SCIENCE AND INNOVATION
INTERNATIONAL SCIENTIFIC JOURNAL VOLUME 2 ISSUE 5 MAY 2023
UIF-2022: 8.2 | ISSN: 2181-3337 | SCIENTISTS.UZ

THE PROBLEM OF COMORBIDITY OF AFFECTIVE DISORDERS AND PERSONALITY DISORDERS

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https://doi.org/10.5281/zenodo.7958187

Abstract. *The problem of studying the comorbidity of affective disorders (AR) and personality disorders (RL), the influence of this comorbidity on clinical symptoms, the course of AR, therapeutic response and the possibility of social adaptation in relevant patients has become particularly relevant in recent years. Data from Internet resources (Medline, Pubmed) served as information sources for this review.*

Keywords: *"hypomanic personality", monopolar depression, schizoid , paranoid, schizotypal personality disorder.*

The consideration of the ratio remains outside the scope of this review AR and RL in the context of an important discussion about the resolution of the manifestations of the dynamics of RL and the actual affective phases, more represented in domestic psychiatry [1, 4, 5].

Correlations of affective disorders and personality disorders. The relationship between manic-depressive psychosis (MDP) and psychopathy has been the subject of serious scientific disputes since the very inception of the concept of MDP [39]. When considering MDP as a constitutional disease, the correlation of MDP with "related " cyclothymic temperament and cycloid psychopathy was quite justified [40]. E.Kraepelin [38] metaphorically assessed the depressive temperament as a vestige of outlined depressive phases, "like how the peak of a mountain grows out of a plain similar in geological structure". At the same time, the inherited depressive temperament in some cases can transform into melancholy, or it can also act as a special form of RL that remains unchanged throughout life. The existence of the distinguished H.Tellenbach [65] special The "typus melancholicus" characteristic of patients with monopolar depression has been confirmed in some modern studies that have revealed a high frequency of this type in patients with recurrent monopolar depression [41]. As a kind of opposite of a depressive personality and, accordingly, a category more compatible with bipolar affective disorders (BAR), an attempt to distinguish the so-called "hypomanic personality" was quite justified [69]. H.S.Akiskal et al. [7] it is believed that the available data suggest that introversion is a possible premorbid trait in non-bipolar depression. In contrast, extroversion, cyclothymic and dysthymic temperaments seem to be precursors of BAR. In a recent paper by D.N.Klein et al. [35] generically presents data on the relationship between personality and depression with the allocation of a significant association between depression with both 3 common personality traits: a high level of neuroticism/ negative emotionality, a low level of extra- version/positive emotionality and kindness, and with various additional traits (for example, avoidance of harm, rumination, self-criticism) and personality types (depressive personality). In recent years, several theoretical models can be identified in the foreign literature that justify modern views on the relationship between affective (depressive spectrum disorders are more often discussed) and personality disorders: general causality, spectrum, predisposition or vulnerability model, pathoplastic and complication model [2, 3, 49]. The search for the neurobiological foundations of comorbidity of AR and RL is a logical vector for the development of theoretical ideas about the relationship of

these disorders. Generalized data indicate that the basis of biological disorders in RL may be dysfunction of the amygdala and orbitofrontal cortex, dysregulation of neurotransmitter systems (especially noradrenergic), but the cause of these disorders is not yet completely clear. These same brain structures are closely related to the pathogenesis of AR [61]. The complexity of the neurobiological interpretation of personality features lies in the fact that personality is a reflection not only of brain biology, but also of the experience of ontogenetic development [42]. In the context of the problem of comorbidity of AR and RL, the system of diagnosis of RL is of great importance, which has undergone fundamental changes with the evolution of ideas about RL. The system of categorical diagnosis of RL prevailing until recently is based on the assumption of the existence of a small number of personality types, each of which has a fundamental character. Within the framework of the American classification DSM-IV (1994), it was proposed to identify three main clusters of RL: cluster A (schizoid, paranoid, schizotypal personality disorder); cluster B (borderline, antisocial, histrionic (hysterical) and narcissistic personality disorder); cluster C (deviant, dependent, obsessive-compulsive personality disorder). However, in clinical practice, most patients with RL meet the criteria of more than one RL, that is, mixed RL is the rule rather than the exception. A meta-analytical study, which included 112 studies, showed that unspecified RL is one of the most common diagnoses of RL in scientific research and clinical practice (17-29%). In reality, this diagnosis is also used to identify mixed RL, that is, in clinical cases when the patient shows features of more than one RL, but does not meet the full criteria of any particular RL [67]. Currently, more and more attention is being paid to the dimensional (Latin dimensio - measurement, size, dimensionality) approach, in which it is assumed that RL is a measurable expression of adaptive and non–adaptive personal characteristics. The importance of this approach in assessing RL is emphasized by the results of various studies, which demonstrate the instability of the diagnosis of RL over time, which does not agree with the idea of the relative stability of personality traits and the diagnosis of RL [27, 29]. Results of The Collaborative Longitudinal Personality Disorders Study (CLPS) also do not support the opinion that the signs of RL are definitive and stable [60].

