International Journal of Mental Health and Addiction (2021) 19:1443–1451
https://doi.org/10.1007/s11469-020-00234-y

ORIGINAL ARTICLE

Clinical-Dynamic Features of Affective Disorders Comorbid with Alcohol Dependence

Svetlana N. Vasilieva[1] · German G. Simutkin[1] · Evgeny D. Schastnyy[1] · Nikolay A. Bokhan[1,2,3]

Published online: 24 February 2020

Abstract
Comorbidity of affective disorders (AD) and alcohol dependence (AlD) worsens prognosis and efficiency of therapy, exacerbates non-compliance in patients, and lowers their level of social adjustment. To study the influence of AlD on clinical-dynamic characteristics of AD, two groups of patients were examined and compared. The study group included 32 patients with AD and comorbid AlD. The comparison group included 31 AD patients without comorbid addictive pathology. The patients of compared groups did not have statistical differences ($p > 0.05$) according to sex, age, and AD. The Clinical Global Impression scale (CGI), Hamilton Depression Rating Scale (HDRS-17), Hamilton Anxiety Rating Scale (HARS), and Social Adaptation Self-evaluation Scale (SASS) were used. Compared to the group without comorbidity, the group of patients with comorbid AD and AlD had more frequent suicide attempts in their medical history, a high level of anxiety according to HARS, severe disorders according to CGI-S, and difficult and impaired social adaptation according to SASS; patients with recurrent depressive disorder (RDD) and bipolar disorder (BD) also experienced a larger number of affective episodes per year. AlD comorbid with AD affects clinical-dynamic indicators and levels of social adjustment in patients.

Keywords affective disorders · alcoholism · comorbidity

✉ Svetlana N. Vasilieva
vasilievasn@yandex.ru

German G. Simutkin
ggsimutkin@gmail.com

Evgeny D. Schastnyy
evgeny.schastnyy@gmail.com

Nikolay A. Bokhan
bna909@gmail.com

Extended author information available on the last page of the article

In previous decades, many studies were devoted to the comorbidity of mental disorders (Kessler et al. 2015). Both epidemiological and clinical studies revealed a high level of comorbidity of affective disorders (AD) with other mental disorders (Merikangas et al. 2011; Kessler et al. 2011). Alcohol dependence (AlD) is considered the most prevalent comorbid pathology with AD, along with anxiety disorders and personality disorders (Boschloo et al. 2011; Perugi et al. 2013; Nabavi et al. 2015). The prevalence of AlD among patients with AD exceeds several times that of the general population. According to data from Schuch et al. (2014), AlD develops more frequently in men with AD, while anxiety disorders are a more frequent comorbid pathology in women. The risk for development of AlD in those with bipolar disorder (BD) is 6–7 times higher than in the general population (Mosolov et al. 2008). Patients with AD quite frequently use alcohol to alleviate symptoms of depression and anxiety (Terra et al. 2006; Crum et al. 2013a, b). In patients with addictive pathology, the frequency of mood disorders also reaches a high level. According to results of the data collected from specialized institutions of eight European countries among patients with AlD ($n = 1767$) aged 18–64 years, depression was revealed in 43.2% of cases (95% CI 40.7–45.8) (Rehm et al. 2015). During national epidemiological survey on alcohol consumption and related states in 2001–2002 of 43,093 respondents from general population, 1643 persons with diagnosis of bipolar disorders according to DSM-IV were revealed. Of them, 54% also reported alcohol use disorder (Oquendo et al. 2010). AD and AlD heighten the risk for development of each other, but according to some authors, this pattern is noted only in males (Bulloch et al. 2012).

Many studies have attempted to reveal pathogenic interactions in the comorbidity of AlD and AD. The results that were obtained demonstrate a commonality of genetic factors in the development of both disorders (Katz and Kravitz 1996), specifically involvement of the same neurohumoral mechanisms into the pathogenesis. Personality traits such as alexithymia and social anxiety appear to be common psychological factors of alcoholism and depression (Cristal 2000). Currently, the problem of interrelations of AD and a pathological craving for alcohol remains unsolved.

