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The Renaissance of Psychedelics in Modern Psychiatry: a New Breakthrough or the Myth of a “Magic Bullet”?

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ABSTRACT

In recent years, there has been a significant surge of interest in psychedelic research. These studies encompass both neuroscience and their potential clinical applications. This phenomenon, often referred to as the "Psychedelic Renaissance", includes studies on compounds such as psilocybin, MDMA, DMT, and LSD used for the treatment of depression, post-traumatic stress disorder, anxiety, and obsessive-compulsive disorders. These substances offer a novel treatment paradigm due to their rapid therapeutic effect and their ability to induce long-term mental state changes, particularly when supported by appropriate psychotherapeutic interventions. At the same time, many studies that praise psychedelics remain methodologically weak, limiting integration of these compounds into medical practice.

This article provides a discussion of current perspectives on psychedelics and a critical review of existing scientific evidence. It explores the historical context of psychedelic use, including early research and the psychedelic therapy methodology with ketamine developed in Russia by Professor E.M. Krupitsky. Key challenges are discussed in detail, including the lack of adequate placebo controls and standardized dosing, small sample sizes, and the significant influence of contextual factors that may confound study outcomes. Based on this analysis, the author encourages Russian psychiatrists to critically assess the available data and develop a balanced approach to the use of psychedelics in therapy, considering the quality of the evidence base and the specifics of the Russian regulatory framework.

Keywords: psilocybin; LSD; serotonin receptors; drug therapy.

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Ренессанс психоделиков в современной психиатрии: новое слово или миф о «волшебной пуле»?

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АННОТАЦИЯ

В последние годы отмечается значительный рост интереса к исследованиям психоделиков. Эти исследования охватывают как нейронауку, так и их потенциальное клиническое применение. Данное явление, которое часто называют «ренессансом психоделиков», включает в себя исследования таких соединений, как псилоцибин, MDMA, DMT и LSD, применяемых при депрессии, посттравматическом стрессовом расстройстве, тревожных и обсессивно-компульсивных расстройствах. Перечисленные вещества предлагают иную парадигму лечения благодаря быстрому наступлению терапевтического эффекта и способности стимулировать долгосрочные изменения психического состояния, поддержанные определённым психотерапевтическим сопровождением. В то же время многие исследования, восхваляющие психоделики, остаются методологически слабыми, что препятствует интеграции этих средств в медицинскую практику. Данная статья предлагает обсуждение современных представлений о психоделиках, а также критическое рассмотрение существующих научных данных. Анализируется исторический контекст использования психоделических средств, включая ранние исследования, в том числе методику психоделической терапии кетамином, разработанную в России профессором Е.М. Крупицким. Подробно рассматриваются существующие сложности, такие как отсутствие адекватных плацебо и стандартов дозирования, малые размеры выборок и сильное влияние контекстуальных факторов, которые могут исказить результаты. На основе этого автор призывает российских психиатров к критичному осмыслению данных и к готовности выработать взвешенное отношение к применению психоделиков в терапии, исходя из качества доказательной базы и особенностей российской нормативно-правовой базы.

Ключевые слова: псилоцибин; ЛСД; серотониновые рецепторы; лекарственная терапия.

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Хәзерге заман психиатриясендә психоделиклар ренесансы: яңа сүзме, әллә “тылсымлы ядрә” турындагы уйдырмамы?

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Соңгы елларда психоделикларны өйрәнү-тикшерү белән кызыксыну арта бара. Бу тикшеренүләр нейрофәнне дә, аларны потенциаль клиник кулланууны да үз эченә ала. Еш кына «психоделиклар ренессансы» дип атала торган әлеге күренеш үз эченә депрессия, травмадан соңгы стресс тайпылышлары, шомлану һәм обсессив-компульсив тайпылышлар вакытында кулланыла торган псилоцибин, MDMA, DMT һәм LSD кебек кушылмаларны өйрәнүне үз эченә ала. Санап үтелгән матдәләр, тиз арада дәвалау таэсиренә һәм психик халәтне озак вакытларга көйләү-стимуляцияләү сәләтенә ия булганлыклары белән, дәвалауның аерым бер, башка парадигмасын тәкъдим итәләр. Шул ук вакытта психоделикларга мактау яудырган күп кенә тикшеренүләр методология ягыннан көчле түгел, бу исә аларны медицина практикасы кертеп җибәрергә мөмкинлек бирми.

Әлеге мәкалә психоделикларны заманча кузаллау турында фикер йөртергә, булган фәнни мәгълүматларга тәнкыйть күзлегеннән карарга тәкъдим итә. Психоделикларны кулланууны тарихи контекстта (профессор Е.М. Крупицкий тарафыннан төзелгән кетамин белән дәвалау методикасын; шулай ук элек булган башка тикшеренүләрне дә кертеп) өйрәнү анализлана. Адекват плацебо һәм доза стандартлары булмау, контекстуаль факторларның тәэсире көчле булу кебек катлаулыклар җентекләп өйрәнелә. Шуларга нигезләнеп, автор Россия психиатрларын булган фәнни мәгълүматларга тәнкыйть күзлегеннән карарга, психоделикларны дәвалау процессында кулланганда, дәлилләргә һәм Рәсәй хокук-норматив базасы үзенчәлекләренә таянып эш итәргә өнди.

