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EARLY SCREENING FOR RISKS OF BIPOLAR DISORDER AT THE PRECLINICAL STAGE

Natalya N. Osipova[1], Leonid M. Bardenshteyn[1], N.I. Beglyankin[1] & M.V. Dmitriev[2]

[1]Moscow State University of Medicine and Dentistry named after A.I. Evdokimov of the Ministry of Healthcare of the Russian Federation, Department of Psychiatry and Narcology, Moscow State University of Medicine and Dentistry named after A. I. Evdokimov, Moscow, Russia

[2]Smolensk State University of Medicine of the Ministry of Healthcare of the Russian Federation, Department of Physics, Mathematics and Medical Informatics Smolensk State University of Medicine, Moscow, Russia

SUMMARY

Introduction: *Bipolar disorder (BD) is characterized by a high rate of prevalence in the general population varying from 0.6% to 5.84% (Yildiz 2015). BD is one of the leading causes of disability and mortality from suicide and comorbid diseases (Johnson et al. 2017). Individual symptoms of the disease in the form of cyclothymia-like mood fluctuations can be detected in adolescence and have potential for predicting risk for BD (Tijssen et al. 2010). The key issue here is untimely diagnosis of BD (Mosolov et al. 2014, Bardenshteyn et al. 2016). Early screening for risks of bipolar disorder at the preclinical stage.*

Subjects and methods: *The study involved 137 students aged from 18 to 20 years (mean age 18.93±0.09). The clinical-psychopathological method as well as the screening method of research were used: the Mini-International Neuropsychiatric Interview (M.I.N.I.), (Sheehan et al. 1998), the Hamilton Depression Rating Scale (HDRS 1960), the Mood Disorder Questionnaire (MDQ) (Hirschfeld 2000). The statistical data processing included descriptive statistical methods ($p<0.05$).*

Results: *Clinical diagnostics of the responders using ICD-10 (WHO, 1992, Chapter V [F00-F99]) excluded the diagnosis of bipolar disorder. The MDQ screening method revealed a statistically significant excess of the average values for hypomania throughout the sample (M±m: 6.46±0.44; $p<0.05$). The total score of 64 interviewees (46.7%; 95% CI: 38.1–55.3) exceeded the threshold value (≥7). 68 responders (49.6%; 95% CI 41.0–55.3) showed one-stage manifestation of certain signs of mood rise. 72 interviewees (52.6%; 95% CI 43.9-58.3) reported absence of mood rise, associated with conflict behaviour, family problems etc.*

According to the HDRS scale, 45 responders (32.85%; 95% CI: 24.14-40.95) showed signs of mild depression (M±m: 6.51±0.39; $p<0.05$). Also, a group of responders (18.2%; 95% CI: 11.78-24.72) manifested exceeding indicators both for hypomania and depression.

Conclusions: *According to the MDQ scale, 46.7% of the responders showed threshold values exceeding; with the one-stage manifestation of hypomania signs in 49.6% of the respondents. 32.85% of the responders showed signs of mild depression (the HAMD scale). 18.2% of the interviewees exceeded threshold values for both hypomania and depression. The discovered cyclothymia-like conditions at the preclinical stage have potential for predicting risk for their transformation to bipolar disorder which directs further outpatient clinical and dynamic observation.*

Key words: *bipolar disorder - early screening - hypomania*

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INTRODUCTION

Bipolar disorder (BD) is characterized by a high rate of prevalence in the general population varying from 0.6% to 5.84% (Yildiz et al. 2015). BD is one of the leading causes of population disability and mortality from suicide and comorbid diseases (substance abuse, anxiety disorders, type II diabetes, obesity, psoriasis, cerebrovascular pathology) (Hayes et al. 2015, Johnson 2014). Individual symptoms of the disease in the form of cyclothymia-like mood fluctuations can be detected in adolescence and have potential for predicting risk for BD (Tijssen 2010).

The key issue here is untimely diagnosis of BD (Bardenshteyn et al. 2016, Mosolov et al. 2014).