Alcohol dependence can develop before and after the development of AD. Mood disorders manifest more frequently, earlier, and alcohol dependence develops already against its background. The comorbidity of AD and AlD makes it difficult to differentiate between the developed AlD on the one hand, and symptomatic alcohol use on the other hand, for instance, depressive disorders and secondary depression due to intoxication with ethanol or response of the individual to social implications of alcoholism. The most significant differential criterion of primary depression is a manifestation of depressive disorder before the development of alcoholism. Difficulties of recognition of depressive disorders with comorbidity of AlD are caused by atypical and masked character of clinical picture of depression and its alexithymic traits in patients. AD with comorbid AlD are characterized by more frequent repetition of depressive episodes, a greater number of suicide attempts, greater degree of inadaptation, and worsened prognosis (Cardoso et al. 2008; Simhandl et al. 2016; Bokhan et al. 2017). Data in the literature concerning the effects of comorbid alcoholism on the efficiency of antidepressant treatment in depressive disorders are varied. Some authors write about the negative effects of alcoholism on the treatment of depression with antidepressants (Hashimoto et al. 2015), whereas others do not confirm such effects (Iovieno et al. 2011). Abuse of alcohol also complicates the collaboration of physician and patient, by lowering the compliance of the patient.

Objective

The aims of this research are to study the cases of comorbidity of affective disorders with alcohol dependence and to assess the influence of alcohol dependence on clinical-dynamic characteristics of affective disorders. In particular, influence on the age to onset of AD, syndromal variant of depression, indices of suicidal behavior of patients, frequency of rise of affective episodes per year (in bipolar disorder and recurrent depressive disorder), level of depression according to HDRS-17, anxiety according to HARS, severity of the disease according to CGI-S, as well as to determine the level of social adaptation of this category of patients.

Material and Methods

Sixty-three patients with AD (20 women and 43 men) were examined. All patients were persons of Slavic nationality.

The median (ME) age of female patients was 45.5 years, and the interquartile range (IQR) was [35; 56]; for males the median age was 38 years, and the IQR was [31; 57]. Depending on AD, patients of the studied sample were divided as follows: BD, current depressive episode—19% ($n = 12$), recurrent depressive disorder (RDD), current depressive episode—42.9% ($n = 27$), depressive episode (DE)—27% ($n = 17$), dysthymia—11.1% ($n = 7$).

Criteria of inclusion in the study consisted of the patient signing informed consent, age of the patient between 18 and 65 years, and diagnosis according to ICD-10: (1) depressive episode, (2) dysthymia, (3) recurrent depressive disorder, and (4) bipolar disorder, current depressive episode. Criteria of exclusion involved a diagnosis of severe cognitive impairment/dementia, and severe or decompensated somatic or neurologic diseases.

The main research methods were as follows: clinical-psychopathological (the record chart of formalized description of the patient was filled in), psychometric, statistical. We assessed the severity of the disease by using the Clinical Global Expression scale-Severity (CGI-S), level of depression using the Hamilton Depression Rating Scale (HDRS-17), and level of anxiety using the Hamilton Anxiety Rating Scale (HARS). The level of quality of life and social functioning of patients in various areas of vital activity was determined with use of the questionnaire "The Social Adaptation Self-Evaluation Scale" developed by M. Bosc, A. Dubini, V. Polin in 1997. This scale included 21 items concerning behavior in the following fields: professional and household, leisure, free time activity; quality of family relationships, relationships beyond the family; estimation of own social and physical attractiveness; interest in new information (intelligent desire for learning); self-control and control over the nearest. The patients evaluated their degree of satisfaction (3—very good, 2—good, 1—poor, 0—very poor) with these areas of the vital activity. Total number of points on this scale provides total score in the range from 0 to 60. The results allow to distinguish four levels of social adaptation: I—social adaptation (0–22 points); II—complicated social adaptation (23–35 points); III—good social adaptation, detected in 80% of the population (36–45 points); and IV—very good social adaptation (46–60 points).

HRDS allows to evaluate clinically the degree of severity of depression and its dynamics in the process of specific treatment. HRDS is considered a "gold standard" in carrying-out the scientific research. Total score of 17 HRDS items: 0–7 points—norm; 8–16 points—mild depressive disorder; 17–23 points—depressive disorder of middle degree of severity; 24 and more points—depressive disorder of massive degree of severity (Zimmerman et al. 2013).

HARS is a clinical rating scale intended for measuring severity of anxiety disorders in patients.