Төп сүзләр: псилоцибин; ЛСД; серотонин рецепторлары; дарулар белән дәвалау.

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BACKGROUND

Modern psychiatry faces significant challenges when treating certain mental disorders that respond poorly to traditional therapeutic approaches, such as depression, post-traumatic stress disorder (PTSD), and chronic anxiety disorders. In this context, there is a growing interest in psychedelics, substances that induce altered perception and states of consciousness and are associated with rapid and sustained changes in patients' mental health [1]. This trend, referred to as the *Psychedelic Renaissance*, has been accompanied by a surge in research exploring the use of psilocybin, MDMA, DMT, LSD, and other compounds for the treatment of depression, PTSD, and anxiety disorders [2].

In 2023, the Australian Therapeutic Goods Administration — the regulatory authority for pharmaceuticals, similar to the U.S. Food and Drug Administration (FDA) — decided to reclassify psilocybin and MDMA as Schedule 8 controlled substances. This reclassification permits authorized psychiatrists to use these compounds for the treatment of treatment-resistant depression and PTSD, respectively [3]. This shift presents both significant opportunities and challenges for the professional psychiatric community in Australia. In several Latin American countries, the use of DMT in the form of ayahuasca has been approved for therapeutic purposes, particularly for combat veterans with PTSD [4].

One reflection of this trend was a 2021 article in The New York Times, which stated that psychedelics will "change psychiatry", heralding a "psychedelic revolution" [5]. Such forecasts contribute to growing enthusiasm both in the society and among professionals. However, they may also lead to inflated and unrealistic expectations, which, if excessively exaggerated, could ultimately result in disappointment and setbacks.

Psychedelics are not new to psychiatric practice; they were actively studied and used in psychotherapy as early as the mid-20th century. In Russia, a significant contribution to the development of psychedelic therapy was made by Professor Krupitsky et al., who described a ketamine-assisted psychotherapy method for the treatment of substance use disorders [6]. At present, psychedelics have once again become the focus of scientific and clinical interest as potentially effective treatments for treatment-resistant depression, PTSD, and other psychiatric disorders. However, their use in psychiatry remains highly controversial, as most psychedelic research faces methodological limitations, which hinder the reliable integration of these findings into clinical practice.

HISTORICAL BACKGROUND AND CONTEMPORARY RESEARCH

The use of psychedelics in psychotherapy has a history spanning several decades. In the mid-20th century, psychedelics gained scientific and clinical interest as potential psychotherapeutic agents. Research was conducted on their application in depression, anxiety disorders, obsessive-compulsive disorder, and substance use disorders. In Russia, a significant achievement was the work of Professor Krupitsky et al., who described a ketamine-assisted psychedelic therapy method [6]. Their studies demonstrated that ketamine therapy is effective in the treatment of alcohol and other substance use disorders, as well as neurotic disorders, suggesting a broad therapeutic potential for psychedelics.

Recent studies have reaffirmed the efficacy of psychedelics in the treatment of depression and PTSD. For example, in 2018, FDA characterized psilocybin as a "breakthrough therapy" for treatment-resistant depression [7]. Clinical data suggest that psilocybin, administered in two sessions, can induce long-term improvements that persist for several months. Similar effects have been observed with other psychedelics. In Brazil, studies on ayahuasca in patients with depression and PTSD demonstrated an improvement in symptoms within one week of administration, with effects lasting up to three weeks [8, 9]. Randomized trials have also shown a sustained reduction in anxiety symptoms in patients with cancer following LSD administration [10]. These findings suggest that psychedelics may offer rapid and long-lasting therapeutic effects, particularly in conditions where conventional treatments often prove ineffective.

CHALLENGES AND LIMITATIONS IN PSYCHEDELIC RESEARCH

Despite promising results, psychedelic research often encounters methodological challenges that raise concerns about efficacy and clinical applicability in psychiatry. Below are some of the key issues.

Lack of an adequate placebo control. Psychedelics produce distinct and intense effects, making it difficult to mask their administration, thereby compromising placebo control and blinding procedures in clinical trials. The use of niacin or diphenhydramine (Benadryl) as a placebo has proven ineffective [11]; participants easily recognize the absence of psychedelic effects, leading to bias and reduced study validity. Similarly, administration of low doses of psychedelics as a placebo is problematic, as even low doses can induce mild therapeutic effects, which are not true placebo responses in the classical sense [12].