The DSM-5 RL description model, along with the categorical diagnosis of RL, suggests using a dimensional assessment of these disorders, including an assessment of the severity of personality pathology, the level of personality functioning and a description of domains/ pathological personality traits. At the same time, it is proposed to correlate the diagnosis of personality disorders and other mental disorders with one axis of diagnosis. Unfortunately, a clear separation of AR and RL is complicated by the fact that in modern diagnostic systems, in some cases, affective symptoms are included in the criteria of certain RL, which is most clearly represented in the case of borderline personality disorder (PRL) [54].

A serious discussion continues about the clinical justification for the allocation of depressive personality disorder (DRL). A number of studies support the idea that DRL is a viable diagnostic category [32]. On the other hand, it is proposed to interpret depressive traits within the framework of a comprehensive model of personality structure [57] or consider DRL a subtype of dysthymia [9]. The problem under discussion is the optimal time for the diagnosis of RL in the case of its comorbidity with AR. It is believed that depressive symptoms can "overshadow" the presentation of personality to such an extent that an up-to-date assessment of personality is impossible, therefore, verification of the diagnosis of RL is preferable during the period of euthymia, especially in the case of BAR.

At the same time, taking into account the possibility of certain personality changes due to the long course of AR, the diagnosis of RL can be more easily verified at the first episode of AR [8]. Nevertheless, P.Bajaj, P.Tyrer [10] , based on a meta-analytical review , conclude that it is practical to diagnose personality even at the time of a detailed clinical picture of depression. In any case, it is important to obtain objective data about the patient from persons who know the patient well for the correct diagnosis of RL [55]. Much attention has been paid in recent years to the development of concise RL screening tools for use in everyday clinical practice and in epidemiological studies: for example, an 8-point structured interview Standardised Assessment of Personality - Abbreviated Scale (SAPAS) [50]. According to the results of the study by S.Germans et al. [23], SAPAS-SR (self-report) or self-reporting version of IPDS (the Iowa Personality Disorder Screen) can be recommended in outpatient clinical practice for screening of RL. Epidemiology. A generalized analysis of the results of modern epidemiological studies on the prevalence of major depressive disorder (major depressive disorder), dysthymia and bipolar affective disorder (BAR) confirms a fairly high prevalence of these disorders among the population during life: 6.7, 3.6 and 0.8 per 100 people, respectively [70]. Taking into account certain differences in terminology and diagnostic criteria of DSM-IV and ICD-10, it should be noted that the concept of BDR by DSM-IV is correlated with moderate or severe depressive episode (single or within recurrent depressive disorder) according to ICD-10. A summary analysis of six modern major American and European studies suggests that the average prevalence of RL is 11.39% without significant differences in gender, that is, almost 1 in 10 people suffer RL [42]. Results of a recent large-scale international study (n=21162, China, Nigeria, South Africa, Colombia, Mexico, USA, Lebanon, Belgium, France, Germany, Italy, Netherlands, Spain) showed that the frequency of RL clusters A, B and C in the general population is 3.6, respectively%, 1.5% and 2.7%. At the same time, RL is significantly more common in men [31]. The representation of RL in outpatient and clinical samples is significantly higher than in the general population [52]. The high frequency of comorbidity of RL with other mental disorders and vice versa, as well as the importance of the clinical consequences of such comorbidity is confirmed by a number of modern studies [71]. In the American NCS-R study (the National Comorbidity Survey Replication) all three RL clusters were significantly often comorbid with a wide range of disorders along the I axis of the DSM-IV, while the greatest comorbidity was for RL from cluster B, most often the comorbidity of RL was observed with AR (38.1%). One of the possible explanations for the found connection may be that dysregulation underlying negative affect, as well as the presence of symptoms of restlessness and impulsivity in the case of RL from cluster B may be a more important factor determining the development of AR than in the case of RL clusters A or C [43]. The results of a major epidemiological study the National Epidemiological Survey on Alcoholism and Related Conditions – NESARC (USA, 43,093 adults aged 18 years and older) showed that with the lifetime prevalence of BDR at 13.23%, the frequency of BDR comorbidity with RL was the highest (30.8% of cases). Cluster C (avoidant, dependent, with the exception of obsessive-compulsive RL) revealed the strongest association with BDR [26, 30]. Similar data on the greatest association between RL from cluster C and AR has also been obtained in other major international studies [31]. A.H.Fan, J.Hassell [20] based on the analysis of data published in PubMed between 1980 and 2006 (32 studies), note that patients with BAR have a significantly higher prevalence of RL than in the general population. A high frequency of comorbidity of BAR I and RL (up to 62%) has been established in a number of studies [63]. A number of studies indicate the predominance

