Bipolar Spectrum Diagnostic Scale (BSDS) to identify the risk of BD in a non-clinical adolescent population.

The study involved 139 adolescents studying at a specialized school in the Smolensk region within the programs of the Federal State Educational Standard of Secondary (Complete) General Education (57 (41.1%) boys and 82 (58.9 %) girls). The average age was 14.61 ± 0.09 years (min = 13; max = 16). The study participants were comparable in age and social and educational status. No significant differences were found by gender ($p > 0.05$).

The informed consent was signed by the parents of the adolescents according to the standard form. The study was conducted in groups of 15–20 people. A preliminary permission had been received to ask clarifying questions from a psychiatrist present during the study. In most cases, adolescents did not have any difficulties with filling out the questionnaire. On average, it took them 30 minutes to fill out the printed copy of the screening questionnaires.

The clinical and psychopathological method and screening methods were used in the work: the Bipolar Spectrum Diagnostic Scale (BSDS; R. Pies, 2005) [33]; the Mood Disorder Questionnaire (MDQ; R.M.A. Hirschfeld, 2000) [32].

Statistical processing of the data included methods of descriptive statistics. The 95% confidence interval (CI) was calculated using the Wald's equation; for small values, it was calculated using the Wald's equation modified according to the method of Agresti – Coull. The significance of the differences between the studied features was assessed using the Pearson's chi-squared test (χ^2) and Fisher transformation. Statistical significance was recognized with a probability of >95% ($p < 0.05$). The relationship between the features was assessed by Spearman's rank correlation coefficient. Statistical analysis of the results was performed in Microsoft Excel 16 using the Data Analysis and AtteStat add-ons and the R statistical package.

RESULTS

During the clinical and psychopathological assessment of the adolescents in accordance with the criteria of ICD-10, class V, mental and behavioral disorders (F00–F99) and mental disorders, including affective pathology, were not identified.

The next stage of the research was to study the risk of developing BD using the Mood Disorder Questionnaire (MDQ). 139 adolescents took part in it. The MDQ consists of 3 sections: the first includes 13 questions reflecting symptoms of mania (hypomania), the second registers the simultaneous presence of one or more symptoms, and the third registers the degree of habitual activity interference due to the presence of symptoms. The average value of positive answers among the respondents in this sample was 7.14 ± 0.26 points (*min* = 1; *max* = 15). These values do not exceed the screening threshold of 7 points [20]. The results of the study are presented in Table 1.

Table 1

The results of the distribution of positive responses according to the MDQ scale, *n* = 139

The distribution of positive answers according to the MDQ scale, points	The number of the respondents who gave a positive answer, *n* (%)	95% CI
15	1 (0.72)	0.13–3.96
14	2 (1.44)	0.4–5.1
13	3 (2.16)	0.74–6.16
12	3 (2.16)	0.74–6.16
11	12 (8.63)	3.96–13.30
10	12 (8.63)	3.96–13.30
9	14 (10.07)	5.07–15.08
8	16 (11.51)	6.21–16.82
7	16 (11.51)	6.21–16.82
6	16 (11.51)	6.21–16.82
5	16 (11.51)	6.21–16.82
4	9 (6.47)	2.38–10.57
3	10 (7.19)	2.90–11.49
2	6 (4.32)	0.94–7.70
1	3 (2.16)	0.74–6.16

Note: 95% CI with respect to the relative rate of a positive response, $p < 0.05$ (here and in Table 2).

To identify the proportion of respondents with an increased level of screening values, grouping was carried out according to the screening threshold. The respondents were divided into two groups. The first group included 76 respondents, which is 54.7% (CI: 46.1–63.1), who scored 7 or less points (not exceeding the screening threshold); the second group included respondents in the amount of 63 individuals, which is 45.3% (CI: 36.8–53.9), who scored more than 7 points (exceeding the screening threshold).