This scale consists of 14 items; 13 items refer to manifestations of anxiety in everyday life, the 14th to manifestation of anxiety during examination. Total score of 0–7 points—norm; 8–16 points—anxiety of mild degree of severity; 17–23 points—anxiety of middle degree of severity; and 24 and more points—anxiety of massive degree of severity.

To study the influence of comorbid alcohol dependence on clinical-dynamic characteristics of AD, the examined patients were divided into two groups. The main group included 32 AD patients with comorbid AlD (9 women and 23 men), aged 44.5 years [36; 51.5]. AD were represented by BD—25% ($n = 8$), RDD—40.6% ($n = 13$), DE—28.1% ($n = 9$), and dysthymia—6.3% ($n = 2$). Duration of alcohol dependence in patients was 8 years [3.5; 11]. In 59.4% of cases ($n = 19$), patients in a state of depression changed their manner of alcohol use, in that they began to drink by themselves. Basic motives of alcohol use during development of depressive symptoms were as follows: to distract from painful/gloomy thoughts, stifle a feeling of anguish, "go out" of their problems, and cope with anxiety and insomnia.

The comparison group included AD patients without comorbid addictive pathology ($n = 31$; 11 women and 20 men), aged 45 years [32; 52]. AD were represented as follows: BD—12.9% ($n = 4$); RDD—45.2% ($n = 14$); DE—25.8% ($n = 8$); dysthymia—16.1% ($n = 5$). The compared groups were matched on sex, age, and AD ($p > 0.05$) (Fig. 1).

Within the groups studied, a comparative assessment of the following characteristics of AD was conducted: age of onset of AD, syndromal variant of depression, indicators of suicidal behavior, number of affective episodes per year (in BD and RDD), level of depression (according to HDRS-17), level of anxiety (according to HARS), and severity of the disease (according to CGI-S). The level of social adaptation in patients was also assessed (according to SASS), as well as the chronologic sequence of development of AD and alcohol dependence.

Statistical data processing was conducted by using the Statistica program for Windows (Version 8.0). For quantitative indices that did not meet the criteria of normal distribution, median, as calculated by the interquartile range—ME [IQR], the statistical significance of

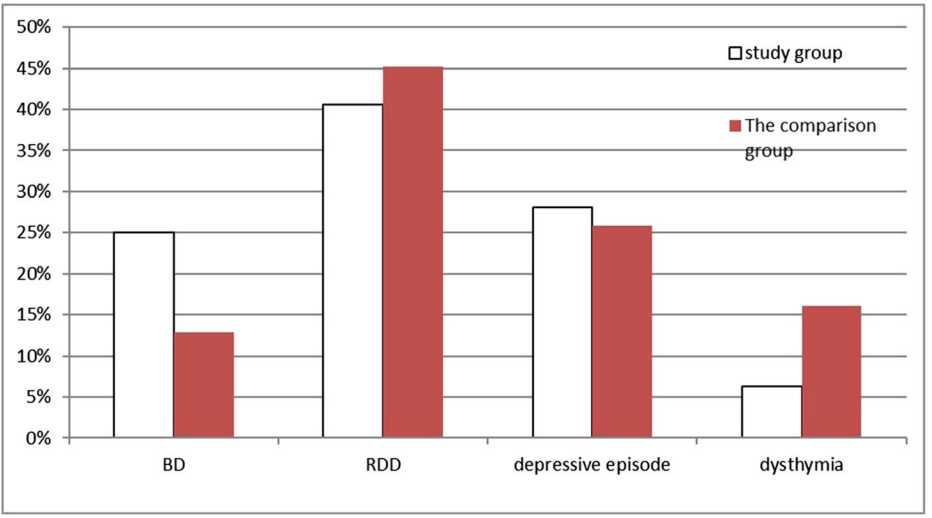

Fig. 1 Structure of affective disorders in compared groups

differences between groups was identified by Mann-Whitney's criteria. Analysis of qualitative signs was conducted through investigation of their frequencies by means contingency table with use of chi-squared test for goodness of fit. In work with small samples, *F* test was used.

Results

The age of onset of AD in the main group was 28.5 years [20; 39.5], and in the comparison group it was 30 years [26; 40]. Groups had no statistically significant differences ($p > 0.05$) according to this indicator.

The distribution of patients in the studied groups depending on the leading syndromal structure of depression is presented in Table 1. Intergroup differences according to the syndrome structure of depression were not found ($p > 0.05$).