It should also be noted that in the temporal aspect of the dynamics of BD, depressive episodes are predominant, and their differentiation from monopolar recurrent depression is a clinical problem. Depression was initially seen as monopolar in over 40% of patients who were later diagnosed with bipolar disorder (Ghaemi et al. 2005). There is evidence that the process of diagnosing BD and, correspondingly, adequate treatment are delayed for 6-8 years or more, especially with the onset of the disease in adolescence (Baldessarini et al. 2020, Vöhringer & Perlis 2016).

Hypomanic states pose significant problems in the diagnosis of type II BD. Episodes of hypomania are difficult to recognize both by the patients themselves and by their relatives; most patients do not consider such conditions painful and, accordingly, do not seek medical help (Pääre n et al. 2013). This is especially true of adolescents who may like the state of a heightened mood and increased energy. They can exacerbate this state by taking psychoactive substances with subsequent risky behavior (Post & Kalivas 2013).

Researchers point out that the average age at which the onset of bipolar disorder occurs, ranges from 20 to

30 years. Some authors have noted two peaks of BD debut: 15-24 and 45-54 years of age. There are indications of an earlier onset of the disease (before 12 years), associated, inter alia, with the impact of a traumatic situation (Goodday et al. 2015). Certain symptoms of BD in the form of cyclothymic mood swings can be found in adolescence and represent a risk of transition to bipolar disorder (Tijssen 2010, Malhi & Bell 2020, Toohey 2019). With the onset of bipolar disorder in childhood, not only is there a more unfavorable course of the disease compared to the onset of the disease in adults (more episodes, substance abuse, deterioration of social functioning), but also a longer delay in starting treatment. The study by J.S. Kroon et al. (2013) found that the first episode of BD experienced at the age of 15 to 24 years subsequently contributes to a more severe course of the disease in patients aged 45-54 years. The early onset of the disease is also associated with a high suicidal risk, the addition of comorbid pathology, and a fast-cycling course (Goldstein et al. 2016, Mota et al. 2016, Jamison 2000

Researchers attach great importance to the identification of prodromal symptoms that precede the onset of the disease. According to the study by G.A. Fava & Tossani (2007), the majority of patients before the onset of clinically defined syndromes had symptoms such as difficulty with falling asleep, irritability, and anxiety. According to A.R. Van Meter et al. (2016), more than half of the respondents revealed a symptom in the form of a significant increase in energy before the onset of a manic episode (Van Meter et al. 2016). There are indications that behavioral disorders, aggressiveness and impulsivity in adolescence also precede bipolar disorder (Axelson et al. 2015).

Early screening for risks of bipolar disorder at the preclinical stage.

SUBJECTS AND METHODS

The study involved 137 students aged from 18 to 20 years (mean age 18.93±0.09). 45 males (32.8%), 92 females (67.2%). The respondents had given written informed consent to participate in the study. The clinical-psychopathological method as well as the screening method of research were used: the Mini-International Neuropsychiatric Interview (M.I.N.I.), (Sheehan et al. 1998), the Hamilton Depression Rating Scale (HDRS, 1960) (Hamilton 1967), the Mood Disorder Questionnaire (MDQ) (Hirschfeld 2000).

The statistical data processing included descriptive statistical methods. The 95% CI confidence interval was constructed through the formula for small values using the Wald method with the Agresti Coull correction. Statistical significance was recognized at a probability of> 95% ($p < 0.05$). Statistical analysis was performed in Microsoft Excel 16.

RESULTS

Clinical diagnostics of the responders using ICD-10 (WHO 1992, Chapter V: mental and behavioral disorders [F00-F99]) and the Mini-international neuropsychiatric interview (M.I.N.I.) excluded the diagnosis of bipolar disorder or any affective pathology. When using the Mood Disorder Questionnaire (MDQ) for the diagnosis of mood disorders, the corresponding recommendations of the developer (Hirschfeld 2000) were considered to confirm the risk of hypomania (total score ≥7). The MDQ screening method revealed a statistically significant excess of the average values for hypomania throughout the sample (M±m: 6.46±0.44; (min=4, max=30); $p<0.05$). The total score of 64 interviewees (46.7%; 95% CI: 38.1–55.3) exceeded the threshold value (≥7).