No significant differences were found between the groups φ *emp = 1.329 ($p > 0.05$), i.e. the proportion of the respondents with screening values not exceeding the screening threshold does not significantly differ from the proportion of the respondents exceeding the screening threshold; the respondents of both groups are seen in the studied social environment with equal likelihood.

The next stage of the study was to investigate the possibilities of using the Bipolar Spectrum Diagnostic Scale (BSDS) screening technique to identify the risk of developing BD. From 139 individuals, the study involved 99 adolescents aged 13–16 years.

BSDS is a technique that, along with the manifestations of depression, takes into account the symptoms of hypomania (mania). The respondent's agreement with any of the proposed statements is equal to 1 point. The total BSDS score can be in the range

of 0–25. The probability of BD is estimated according to the sum of points: 20 points or more – bipolar spectrum disorder is very likely, 13–19 points – a moderate probability of bipolar spectrum disorders, 7–11 points – low probability of bipolar spectrum disorders, less than 7 points – BD is unlikely. The screening threshold is 13 points.

The average score for positive responses among the respondents in this population was 8.93 ± 0.39 (*min* = 1; *max* = 20), which is below the screening threshold (13 points). The results of the study are presented in Table 2.

Table 2

The results of the distribution of the total score for positive responses according to the BSDS, *n* = 99

The total score for positive responses according to the MDQ scale, points	The number of respondents who gave a positive answer, *n* (%)	95% CI
20 and more	1 (1.01)	0.18–5.5
13–19	28 (28.28)	20.35–37.83
7–11	50 (50.51)	40.83–60.15
less than 7	20 (20.20)	13.47–29.15

The table shows the prevalence of low (50.51%) and moderate (28.28%) trends toward BD in the respondents. To identify the proportion of the respondents with an increased level of screening values (13 or more points), grouping was carried out according to the screening threshold. The respondents were divided into two groups. The first group included 83 respondents, which is 83.8%, CI: (75.1–90.5), who scored less than 13 points (not exceeding the screening threshold); the second group consisted of 16 individuals, which is 16.2%, CI: (11.9–28.3), who scored 13 or more points (exceeding the screening threshold).

When comparing the two groups, significant differences were revealed φ *emp = 10.501 ($p < 0.05$), i.e. the proportion of respondents with values not exceeding the screening threshold significantly differs from the proportion of respondents exceeding the screening threshold. This sample is dominated by respondents with values not exceeding the screening threshold (less than 13 points), respectively, who do not have a risk of developing BD.

The next stage of the research was to study the simultaneous (combined) use of the MDQ and BSDS screening techniques; a comparative analysis was carried out. As a result, the MDQ scale revealed a tendency toward BD in a non-clinical population of adolescents to a greater extent than the BSDS; φ *emp = 6.36 ($p < 0.05$) (Fig. 1). The average value according to the MDQ scale approached the screening threshold value of 7 points (7.14 ± 0.26, min = 1; max = 15), and the average value according to the BSDS (8.93 ± 0.39, min = 1; max = 20) was 13 points lower than the screening threshold. The results obtained may indicate difficulties experienced by adolescents in assessing the emotional state, which justifies a comprehensive approach to the diagnosis of a tendency toward affective pathology.

Further, we performed a correlation analysis of the survey results on the BSDS and MDQ scales. A noticeable direct, positive relationship was revealed ($r = 0.55$; $p < 0.05$), which indicates the possibility of combined use of these screening scales (Fig. 2).