Uncertainty in dose optimization. Most studies lack standardized dosing protocols that ensure maximum therapeutic benefit while minimizing adverse effects. The analysis shows that effective doses vary, and the absence of dosing standardization complicates result replication and cross-study comparisons. Several trials have demonstrated a correlation between higher psychedelic doses and more pronounced therapeutic effects; however, dosage should be individualized to account for patient-specific factors and tolerability.

Sample homogeneity and previous psychedelic use. Many studies are conducted on participants with previous psychedelic experience [13]. Recruitment often occurs

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through online psychedelic communities, which may attract individuals with positive past psychedelic experience, whereas those with negative experience may avoid such studies. Additionally, most study samples primarily consist of middle-aged participants of European descent, resulting in homogeneous cohorts and limited generalizability to broader patient populations.

Psychotherapeutic support as an integral study component. Nearly all psychedelic trials incorporate psychotherapy, which itself may significantly influence treatment outcomes. It is well established that psychotherapy — especially cognitive-behavioral therapy — effectively reduces symptoms of depression and anxiety for several months [14]. This makes it challenging to isolate the effects of psychedelics from those of psychotherapy. This issue cannot be resolved within a strict *either/or* framework. To assess the therapeutic value of psychedelics, it is necessary to determine the extent to which their effects depend on psychotherapeutic support and to explore how they interact with various psychotherapy modalities.

BIOLOGICAL MECHANISMS OF PSYCHEDELIC ACTION

At the biological level, psychedelics primarily bind to serotonin receptors, particularly 5-HT2A, leading to the activation of specific brain regions and modulation of neuroplasticity [15]. It is hypothesized that 5-HT2A receptor stimulation increases levels of brain-derived neurotrophic factor (BDNF), potentially promoting neuronal growth and synaptic remodeling. However, findings remain contradictory. Studies indicate that while 5-HT2A activation in the cerebral cortex elevates BDNF levels, it reduces them in the hippocampus, potentially exerting negative effects on cognitive function [16]. Additionally, 5-HT2B receptor activation, associated with certain psychedelics, has been linked to cardiovascular risks [17].

Furthermore, the psychotropic effects of psychedelics are often attributed to altered information processing and neural network desynchronization, which may allow patients to temporarily disengage from maladaptive cognitive and behavioral patterns [18]. While these mechanisms suggest considerable therapeutic potential, further research is necessary to elucidate the long-term consequences of psychedelic-induced neural modulation.

ROLE OF PSYCHEDELICS IN THERAPEUTIC PRACTICE: DOES IT MEAN INTEGRATION OR PARADIGM SHIFT?

A key question surrounding psychedelics is whether they should be integrated into existing therapeutic frameworks, or if they necessitate a fundamental paradigm shift in the treatment of mental disorders. In English-language sources, psychedelics are frequently described as a "new paradigm" in psychiatry. However, this perspective remains disputable. Many researchers argue that psychedelics should be viewed as a complementary tool within established psychotherapy and psychopharmacology, rather than a revolutionary approach. For example, the REBUS model, proposed by Carhart-Harris and Friston [19], conceptualizes the action of serotonergic psychedelics as a temporary "flattening" of the brain's attractor landscape. This model suggests that psychedelics may reduce the stability of pathological cognitive and emotional states, facilitating transitions toward healthier mental states. However, since the REBUS model does not explicitly define these pathological attractors, it provides a theoretical rather than mechanistic framework for understanding psychedelic-induced therapeutic change and requires further empirical validation.

Psychedelics may function as psychotherapeutic adjuncts, enhancing perception, introspection, and emotional processing. This perspective broadens the biological paradigm of psychiatry, emphasizing the importance of taking into account set and setting and advocating for the integration of the biopsychosocial model in psychedelic-assisted therapy. Furthermore, psychedelics demonstrate potential transdiagnostic effects, suggesting that therapeutic protocols could be developed based on shared pathophysiological mechanisms rather than diagnostic categories.

However, it should be emphasized once again that by referring to psychedelic therapy as "new" we risk repeating historical missteps from the 1950s and 1960s, while simultaneously overlooking the substantial empirical data accumulated during that era. Many of the concepts and ideas currently being revisited as "innovative" were previously investigated and critiqued decades ago. For instance, early psychedelic researchers emphasized the importance of set and setting in shaping therapeutic outcomes — a principle that remains critical to optimizing psychedelic therapy today.

CONCLUSION

The *Psychedelic Renaissance* has reinvigorated psychiatry, offering potential solutions for treatment-resistant mental disorders. However, the lack of high-quality evidence, methodological challenges in research, and unclear biological mechanisms necessitate a cautious and evidence-based approach. Russian psychiatrists should evaluate psychedelic therapy through a critical lens, adhering to rigorous scientific standards and established principles of evidence-based medicine. The question of whether psychedelics represent a powerful therapeutic tool or if their effects are overestimated remains unresolved. Further well-designed studies, free from methodological bias and cognitive distortions, are needed to determine their true clinical value.

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