of cases of obsessive-compulsive, borderline and narcissistic RL in patients with BAR, and avoidant RL in monopolar patients [16]. Due to the overlap of phenomenology between BAR and RL from cluster B (especially PRL) erroneous diagnosis can be biased in any direction, so the assessment of the comorbidity of these disorders in practice can be very difficult [56]. A review of publications in Medline over a 20-year period confirms a more frequent association of PRL with BAR than with other mental disorders. In the differential diagnosis of PRL and AR, it is important to take into account whether the relevant patient has affective instability and impulsivity in the context of discrete episodes or whether these symptoms represent a permanent pattern of functioning; however, the situation may be complicated by the fact that these symptoms may be a combination of both [46].

Clinical significance of comorbidity of affective disorders and personality disorders in various studies. There are quite contradictory data regarding the clinical significance of the comorbidity of RL and BDR. On the one hand, there are separate studies that deny the presence of a significant negative effect of comorbid RL on the main clinical and dynamic characteristics of BDR, with the exception of an earlier age at the beginning of AR, the number of suicide attempts and quality of life [15]. On the other hand, most studies state the fact that the comorbidity of AR with RL has a negative effect on the course of AR and causes not only an earlier manifestation of AR and a greater number of suicidal attempts, but also more severe symptoms, an increase in the recurrence of affective disorders, and a worse prognosis. RL itself and certain dysfunctional personality traits reduce the effectiveness of treatment of current depression (both medicamental and psychotherapeutic), as well as reduce compliance [24, 51, 59].

On the other hand, most studies state the fact that the comorbidity of AR with RL has a negative effect on the course of AR and causes not only an earlier manifestation of AR and a greater number of suicidal attempts, but also more severe symptoms, an increase in the recurrence of affective disorders, and a worse prognosis. RL itself and certain dysfunctional personality traits reduce the effectiveness of treatment of current depression (both medicamental and psychotherapeutic), as well as reduce compliance [24, 51, 59]. A possible mechanism for a more unfavorable course of BDR in comorbidity with RL may be increased vulnerability to stress in the corresponding cases [28]. In recent years, data began to accumulate on the effect of comorbidity of RL on the course of BAR, which showed that RL was associated with the incompetence of such patients, a decrease in response to lithium therapy, a worse outcome of therapy, an increased risk of alcohol and other substances, and an increase in the severity of residual affective symptoms [12, 22]. Bipolar patients with comorbid RL in comparison with bipolar patients without comorbid RL have more severe symptoms of AR and a lower level of functioning [17]. P.J.Bieling et al. [12] revealed that RL from cluster A are the most significant predictors of poorer output in patients with bipolar depression. With prolonged observation of bipolar patients (about 3 years, n=648), it turned out that the presence of comorbid RL (especially cluster B) caused an increased risk of suicide in appropriate cases [45]. A review of 32 studies confirmed that bipolar patients with the presence of RL have a worse response to therapy and a more severe course of BAR than in the case of ≪clean≫ BAR [20]. However, the results of individual studies do not confirm a significant negative impact RL for the course of BAR, with the exception of an earlier age to the beginning of BAR I [8] or a higher frequency of suicidal behavior [68]. Some domestic studies [6] show that among patients with AR (n=85) , cluster C RL prevails (26%). At the same time, patients with concomitant RL were younger and had an earlier onset of the disease. In individuals with

concomitant RL from cluster C, a significantly longer course of the depressive phase was noted. According to the general clinical impression, patients with concomitant personality pathology of this type reacted worse to treatment, they were prescribed more drugs, they often retained and had more pronounced residual symptoms. The presence of personality pathology was also reflected in a higher level of anxiety and a subjectively higher assessment of the severity of depression in the corresponding patients. The issues of social adaptation and quality of life in the application to cases of comorbidity of AR and RL have been studied quite little. According to 2-year follow-up (CLPS) of psychosocial functioning disorders in patients with BDR and comorbid RL causes insufficient output and a worse level of psychosocial functioning than in the case of "pure" BDR [47]. Approaches to therapy and its features in comorbidity of affective and personality disorders Although the majority of patients with AR have psychiatric and/or medical comorbidity, the existing guidelines for AR therapy are more focused on AR itself without taking into account the existing comorbidity. Only recently, recommendations for the treatment of cases of AR and RL comorbidity have begun to appear [55].