We conducted a comparative assessment of the following indicators of suicidal behavior: availability of suicidal thoughts in the current episode, and suicide attempts in the anamnesis. Distribution of patients depending on availability of suicidal thoughts in their current state had no statistically significant intergroup differences ($p > 0.05$); in the main group, suicidal thoughts were available in the clinical picture in 65.6% of cases ($n = 21$), and in 48.4% of cases ($n = 15$) in the comparison group. In patients of the main group, suicidal thoughts became the most painful against the background of withdrawal syndrome, and acquired a frequently obsessive character. The analysis of anamnestic and follow-up data showed more frequent incidence of suicide attempts in the anamnesis of patients within the main group than in the comparison group: 25% and 6.5%, respectively ($p < 0.05$). To the rise of suicidal ideation in the main group, not only painful depressive experiences contributed most significantly but also psychotraumatic circumstances which were frequently social implications of alcoholization.

Assessment of the number of affective episodes per year in patients diagnosed with RDD and BD showed that this indicator was higher in the main group than in the comparison group: 1.5 [0.9; 2.0] and 0.9 [0.7; 1.6] respectively ($U = 200.0000$, $Z = 2.509120$, $p = 0.012$).

Degree of the severity of depressive symptoms according to HDRS-17 in both groups had no statistically significant differences (Table 2).

Table 1 Socio-demographic characteristics of the studied patients

Characteristics		% (*n*)
Sex	Female	31.7 ($n = 20$)
	Male	68.3 ($n = 43$)
Marital status	Married	61.9 ($n = 39$)
	Single	11.1 ($n = 7$)
	Divorced	14.3 ($n = 9$)
	Widowed	12.7 ($n = 8$)
Level of education	Secondary	19.1 (12)
	Secondary vocational	20.6 (13)
	Higher	60.3 (38)
Professional status	Employed	52.4 (33)
	Unemployed	33.3 (21)
	Unemployed due to mental pathology	14.3 (9)

Table 2 Distribution of patients in the main and control groups, depending on the syndromal variant of depression

Syndromal variants of depression	Main group		Comparison group	
	Abs.	%	Abs.	%
Anxiety	12	37.5	9	29.1
Dysphoric	13	40.6	8	25.8
Hypochondriac	3	9.3	4	12.9
Conversion	2	6.3	5	16.1
Adynamic	2	6.3	5	16.1
Total	32	100	31	100

Scoring according to HARS in the examined patients (Table 2) showed that there were more patients with a high level of anxiety in the main group than in the comparison group ($p = 0.03$, $\chi^2 = 4.58$).

It was revealed that the diagnosis of a severe disorder (CGI-S = 6 points) in the main group occurred more frequently than in the comparison group: 34.4% (11) and 12.9% (4), respectively ($p = 0.04$, $\chi 2 = 4.00$).

Depending on the total score obtained from the SASS, patients of the compared groups were divided into 3 subgroups: with poor social adaptation (from 0 to 22 points), with complicated social adaptation (from 22 to 35 points), and with good social adaptation (from 35 to 52 points). Assessment of the level of social adaptation in the patients studied showed that, in both the main group and the comparison group, the greatest amount of patients had complicated social adaptation (Table 3).

According to the SASS, there were fewer patients with good social adaptation in the main group than in the comparison group: 9.4% and 35.5%, respectively ($p = 0.03$, $\chi 2 = 4.79$) (Table 4).

Assessment of the chronological sequence of the onset of comorbid disorders in the main group showed that AD preceded the development of AlD in 75% of cases ($n = 24$).

Discussion

In analyzing the data in Table 1, it is noteworthy that in patients with AD, both with comorbidity of AlD and without it, anxiety and dysphoric variants of depression were revealed in more than half of the cases. According to the results of epidemiological and clinical studies, the prevalence of full-blown anxiety disorders in patients with both AD and AlD is high

Table 3 Distribution of patients in the compared groups, depending on degree of severity of depression and anxiety

	Main group, *n* (%)			Comparison group, *n* (%)		
	Mild	Moderate	Severe	Mild	Moderate	Severe
HDRS-17	2 (6.3)	22 (68.7)	8 (25)	4 (12.9)	23 (74.2)	4 (12.9)
HARS	1 (3.1)	9 (28.1)	22 (68.8)#	1 (3.2)	17 (54.9)	13 (41.9)