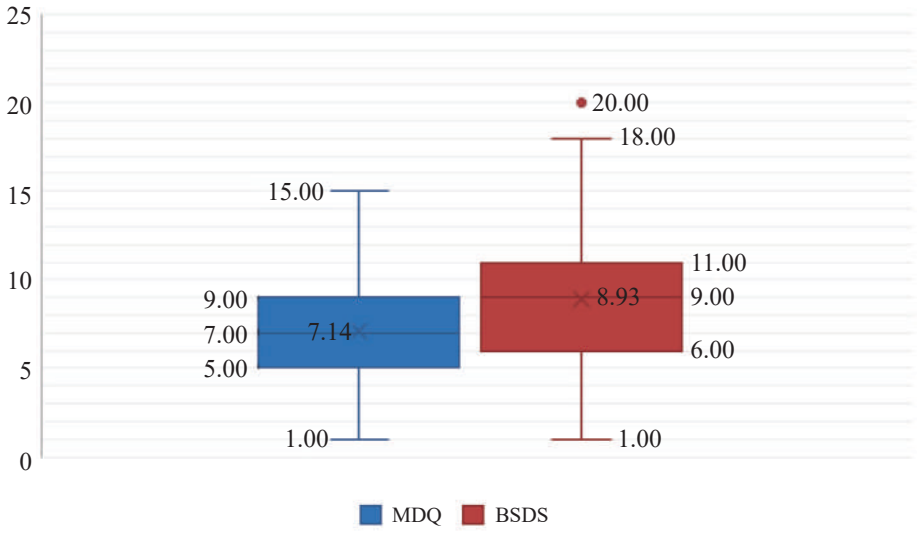

Fig. 1. Distribution of average values on the BSDS and MDQ scales

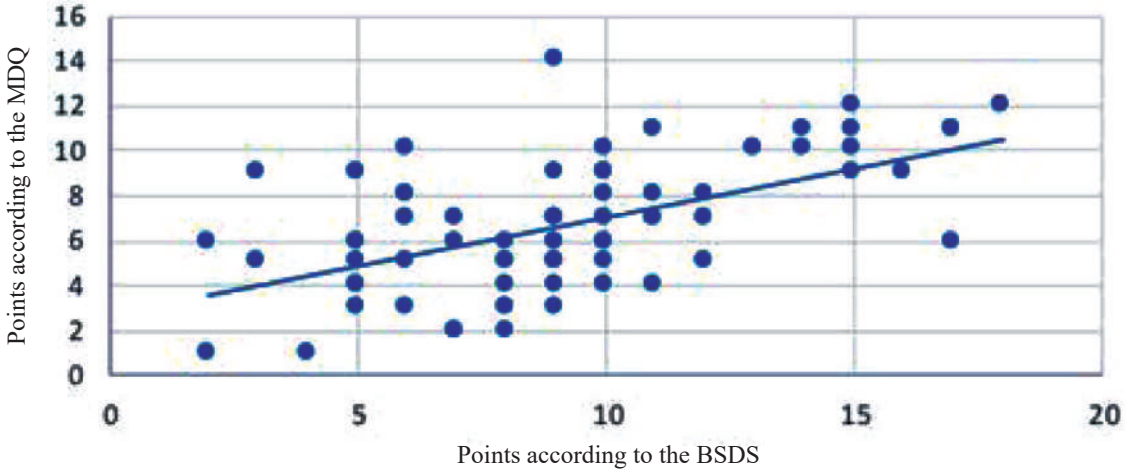

Fig. 2. Study of the correlation between the MDQ and BSDS

To assess the possibility of combined use of the two scales, the Pearson's test was used. When analyzing the statistical relationship between the parameters of the MDQ and BSDS screening methods (above / below the screening value for both scales), $\chi 2$ was 12.6, which indicates a high degree of its statistical significance (p = 0.0004). Combined use of the two techniques in the groups exceeding the screening threshold was revealed in 17.1% of cases. In the groups of respondents where the screening values on both scales did not exceed the threshold values, the combined use of the methods was detected in 48.7% of cases.

The data obtained may indicate the effectiveness of comprehensive research in non-clinical samples. In this study, the combined use of the two screening scales (MDQ and BSDS) revealed a risk of developing affective disorders in 17% of the respondents. At the same time, with the use of each of these techniques separately, contradictory results were obtained: according to the MDQ data, a tendency toward affective pathology was revealed in 45.3% of the respondents, while according to the BSDS, only 16.2% of the respondents in the non-clinical sample were found to exceed the screening threshold.

The findings obtained are consistent with the results of studies on possibilities of applying screening scales in the general population. Scholars discuss a significant variation in the sensitivity and specificity of screening methods in non-clinical samples. R.M. Hirschfeld et al. (2003), when studying validity of the MDQ scale for application in the general population, found that the sensitivity of the method was 28.1% and the specificity was 97.2%, which significantly limits its use [39].

The study of possibilities of the BSDS in outpatient psychiatric practice shows greater sensitivity with regard to exclusion of the diagnosis of BD. At the same time, some experts consider the BSDS a useful screening tool for detecting subclinical manifestations of hypomania [40]. In order to optimize screening for BD, according to many researchers, the combined use of several diagnostic questionnaires may be recommended. An increase in the efficiency of BD screening was shown with the combined use of the MDQ and the HCL-32, the BSDS and the HCL-32, as well as the BSDS and the MDQ [41, 42].

Therefore, this analysis has shown that the combined use of two screening scales and clinical and psychopathological assessment can contribute to more reliable results in detecting mood disorders in non-clinical populations of adolescents and minimize the problem of over- and underdiagnosis of subdepression and hypomanic states.

CONCLUSION

In the clinical and psychopathological assessment of adolescents in accordance with the criteria of ICD-10, class V (mental disorders and behavioral disorders (F00–F99)), mental disorders, including affective pathology, were not detected. Based on the results obtained, it may be assumed that in this study, the MDQ and BSDS screening methods can work in unison, to detect respondents with values both not exceeding and exceeding the screening threshold. In particular, consistency of measurements of the methods in iden-

tifying values that do not exceed the screening threshold is confirmed in 48.7% of cases, which indicates that there is no risk of BD in the studied population of healthy adolescents. In 17.1% of cases, the consistency of measurements of the two methods in identifying the excess of the screening threshold corresponds to the risk of developing BD in this population of respondents.

Identifying the risk of BD in adolescents is very complicated due to significant polymorphism of both prodromal and initial manifestations of BD. Adolescence, characterized by complex neuroendocrine changes in the body, also causes certain alterations in the initial manifestations of BD. Psychological features typical of adolescence (reactions of emancipation, opposition; active and passive protest; aggravation of characterologic traits, etc.) can act both as psychological phenomena and psychopathological symptoms and require thorough differential diagnosis.

Early diagnosis of the risk of BD in adolescents, along with the clinical and psychopathological assessment, may include the use of screening scales. The combined use of several screening methods is justified by polymorphism of initial hypomanic and depressive states, as well as the by difficulties in subjective assessment of BD symptoms by adolescents. Further research on possibilities of early diagnosis of the risk of BD requires a comprehensive approach with use of the basic clinical and psychopathological assessment and additional psychometric scales, a thorough assessment of anamnestic data, and subsequent follow-up.

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Authors information

Osipova Natalia N. – Cand. Sci. (Med.), Associate Professor, Department of Psychiatry and Narcology, A.I. Yevdokimov Moscow State University of Medicine and Dentistry, Moscow, natinen@yandex.ru, https://orcid.org/0000-0002-8034-4457

Bardensteyn Leonid M. – Dr. Sci. (Med.), Professor, Honored Doctor of the Russian Federation, Head of the Department of Psychiatry and Narcology, A.I. Yevdokimov Moscow State University of Medicine and Dentistry, Moscow, barden@mail.ru, https://orcid.org/0000-0002-1171-5517

Lyamets Leonid L. – Cand. Sci. (Technical Sciences), Associate Professor, Head of the Department of Physics, Mathematics, and Medical Informatics, Smolensk State Medical University, Smolensk, LLL1965@mail.ru , https://orcid.org/0000-0002-9173-3044

Dmitrieva Elena V. – Senior Lecturer, Department of Physics, Mathematics, and Medical Informatics, Smolensk State Medical University, Smolensk, vernulas@mail.ru , https://orcid.org/0000-0003-0375-0870

(✉) **Osipova Natalia N.,** natinen@yandex.ru

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