While studying the structure of mood elevation episodes on the MDQ scale, 68 responders (49.6%; 95% CI 41.0–55.3) showed a one-stage manifestation of certain signs of mood rise. 72 interviewees (52.6%; 95% CI 43.9–58.3) reported the absence of a mood rise associated with conflicting behaviour, family problems, financial problems, etc. Moderate and serious problems in mood increase were found in 25 (18.2%; 95% CI 11.6-0.0) and 4 respondents (2.9%; 95% CI 0.0-61.2), respectively.

Complicated heredity for bipolar disorder was noted with 4 subjects (2.9%; 95% CI 0.0-5.8). 3 respondents (2.2%; 95% CI -0.3-5.8) noted the indication of medical workers that the respondents had had bipolar disorder (Table 1).

While studying episodes of declines in mood on the Hamilton Depression Scale (HAMD-17)-the average value for the entire sample was 6.51±0.39. 92 respondents (67.15%; 95% CI 59.05-75.26) showed no clinical signs of depression. According to the HDRS scale, 45 responders (32.85%; 95% CI: 24.14–40.95) showed signs of mild depression (8-13 points) (M±m: 6.51±0.39; $p<0.05$) (Table 2).

This group is dominated by indicators such as: depressive mood, stress, and mental anxiety.

In the general sample, a group of respondents (n=25; 18.2%) was identified with exceeding indicators for both hypomania and depression. Also, a group of responders (18.2%; 95% CI:11.78–24.72) manifested exceeding indicators both for hypomania and depression ("risk group"). Results shown in Table 3 and Picture 1.

DISCUSSION

The findings are consistent with the concept of subthreshold depression, which has a high prevalence in adolescence and is associated with concomitant somatic pathology and functional impairment. The findings of Crockett (2020), have shown that subthreshold depression in girls, in addition to low mood, manifested

Table 1. Structure of indicators on the MDQ scale in the entire sample

1. Has there ever been a period of time when you were not your usual self and...

Total answers for «yes»	Absolute Indicator, n=137	Relative Indicator, %	95% Confidence Interval
13	0	0.0	0.0-0.0
12	3	2.2	0.3-4.7
11	11	8.0	3.3-12.7
10	10	7.3	2.8-11.8
9	17	12.4	6.7-18.1
8	14	10.2	5.0-15.4
7	9	6.6	2.3-10.8
6	12	8.8	3.9-13.6
5	16	11.7	6.1-17.2
4	6	4.4	0.8-7.9
3	16	11.7	6.1-17.2
2	9	6.6	2.3-10.8
1	14	10.2	5.0-15.4
Total			
more than 7 answers for «yes»	64	46.7	38.1-55.3
less than 7 answers for «yes»	73	53.3	44.7-61.9

2. If you checked YES to more than one of the above, have several of these ever happened during the same period of time?

Answer Options:	Absolute Indicator, n=137	Relative Indicator, %	95% Confidence Interval
yes	68	49.6	41.0-55.3
no	69	50.4	41.7-61.9

3. How much of a problem did any of these cause you - like being able to work; having family, money, or legal troubles; getting into arguments or fights?

Answer Options:	Absolute Interval, n=137	Relative Interval, %	95% Confidence Interval
no problems	72	52.6	43.9-58.3
insignificant	36	26.3	18.7-59.0
moderate	25	18.2	11.6-24.9
serious	4	2.9	0.0-5.8

4. Have any of your blood relatives (ie, children, siblings, parents, grandparents, aunts, uncles) had manic-depressive illness or bipolar disorder?