#$p < 0.05$, where # intergroup differences

Table 4 Distribution of patients with different levels of social adaptation in the studied groups

	Main group, *n* (%)	Comparison group, *n* (%)
Poor social adaptation	6 (18.7)	3 (9.7)
Complicated social adaptation	23 (71.9)	17 (54.8)
Good social adaptation	3 (9.4)	11 (35.5) #

# $p < 0.05$, where # intergroup differences

(Merikangas and Pato 2009; Nabavi et al. 2015; Terra et al. 2006). While patients with anxiety disorders were not included in our sample, the available symptoms of anxiety were an integral part of the clinical picture of AD and AlD. Furthermore, assessment of the severity of anxiety in groups revealed a higher level of anxiety in patients with a combination of AD and AlD, compared with patients who had AD without comorbid AlD.

The age of patients at the onset of AD with and without comorbidity of AlD had no statistically significant differences, according to the findings of our study—although data exists in the literature that supports the manifestation of AD that is comorbid with other mental disorders at a younger age (Joslyn et al. 2016). The results of our previous studies also indicated an earlier age of patients at the onset of depressive disorders comorbid with anxiety disorders, compared with depressive disorders without comorbid pathology (Vasilieva 2010).

According to current knowledge, AD and AlD are often accompanied by suicidal behavior (Morin et al. 2013; Orui et al. 2011), and the comorbidity of these disorders leads to an even greater risk of suicide (Oquendo et al. 2010). Our data on suicide attempts in the anamnesis have confirmed that comorbidity of AlD and AD increases the risk of suicidal behavior in patients.

The indices presented in Table 3 confirm data in the previous literature on the negative effects of AD and AlD on the social adaptation of patients. The combination of the above disorders leads to a more pronounced decrease in this indicator.

In most of the patients studied, AD preceded the development of AlD, which is consistent with the literature (Crum et al. 2015; Zimmermann et al. 2003). At the same time, a group of authors indicates that alcohol abuse occurs more often prior to the manifestation of AD, but not AlD (Falk et al. 2008).

Conclusions

The results of our study testify that in AD with comorbid AlD, compared to AD without AlD, there are more frequent exacerbations of affective pathology and higher levels of anxiety, disease severity, and risk of suicidal behavior. Also, patients with comorbidity of the above-mentioned disorders have a lower level of social adaptation than patients with “pure” AD. In most cases, AlD develops against the background of AD. Supported by the above data, it is possible to draw the following conclusion: AlD comorbid with AD has a negative effect on the clinical-dynamic indices and level of social adaptation in patients.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

References

Bokhan, N. A., Mandel, A. I., Kuznetsov, V. N., Rakhmazova, L. D., Axenov, M. M., Perchatkina, O. E., & Repetsky, D. N. (2017). Alkogolizm i faktory suitsidal'nosti sredi korennogo naseleniya rayonov, priravnennykh k Kraynemu Severu [alcoholism and suicidality factors among indigenous population of territories given the same status as far north]. *Suicidology, 8*(1), 68–76 (in Russ.).

Boschloo, L., Vogelzangs, N., Smit, J. H., van den Brink, W., Veltman, D. J., Beekman, A. T., & Penninx, B. W. (2011). Comorbidity and risk indicators for alcohol use disorders among persons with anxiety and/or depressive disorders: Findings from the Netherlands study of depression and anxiety (NESDA). *Journal of Affective Disorders, 131*(1–3), 233–242. https://doi.org/10.1016/j.jad.2010.12.014.

Bulloch, A., Lavorato, D., Williams, J., & Patten, S. (2012). Alcohol consumption and major depression in the general population: critical importance of dependence. *Depression and Anxiety, 29*(12), 1058–1064. https://doi.org/10.1002/da.22001.

Cardoso, B. M., Kauer Sant'Anna, M., Dias, V. V., Andreazza, A. C., Ceresér, K. M., & Kapczinski, F. (2008). The impact of co-morbid alcohol use disorder in bipolar patients. *Alcohol, 42*(6), 451–457. https://doi.org/10.1016/j.alcohol.2008.05.003.

Cristal, G. (2000). Narushenie emotsional'nogo razvitiya pri addiktivnom povedenii [impairment of emotional development in addictive behavior]. In S. Dauling (Ed.), *Psikhologiya i lechenie zavisimogo povedeniya [Psychology and treatment of dependent behavior]* (pp. 11–27). Moscow: Klass (in Russ.).

Crum, R. M., La Flair, L., Storr, C. L., Green, K. M., Stuart, E. A., Alvanzo, A. A., et al. (2013a). Reports of drinking to self-medicate anxiety symptoms: Longitudinal assessment for subgroups of individuals with alcohol dependence. *Depression and Anxiety, 30*(2), 174–183. https://doi.org/10.1002/da.22024.

Crum, R. M., Mojtabai, R., Lazareck, R., Bolton, J. M., Robinson, J., Sareen, J., et al. (2013b). Drinking to self-medicate mood symptoms: association with development of alcohol dependence. *JAMA Psychiatry, 70*(7), 718–726. https://doi.org/10.1001/jamapsychiatry.2013.1098.

Falk, D. E., Yi, H. Y., & Hilton, M. E. (2008). Age of onset and temporal sequencing of lifetime DSM-IV alcohol use disorders relative to comorbid mood and anxiety disorders. *Drug and Alcohol Dependence, 94*(1–3), 234–245. https://doi.org/10.1016/j.drugalcdep.2007.11.022.

Hashimoto, E., Tayama, M., Ishikawa, H., Yamamoto, M., & Saito, T. (2015). Influence of comorbid alcohol use disorder on treatment response of depressive patients. *Journal of Neural Transmission, 122*(2), 301–306. https://doi.org/10.1007/s00702-014-1254-7.

Iovieno, N., Tedeschini, E., Bentley, K. H., Evins, A. E., & Papakostas, G. I. (2011). Antidepressants for major depressive disorder and dysthymic disorder in patients with comorbid alcohol use disorders: meta-analysis of placebo-controlled randomized trials. *Journal of Clinical Psychiatry, 72*(8), 1144–1151. https://doi.org/10.4088/JCP.10m06217.

Joslyn, C., Hawes, D. J., Hunt, C., & Mitchell, P. B. (2016). Is age of onset associated with severity, prognosis, and clinical features in bipolar disorder? A meta-analytic review. *Bipolar Disorders, 18*(5), 389–403. https://doi.org/10.1111/bdi.12419.

Katz, R. S., & Kravitz, H. M. (1996). Fibromyalgia, depression and alcoholism: A family history study. *The Journal of Rheumatology, 23*(1), 149–154.

Kessler, R. C., Petukhova, M., & Zaslavsky, A. M. (2011). The role of latent internalizing and externalizing predispositions in accounting for the development of comorbidity among common mental disorders. *Current Opinion in Psychiatry, 24*(4), 307–312. https://doi.org/10.1097/YCO.0b013e3283477b22.

Kessler, R. C., Sampson, N. A., Berglund, P., Gruber, M. J., Al-Hamzawi, A., Andrade, L., et al. (2015). Anxious and non-anxious major depressive disorder in the World Health Organization world mental health surveys. *Epidemiology and Psychiatric Sciences, 24*(3), 210–226. https://doi.org/10.1017/S2045796015000189.

Merikangas, K. R., & Pato, M. (2009). Recent developments in the epidemiology of bipolar disorder in adults and children: Magnitude, correlates, and future direction. *Clinical Psychology: Science and Practice, 16*(2), 121–133.

Merikangas, K. R., Jin, R., He, J. P., Kessler, R. C., Lee, S., Sampson, N. A., Viana, M. C., Andrade, L. H., Hu, C., Karam, E. G., Ladea, M., Medina-Mora, M. E., Ono, Y., Posada-Villa, J., Sagar, R., Wells, J. E., & Zarkov, Z. (2011). Prevalence and correlates of bipolar spectrum disorder in the world mental health survey initiative. *Archives of General Psychiatry, 68*(3), 241–251. https://doi.org/10.1001/archgenpsychiatry.2011.12.

Morin, J., Wiktorsson, S., Marlow, T., Olesen, P. J., Skoog, I., & Waern, M. (2013). Alcohol use disorder in elderly suicide attempters: a comparison study. *The American Journal of Geriatric Psychiatry, 21*(2), 196–203. https://doi.org/10.1016/j.jagp.2012.10.020.

Mosolov, S. N., Kostyukova, E. G., & Kuzavkova, M. V. (2008). Bipolyarnoe affektivnoe rasstroystvo: diagnostika i terapiya [bipolar disorder: diagnosis and therapy]. Moscow, Russia: MEDpressinform (in Russ.).

Nabavi, B., Mitchell, A. J., & Nutt, D. (2015). A lifetime prevalence of comorbidity between bipolar affective disorder and anxiety disorders: A meta-analysis of 52 interview-based studies of psychiatric population. *EBioMedicine, 2*(10), 1405–1419. https://doi.org/10.1016/j.ebiom.2015.09.006.

Oquendo, M. A., Currier, D., Liu, S., Hasin, D., Grant, B., & Blanco, C. (2010). Increased risk for suicidal behavior in comorbid bipolar disorder and alcohol use disorders. *Journal of Clinical Psychiatry, 71*(7), 902–909. https://doi.org/10.4088/JCP.09m05198gry.

Orui, M., Kawakami, N., Iwata, N., Takeshima, T., & Fukao, A. (2011). Lifetime prevalence of mental disorders and its relationship to suicidal ideation in a Japanese rural community with high suicide and alcohol consumption rates. *Environmental Health and Preventive Medicine, 16*, 384–389. https://doi.org/10.1007/s12199-011-0209-y.

Perugi, G., Angst, J., Azorin, J. M., Bowden, C., Vieta, E., & Young, A. H. (2013). Is comorbid borderline personality disorder in patients with major depressive episode and bipolarity a developmental subtype? Findings from the international BRIDGE study. *Journal of Affective Disorders, 144*(1–2), 72–78. https://doi.org/10.1016/j.jad.2012.06.008.

Rehm, J., Allamani, A., Aubin, H. J., Della Vedova, R., Elekes, Z., Frick, U., et al. (2015). People with alcohol use disorders in specialized care in eight different European countries. *Alcohol and Alcoholism, 50*(3), 310–318. https://doi.org/10.1093/alcalc/agv009.

Schuch, J. J., Roest, A. M., Nolen, W. A., Penninx, B. W., & de Jonge, P. (2014). Gender differences in major depressive disorder: results from the Netherlands study of depression and anxiety. *Journal of Affective Disorders, 56*, 156–163. https://doi.org/10.1016/j.jad.2013.12.011.

Simhandl, C., Radua, J., König, B., & Amann, B. L. (2016). Prevalence and impact of comorbid alcohol use disorder in bipolar disorder: a prospective follow-up study. *Australian and New Zealand Journal of Psychiatry, 50*(4), 345–351.

Terra, M. B., Barros, H. M., Stein, A. T., Figueira, I., Jorge, M. R., Palermo, L. H., et al. (2006). Social anxiety disorder in 300 patients hospitalized for alcoholism in Brazil: High prevalence and undertreatment. *Comprehensive Psychiatry, 47*(6), 463–467.

Vasilieva, S. N. (2010). Clinical-dynamic characteristics of depressive disorders comorbid with anxiety disorders [supplemental material]. *European Psychiatry, 25*, 225. https://doi.org/10.1016/S0924-9338(10)70225-X.

Zimmerman, M., Martinez, J. H., Young, D., Chelminski, I., & Dalrymple, K. (2013). Severity classification on the Hamilton depression rating scale. *Journal of Affective Disorders, 150*(2), 384–388. https://doi.org/10.1016/j.jad.2013.04.028.

Zimmermann, P., Zardi, G., Lehmann, M., Zeder, C., Amrhein, N., Frossard, E., & Bucher, M. (2003). Engineering the root-soil interface via targeted expression of a synthetic phytase gene in trichoblasts. *Plant Biotechnology Journal, 1*(5), 353–360.

Affiliations

Svetlana N. Vasilieva[1] · German G. Simutkin[1] · Evgeny D. Schastnyy[1] · Nikolay A. Bokhan[1,2,3]

[1] Tomsk National Research Medical Center of the Russian Academy of Sciences, Mental Health Research Institute of Tomsk, Aleutskaya Street 4, 634014 Tomsk, Russia

[2] Department of Psychiatry, Narcology and Psychotherapy, Siberian State Medical University, Tomsk, Russia

[3] Department of Psychotherapy and Psychological Counseling of the Faculty of Psychology, National Research Tomsk State University, Tomsk, Russia