Despite the existing ideas and research data on the impossibility of psychopharmacological influence on personal disorders [62], evidence of the effectiveness of psychotropic drugs in such clinical cases is accumulating, which is confirmed by meta-analysis 21 studies [33], according to which drug therapy aimed at clearly defined domains of symptoms may have a beneficial effect on patients with severe RL. Nevertheless, according to experts, the available evidence on the effectiveness of pharmacotherapy in comorbidity of RL and AR is still weak [62]. A concordant point of view is that with comorbidity of AR and RL, treatment of both RL and AR is required, but despite all the efforts of researchers and clinicians, the corresponding patients remain one of the most difficult groups in psychiatric practice [53]. Meta-analytical reviews confirm that RL, as a rule, have a negative impact on the outcome of treatment of both unipolar and bipolar AR. The chances of having a poor result in the treatment of current depression with comorbidity of AR with RL are on average 2-3 times greater than in the case of pure AR [11, 53, 66], which allows us to consider RL as an important predictor of chronification of affective pathology. At the same time, all variants of antidepressant treatment, except for electroconvulsive therapy, give the indicated insufficient result of therapy. However, some studies have shown that although the presence of comorbid RL was associated with a twofold increase (2.2) in the probability of non–remission in a depressive episode, this applied only to cases of the first attempt of treatment with antidepressants [14]. A recent study by P.Gorwood et al. [25], covering 8,229 outpatient patients with BDR also revealed that personality dysfunction is associated with a violation of the short-term response to treatment with antidepressants.

Early studies have shown that the presence of RL complicates the therapeutic response of depressed patients to tricyclic antidepressants [13]. There are separate studies confirming the high efficacy of SSRIs in the treatment of current depression, comorbid with RL: fluoxetine [21], sertraline and citalopram [19]. At the same time, practically in all studies, a positive effect of SSRIs is noted both on the actual depressive symptoms and on the manifestations of RL. For example, according to a placebo-controlled study, paroxetine probably has a specific pharmacological effect on characteristics such as neuroticism and extraversion, which differs from its effect on depression and complements the antidepressant effect of SSRIs [64]. The importance of psychotherapy for comorbidity of AR and RL is emphasized in a number of works, while it was found that RL does not have an unfavorable effect on the therapeutic response in patients with depression receiving

cognitive behavioral therapy. On the contrary, the presence of RL negatively affected the effectiveness of treatment for patients undergoing interpersonal therapy [34]. Combination therapy: a combination of anti- depressants and various types of psychotherapy (cognitive-behavioral, short-term psycho- dynamic, interpersonal) in depressive (both monopolar and bipolar) patients with RL is evaluated as the most effective, while it is important to focus psychotherapy not on the symptoms and complaints of the patient, but on all aspects of the patient's current relationships [36].

Despite the fact that the majority of modern literature data speaks in favor of the negative impact of AR comorbidity with RL on the results of treatment of mood disorders [55], there are certain empirical data that are not so unambiguous in assessing such a negative impact [37, 48], and even directly showing that personal pathology does not she moderated the effect of therapy AR [44]. Meta-analysis of the results of randomized controlled studies of depression pharmacotherapy (in adult outpatient patients with BDR) with comorbid RL showed that in methodically high- quality studies, the difference in the proportion of remission between groups with "pure" BDR and BDR comorbid with RL was only 3%, which is neither statistically nor clinically significant [37]. The limitation of this work is the inclusion of a small number (six) studies in the meta-analysis. Another analysis of the results of studies that are correct from the point of view of design also does not confirm the negative effect of comorbid RL on the outcome of AR treatment (especially when evaluating short-term results), which can be interpreted as a clinically optimistic approach when assessing the prospects of therapy in the case of comorbidity of AR and RL [51].

In his review of foreign literature N.G.Garanyan [2, 3] expresses the opinion that there is a problematic situation in the research of personal factors of therapeutic resistance in the treatment of depression. It seems that individual personality traits and certain RL can act as counter - therapeutic (reducing the effectiveness) factors in some types of depression treatment (for example, long -term drug treatment with antidepressants, psychodynamic and interpersonal forms of psychotherapy), not being such for other forms of therapy (for example, for short- term drug treatment, ECT, cognitive-behavioral psychotherapy). Therefore, further research is needed to clarify which RL or dysfunctional personality traits in which forms of therapy act as counter–therapeutic agents. Thus, cases of comorbid combination AR and RL in clinical practice are quite frequent, which must be taken into account when diagnosing AR, especially in the presence of resistance to ongoing therapy. RL can have a significant impact on the main clinical and dynamic characteristics of AR and the effectiveness of psychopharmacotherapy and psychotherapy, as well as increase the risk of suicidal behavior in appropriate clinical cases. Therapy of patients with comorbid AR and RL should be comprehensive and take into account current recommendations regarding the treatment of both AR and RL.

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