Answer Options:	Absolute Indicator, n=137	Relative Indicator, %	95% Confidence Interval
yes	4	2.9	0.0-5.8
no	133	97.1	94.2-100.0

5. Has a health professional ever told you that you have manic-depressive illness or bipolar disorder?

Answer Options:	Absolute Indicator, n=137	Relative Indicator, %	95% Confidence Interval
yes	3	2.2	0.3-5.8
no	134	97.8	95.3-100.0

Table 2. Results of studying sub-depressive mood swings

Total indicators of the HAMD-17 scale	Absolute Indicator, n=137	Relative Indicator, %	95% Confidence Interval
0-7 points - norm	92	67.15	59.05-75.26
8-13 points - mild depressive disorder	45	32.85	24.74-40.95

Table 3. Indicators of values on the MDQ and HAMD-17 scales among the respondents of the "risk group"

	Age	MDQ	HAMD-17
Average	18.84	9.56	10.44
Standard Deviation	0.69	1.33	1.50
Median	19.00	9.00	10.00
25% quartile	18.50	8.50	9.00
75% quartile	19.00	10.50	11.00
Minimum	17.00	7.00	8.00
Maximum	20.00	12.00	13.00

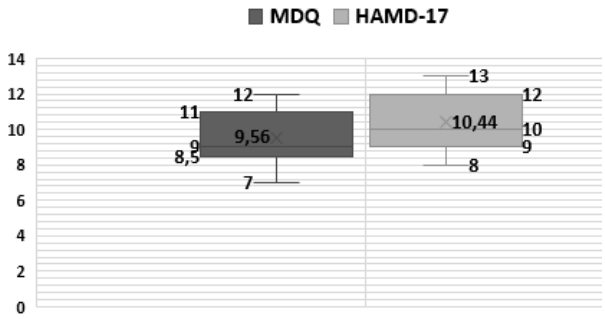

Figure1. Indicators of values on the MDQ and HAMD-17 scales among the respondents of the "risk group"

itself in the form of sleeping problems; boys had more pronounced anhedonia, impaired concentration, psychomotor retardation or agitation (Crockett et al. 2020). Van Meter et al. (2019) identified prodromal symptoms preceding the first episode of mood disorder. In more than half of the participants (51%), the affective episode was preceded by a symptom of increased energy. Researchers identified more than 40 different prenosological symptoms, which generally indicated the heterogeneity of premorbid manifestations. This study also showed that the onset of BD was gradual (Van Meter et al. 2016). The existing data on the presence of more than one prodromal symptom in the majority of patients may further facilitate the identification of more accurate clusters of signs that could serve as convincing criteria for the prognosis, prevention, and early intervention in bipolar disorder. However, according to many researchers, the use of screening techniques in non-clinical samples to identify the risk of BR causes many difficulties, since the indicators of sensitivity and specificity vary widely. Subjective assessment of the emotional state (in particular, hypomania) in adolescents is also a complicated procedure. In addition, the onset of BR is characterized by a high degree of polymorphism, which, in general, introduces additional difficulties in the diagnosis of the disease in the early stages (Georgina et al. 2017, Vázquez et al. 2010, Goodday et al. 2015).

CONCLUSION

During preclinical screening of mood elevation episodes using the MDQ scale, 46.7% of the responders exceeded threshold values; with the one-stage manifestation of hypomania signs in 49.6% of the respondents. The majority of respondents (52.6%) did not associate the rise in mood with the deterioration of habitual functioning and the appearance of problems in interpersonal relationships, which confirms the difficulties in recognizing episodes of the rise in mood both by the respondents themselves and by those around them, including close people. 32.85% of the responders showed signs of mild depression (according to the HAMD scale), corresponding, with a mild degree, to increased indicators of low mood, tension and mental anxiety. 18.2% of the interviewees exceeded threshold values for both hypomania and depression.

The discovered cyclothymia-like conditions at the preclinical stage have potential for predicting risk of their transformation into bipolar disorder which presumes further outpatient clinical and dynamic observation with the expansion of diagnostic tools and retrospective analysis of subjective and objective anamnestic data.

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Contribution of individual authors:

Natalya N. Osipova - development of research design, writing the abstract.

Leonid M. Bardensteyn - the main idea of the research, preparation of the draft abstract.

N.I. Beglyankin – accumulation of material.

M.V. Dmitriev – statistical processing of material.

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Correspondence:

Natalya N. Osipova, MD
Moscow State University of Medicine and Dentistry named after A.I. Evdokimov
of the Ministry of Healthcare of the Russian Federation
Moscow, Russia
E-mail: