Personalized Psychiatry and Neurology

Review

Modern Psychiatry: from Theory to Practice

Nataliia N. Petrova

St. Petersburg State University, Saint Petersburg, Russia;
* Correspondence: petrova_nn@mail.ru

Abstract: In this review scientific papers published on eLibrary, PubMed, Google Scholar were searched and analyzed for all time till 2024 year on the problem of neuropsychiatry, translational neuro-science, biomarkers. The issues of precision psychiatry and targeted therapy of mental disorders are considered. The ways of bridging the gap between theoretical and practical (clinical) psychiatry are discussed.

Keywords: *translational neuroscience; neuropsychiatry; biomarkers*.

Citation: Petrova, N.N. Modern Psychiatry: from Theory to Practice. *Personalized Psychiatry and Neurology* **2024**, *4 (4)*: 11-25. https://doi.org/10.52667/2712-9179-2024-4-4-11-25

Chief Editor: Nikolaj G. Neznanov, D Med Sci, Professor

Received: 30 November 2024
Accepted: 2 December 2024
Published: 15 December 2024

1. INTRODUCTION

There is a remarkable need for progress in the practice of clinical psychiatry. Mental illness and substance use disorders are the leading cause of disability worldwide with major depressive disorder being the most common cause [1]. According to the World Health Organization, psychiatric disorders affect a significant portion of the global population, with an estimated one in four individuals experiencing a mental health condition at some point in their lives. Suicide is a leading cause of death in young adults [2], and severe and enduring mental illness is associated with a reduction of lifespan of about a decade [3].

Mental disorders also magnify the risk of multiple other chronic conditions including heart disease, as reported by Teng et al. [4]. Psychiatric disorders represent a significant social problem worldwide, given their profound impact on both the individual and society. Despite growing awareness of the need for targeted and personalized treatments, there is a gap between research and clinical practice, with pharmacological management often being empirical and based on outdated biological hypotheses.

While modern psychotropics have fewer adverse effects than earlier drugs, they are still often unfocused in their mode of action. This suggests that current treatments may not be fully effective or tailored to the individual needs of patients. Current treatments are effective in only 40–60% of individuals [5], providing symptomatic relief as opposed to a cure. Other limitations include debilitating side effects such as oversedation and delayed onset of therapeutic efficacy [6]. Despite this urgent medical need, no drugs with fundamentally new mechanisms of action have emerged for over two decades [7] and many pharmaceutical companies have abandoned their neuropsychiatric R&D initiatives altogether [8]. So, it is widely recognized that clinical practice in psychiatry has not fundamentally changed for over half a century [9, 10]. It is obvious that there is a pressing need for innovative approaches to psychiatric treatment, including the development of novel biomarkers that can help identify the underlying causes of psychiatric disorders and guide the development of targeted more effective and personalized treatments [11].

2. MATERIAL AND METHODS

Scientific papers published on eLibrary, PubMed, Google Scholar were searched and analyzed for all time till 2024 year. Such keywords as translational neuroscience, neuro-psychiatry, biomarkers were used.

3. RESULTS

3.1. Neuroscience

The term "neuroscience" was proposed in the 1960s by Francis O. Schmitt to refer to a collection of disciplines that study the functioning of the nervous system. Today, it includes psychiatry, neuroanatomy, neurochemistry, neurophysiology, neuropsychology, molecular biology, biochemistry, physics, cellular and evolutionary biology, developmental biology, engineering, informatics, ethology, psychology, and neuroeconomics. While clinicians are immersed in practice, scientists are deeply involved in studying fine mechanisms using models that can only partially reproduce real manifestations of psychiatric disorders, and the possibilities for dialogue between these two groups of people remain limited. Neuroscience can be simply described as scientific investigation of the central nervous system and its functions. It is a multidisciplinary area of science that connects various disciplines such as physiology, anatomy, molecular biology, cytology, psychology, physics, computer science, chemistry, medicine, statistics, mathematical modelling and many more [12-14]. The main goal of neuroscience is understanding the biological basis of the functioning of central nervous system, and this effort has been described by Eric Kandel, the renowned master of neuroscience, as the “epic challenge” of biological sciences [15]. Despite significant progress in recent decades, there is still much to be learned about how the brain works, and researchers continue to make new discoveries that shed light on its functions and mechanisms. The connections between neuroscience and other fields are crucial to understanding the brain. For example, advances in computer science and mathematics have enabled the development of new imaging techniques and statistical methods for analyzing brain data. Similarly, advances in molecular biology and genetics have helped to understand the genetic and molecular mechanisms that underlie brain function and behavior. Samancı Marangozoğlu et al. highlight the significant advancements in neuroscience research over the 20th century, which have enabled a more comprehensive understanding of the central nervous system (CNS). The convergence of various disciplines, including molecular biology, electrophysiology, neuroimaging, genetics, genomics, and computational neuroscience, has revolutionized the field [16].

Genetic studies have played a pivotal role in unraveling the genetic basis of psychiatric disorders. Genome-Wide Association Studies (GWAS) have identified numerous genetic variants associated with various psychiatric conditions, shedding light on the bio-logical pathways involved [17]. These findings provide valuable clues about disease etiology, potential therapeutic targets, and personalized treatment approaches. Additionally, advancements in gene-editing technologies, such as CRISPR-Cas9, offer exciting possibilities for studying the functional consequences of genetic variants and exploring potential interventions [18]. Neuroimaging techniques have revolutionized our understanding of the brain and its relevance to psychiatric disorders. Functional Magnetic Resonance Imaging (FMRI), Positron Emission Tomography (PET), and Electroencephalography (EEG) enable researchers to investigate the neural correlates of psychiatric symptoms, identify biomarkers, and monitor treatment response [19, 20]. Neuroimaging studies have provided valuable insights into the alterations in brain structure, connectivity, neurotransmitter systems associated with various psychiatric disorders. Integration of multimodal imaging approaches and advanced analytical methods, such as machine learning algorithms, enhance the ability to characterize and classify psychiatric disorders [21]. Advancements in molecular

biology approaches have deepened our understanding of the molecular mechanisms underlying psychiatric disorders. Studies focusing on gene expression, epigenetic, and protein signaling pathways have revealed critical information about the dysregulation of biological processes in psychiatric conditions. For instance, investigations into the role of epigenetic modifications, such as DNA methylation and his-tone modifications have illuminated the influence of environmental factors on gene expression and their potential contribution to psychiatric vulnerability [22]. By understanding the intricate interplay between genetic factors, brain structure and function, and molecular mechanisms, researchers can develop more targeted and personalized treatments. This approach can help identify subgroups of patients who are more likely to respond to specific interventions, leading to improved treatment outcomes and better patient care [23].

Understanding and management of neuropsychiatric diseases requires an integrated and interdisciplinary approach. The investigation of neuropsychiatry highlights the complex interaction between shared neurobiological pathways, similar clinical manifestations, and the difficulties associated with conventional diagnostic paradigms in psychiatry and neurology. It is crucial to adopt collaborative care models that recognize the com-mon pathways and clinical manifestations to connect the fields of psychiatry and neurology. To advance research and practice in the dynamic field of neuropsychiatry, it is important to promote a culture of multidisciplinary collaboration, improve training pro-grams, and support integrated care models. In this way the field can make progress, facilitating the development of individualized methods for diagnosis and treatment [24].

Neuropsychiatry combines the knowledge and expertise of psychiatry, neurology/neuroscience, and neuropsychology to provide a comprehensive approach to under-standing and treating complex patients with mental health issues. This interdisciplinary field, skillfully blending elements of neurology and psychiatry, has evolved significantly over the past century. Such a combined expertise is extremely helpful in the formulation and management of complex patients, especially patients in whom neuropathology is a primary cause or mechanism of psychopathology. Complex psychopharmacological cases may also benefit from expert neuropsychiatric management. Progress along this path will depend on both a careful synthesis of diverse findings but also the critical evaluation of ever-accumulating clinical and research data. Developing a clear and accessible conceptual framework for neuropsychiatry remains a paramount goal. It integrates insights and methodologies from diverse areas, such as behavioral neurology and biological psychiatry, evolving through rigorous debate and gradual refinement within the medical and scientific communities [25].

The future trajectory of neuropsychiatry relies on its capacity to fuse the insights of neuroscience seamlessly with the wisdom of psychosocial sciences and philosophy. Such a unification promises to transform our approach to mental health care, potentially elevating the quality of life for those living with neuropsychiatric disorders significantly. Furthermore, the incorporation of phenomenology and the philosophy of mind into neuropsychiatry presents a fertile ground for innovation. While there are hurdles due to the fluid nature of the field's boundaries, overcoming these challenges can significantly enrich our understanding of patients' subjective experiences and the nuances of mental disorders [26].

3.2. Precision psychiatry

The emergence of precision psychiatry is obvious. Precision medicine is successful in many areas and the concept of precision medicine is well defined in research disciplines, such as oncology and infectious diseases, where it is conceptually linked to molecular biological properties of the disease (or causative agent) that are relevant for the drug's mechanism of action. But 'precision therapy' is still an emerging field in psychiatry. Developing innovative therapies for psychiatric disorders will require new approaches

and a more nuanced understanding of the biology of these disorders. Yatham et Thibaut emphasize the need for a multifaceted and interactive approach to treatment and note that even incremental improvements can lead to significant clinical benefits over time [27].

The population of psychiatric patients are separated into various groups by specific biomarkers. Multi-omics and/or neuroimaging datasets are available to represent these specific biomarkers within the context of precision psychiatry. Psychopharmacotherapy can be individualized based on the use of appropriate or proportional genetic biomarkers and/or imaging techniques [28]. There is a growing number of genetic and neuroimaging biomarkers that may improve the ability to predict treatment response [29]. For example, genetic biomarkers such as gene expression profiles and single nucleotide polymorphisms (SNPs) can be used to assess adverse events and response to antidepressant therapy [30].

Recently, there has been significant progress in the areas of machine learning, artificial intelligence, pharmacogenomics, multi-omics, neuroimaging, and precision psychiatry [31-33].

The identification of biomarkers, genetic variants, and specific patient characteristics can help guide treatment selection and predict individual responses to medications. Genetic research has played a significant role in precision psychiatry, with studies uncovering genetic variations associated with treatment response and susceptibility to psychiatric disorders. Pharmacogenomics is one of the research fields to further advance precision psychiatry, where pharmacogenomics is defined as the study of how genes and their functions can influence a person's response to medications, drug metabolism, efficacy and adverse effects. GWAS have identified genetic markers that can predict response, such as polymorphisms in genes involved in drug metabolism and neurotransmitter pathways [34]. Additionally, advances in pharmacogenetics have provided valuable insights into the influence of genetic factors on drug efficacy and adverse reactions [35]. Incorporating genetic information into treatment decision-making can enhance treatment outcomes and minimize potential adverse effects. Furthermore, the identification of biomarkers has opened new avenues for precision psychiatry. Biomarkers, including neuroimaging measures, blood-based molecular markers, and physiological indicators, hold promise for predicting treatment response and monitoring disease progression. For instance, neuroimaging studies have revealed specific brain circuitry alterations associated with different psychiatric disorders, offering potential targets for personalized interventions [36]. Additionally, blood-based biomarkers, such as inflammatory markers and neuro trophic factors, may provide valuable insights into disease mechanisms and treatment response [37]. Machine learning algorithms have demonstrated the ability to analyze complex clinical data and identify subgroups of patients who are more likely to respond to specific treatments or require alternative interventions [38].

In terms of neuroimaging-driven and multi-omics-driven techniques, it is of great interest that future prospective clinical trials concerning artificial intelligence and machine learning approaches to forecast medical outcomes and/or drug treatments may contribute to feasible explanations in public health as well as global health. Therapies for psychiatric disorders must take into consideration of the interactions between neuroimaging datasets and multi-omics as well as epigenetics and gene–environment interactions [39]. The pre-treatment prediction tests involving artificial intelligence and machine learning-based precision psychiatry and pharmacogenomics would become a reality in individual-specific clinical care [40, 41]. The guideline of an artificial intelligence and machine learning approach is comprised of the following three steps: we firstly build the predictive model from the initial input data in the beginning step, then secondly fine-tune and gauge the predictive model in the intermediate step, and thirdly utilize the predictive model for presenting an estimated outcome in the final step [42]. The recent advancements in da-ta-intensive health sciences and single cell

sequencing technologies could assuredly trigger new artificial intelligence and machine learning software frameworks, such as deep learning algorithms [43], for population health, public health, and global health [44, 45].

The integration of genetic studies, neuroimaging techniques, and molecular biology approaches holds great potential for precision psychiatry. So, precision psychiatry is an integrative approach, one that pulls together the scientific foundation of the discipline and recent neuroscientific, technological, and computational advances and directs them at closing the gap between discovery and clinical translation. Neuroscience insights offer new ways to account for the heterogeneity of mental disorders and to consider treatment selections. These insights link clinical phenotypes to an individual's biotypes, opening the possibility that treatments can be adapted and selected to target specific clinical features and biotypes. For precision psychiatry be useful to clinicians, it must be driven by clinical translational goals. Clinical decision-making is complemented by measures that help to diagnose clinical biotype profiles and tailor treatments to these profiles. Realizing this perspective will involve an integration of findings from basic and clinical neuroscience, population-level data from clinical practice and new forms of clinician-researcher partnership. Precision in the context of psychiatry is an approach that focuses on under-standing the underlying neurobiological mechanisms that cause the symptoms of psychiatric disorders. Using this understanding, we can develop treatments, which will ad-dress previously untreatable aspects of psychiatric disorders by providing more specific symptom control and altering the trajectory of the disease. Rather than focusing on diagnostic categories, the emphasis is on solutions that span pharmacological, behavioral, neuromodulation, and novel therapeutics and can alter the specific biological processes that lead to the manifestation of symptoms and phenotypes.

Precision psychiatry can be described by three terms: stratified medicine, personalized medicine, and precision mental health. "Stratified medicine" focuses on identifying subgroups of patients who will benefit from treatments as a step toward a fully personalized approach. "Personalized medicine" focuses on harnessing new advances in genomics to select treatment options with the greatest likelihood of success, now it is being expanded to include neuroscience-based assessments. "Precision mental health" is a new frontier, expanding on precision medicine to a wider concept of health and prevention. There are three main goals for developing a precision approach to psychiatry [46]: 1) precise classification (that is, a specific understanding of the pathophysiology of each individual patient) hinges on the identification of subtype profiles that map neurobiology and symptoms, taking into account life experience, and are relevant to guiding treatment choices; these profiles and biotypes may align with our current diagnostic categories, but may also cut across them or represent new subgroups; 2) precise treatment planning (tailoring treatment plans in a personalized manner); although many effective treatments are available, treatment selection is not linked to a precise understanding of an individual patient's neurobiology; 3) precise prevention (targeted and tailored prevention strategies).

So, precision psychiatry affirms to provide novel diagnostic and therapeutic approaches for treatment prediction, prognosis prediction, diagnosis prediction, and the detection of potential biomarkers in an individual-specific and treatment-specific manner in psychiatric disorders [47, 48]. It means that medical decisions and practices are adapted to specific patients [49]. Furthermore, individual-oriented results will be progressively generated towards the fields of population health, public health, and global health in light of the pressing needs of innovative diagnostics in precision psychiatry and pharmacogenomics for psychiatric disorders [50, 51]. Integrating genetics, biomarkers, and clinical profiles can guide the development of tailored interventions, leading to improved treatment outcomes. Biological and/or clinical implications can serve as decision support aides for treatment prediction, prognosis

prediction, and diagnosis prediction in translational and precision psychiatry [38]. Precision psychiatry, developing a more comprehensive understanding of the physiological underpinnings of mental illness, has the potential to revolutionize psychiatric care [52].

3.3. Psychotropic drug development

There is currently no significant progress in the search for new treatments for mental illness. There are many challenges along the path to the approval of new drugs to treat CNS disorders, one of the greatest areas of unmet medical need with a large societal burden and health-care impact. The concepts of target identification and validation are considered promising. Unfortunately, in the last decades, not much progress has been made in finding new treatments for CNS diseases and few CNS drug approvals have succeeded. Selecting the most biologically plausible molecular targets that are relevant to the disorder is a critical first step to improve the probability of success [53].

The well-established concepts of target identification and validation are at the core for drug discovery and development programs. Drug target finding has been pursued using GWAS methods, but this has not been proven successful for CNS diseases yet. Various potential issues with the GWAS approach are listed and may dampen the validity of using GWAS for target finding. Two recent alternative methods for target finding are dis-cussed. One approach is related to the Research Domain Criteria (RDoC) initiative in which different functional domains are connected with neurodevelopmental and biological mechanisms in a matrix format. Thereby, drug targets could be identified for these brain functions. Another approach mentioned here is based on the "diseaseome" (net-work medicine), which is a data-driven approach using molecular biology and genetic information to find treatment-based mechanism. Although these two approaches may seem promising, no promising clinical treatments are available yet. Target identification still remains the most important and challenging step in drug discovery and development for CNS diseases [54].

Advancements in neuroscience and an improved understanding of the pathophysiology of psychiatric disorders have opened new avenues for drug development. Studies examining the signaling pathways implicated in psychiatric disorders have identified potential targets for drug development and personalized treatment approaches [55]. Re-searchers are exploring novel targets and mechanisms of the glutamatergic system has gained attention as a potential target for novel antidepressant and antipsychotic medications [56]. Modulating glutamate receptors or targeting specific subtypes holds promise in addressing treatment-resistant depression and enhancing the efficacy of antipsychotics [57]. Another emerging area of research is the investigation of neuropeptide systems in psychiatric disorders. Neuropeptide, such as oxytocin, vasopressin, and corticotrophin-releasing factor, have been implicated in social cognition, stress regulation, and emotional processing [58]. Targeting these neuropeptide systems may provide new avenues for the development of medications that address specific symptoms or domains of dysfunction in psychiatric disorders. Repurposing existing medications for psychiatric indications offers a cost-effective and expedited approach to drug development. Drug candidates that have demonstrated safety and efficacy in other medical conditions are being investigated for their potential benefits in psychiatric disorders. For example, some anti-inflammatory agents and NMDA receptor modulators are being explored for their therapeutic potential in major depressive disorder and schizophrenia [59, 60].

While the development of new psychotropic medications and the exploration of novel targets for drug therapy hold promise, several challenges need to be addressed. Actually, in the modern era of drug development, the first step is the selection of a therapeutic target, which is largely determined by its putative pathogenic involvement. However, the preclinical stage of developing new psychotropic drugs is plagued by the

challenges of finding molecules that penetrate the blood-brain barrier, coupled with the low predictive value of many preclinical models of nervous system diseases [61]. In addition to the difficulty to overcome the blood-brain barrier and to assess target interactions the complexity of developing psychotropic drugs is related to several factors. Complex methods (positron emission tomography, CNS functional tests, postmortem studies, CSF analysis) are required. There is a gap between the definition of the biological processes underlying animal models and studies in humans, which has limited the identification of cross-species clinically significant mechanisms. The results of animal studies cannot be directly translated into targets for psychotropic drugs. The classification of mental disorders is based primarily on a phenomenological approach, and the neurobiological mechanisms of most CNS disorders are only partially used for diagnosis [62]. The heterogeneity of psychiatric dis-orders complicates their definition, which is partly explained by genetic variability. Evidence for different subtypes of psychiatric disorders has been found, which explains treatment resistance in several indications, such as depression and schizophrenia. Precision medicine involves clustering of individuals with psychiatric symptoms based on relevant biological phenotypes (biotypes) rather than clinical phenomenological classifications. For drug development in precision psychiatry, it will also be essential that psychiatric biotypes are based on 'drugable' characteristics, and to some extent the patient will have to be matched to the most appropriate drug. The search for target drugs has been conducted using GWAS methods, but its effectiveness in CNS diseases has not been proven. Alternative methods for target search are associated with the Research Domain Criteria (RDoC) initiative in which different functional domains are connected with neurodevelopmental and biological mechanisms in a matrix format and drug targets could be identified for these brain functions; another approach is based on the "diseaseome" (net-work medicine), which is a data-driven approach using molecular biology and genetic information to find treatment-based mechanism. Although these two approaches may seem promising, no promising clinical treatments are available yet. Target identification still remains the most important and challenging step in drug discovery and development for CNS diseases [54]. Nevertheless, due to the large social, economic and personal burden of psychiatric diseases, it is important to develop innovative treatments.

3.4. Translational psychiatry

Although the term "translational" has various definitions, all focus on a better understanding of the pathophysiology and development of new diagnostic tests, aiming to develop more effective treatments. It means the process of obtaining benefit for patients by converting scientific discoveries into clinical applications in order to improve health and decrease morbidity and mortality. Translational research refers to activities conducted to bridge the gap between drug discovery in preclinical models and drug development in humans [63-65].

Translational psychiatry holds the promise of revolutionizing mental health treatment and enhancing patient outcomes [66]. Better understanding on the response variability, cognitive functioning, role of comorbidities and treatment resistance are critical for the development of prevention and treatment strategies that are more effective [67]. One of the primary challenges of translational psychiatry lies in the design and execution of translational research studies. However, designing studies that can be seamlessly translated into real-world clinical settings presents a unique set of difficulties. Factors such as the selection of appropriate study end points, the use of relevant outcome measures, and the inclusion of diverse patient populations pose challenges in effectively bridging the research-to-practice gap [68]. Reproducibility is another pressing concern in translational psychiatry. Efforts to enhance reproducibility include the adoption of transparent reporting standards, preregistration of study protocols, and promoting data sharing and collaboration [69].

Improved communication and coordination between different disciplines, including psychiatry, neuroscience, and genetics, and pharmacology, can foster a more comprehensive and interdisciplinary approach to translational psychiatry [66]. Funding constraints also pose challenges to translational psychiatry. Limited funding opportunities for translational research can impede the progress of projects, hindering the translation of promising findings into clinical practice. Addressing this challenge requires increased investment and support from funding agencies, as well as the development of public-private partnerships to ensure sustained funding for translational research endeavors [70].

Furthermore, regulatory considerations play a crucial role in the translation of re-search findings into clinical applications. Striking a balance between regulatory oversight and timely translation is essential for expediting the implementation of evidence-based practices [71]. Emerging translational research in psychiatric and neurological diseases develop from in vitro to in vivo models, from animals to humans, from qualitative to quantitative psychiatric disorders. Collaborative efforts of scientists and clinicians are committed to unraveling the complexities of the brain and mind. Multidisciplinary but integrative approaches synthesize knowledge from in vitro experiments, animal models, and human clinical trials to pave the way for transformative breakthroughs that can be translated into effective interventions [72]. Current policies regulating the use of animals for scientific purposes are based on balancing between potential gain of knowledge and suffering of animals used in experimentation. Neuropsychiatry-related preclinical re-search is an especially interesting case from an ethical perspective. The 3R principles (Replacement, Reduction and Refinement) are used to minimize the negative consequences for the animals used in research. However, neuropsychiatric research is characterized by specific challenges in assessing the probability of success of reaching the final aim, due to our limited mechanistic knowledge of human neuropsychiatric illness. The translational value of the currently used animal models may be difficult to prove, which undermines the validity of these models and complicated the ethical assessment. Combined approach that deals with both science and the ethical dimensions is necessary in neuropsychiatry-related preclinical research. This approach will improve experimental methods by using systematic reviews, patients-based approach that leads to models that reflect interindividual variation better and more interdisciplinary cooperation [73].

The steps to improve translational research in psychiatry focus on deconstructing complex psychiatric disorders into distinct neurobiological functional abnormalities, clustering patients based on biological phenotypes, developing and validating biomarkers, and incorporating digital technologies and patient involvement in the research process. These steps include [62]:

1) deconstructing psychiatric disorders (identify the underlying neurobiological functional abnormalities that contribute to the development and maintenance of psychiatric disorders; this involves understanding the complex interactions between genetic, environmental, and neurobiological factors that contribute to disease pathophysiology.);

2) clustering patients based on biological phenotypes (group patients based on their underlying biological characteristics, such as biomarkers or molecular signatures, which reflect pathophysiologically relevant processes; this allows for a more personalized approach to treatment and increased potential for targeted therapies);

3) developing and validating biomarkers (identify and validate biomarkers that are associated with the pathophysiology of psychiatric disorders or represent pharmacological processes; biomarkers can be used to diagnose, monitor treatment response, and predict disease progression);

4) reverse translation from clinical to preclinical research (conduct research in humans using preclinical findings as a starting point, focusing on evolutionarily

preserved neurobiological and neuropharmacological systems; this approach can help bridge the gap between basic science discoveries and clinical applications);

5) digital technologies (utilize digital technologies to quantify pathophysiologically relevant biological parameters, such as neuroimaging, genomics, or wearable devices; these technologies can provide mechanism-based characterizations of patient subgroups and clinical effects);

6) collaboration with industry and regulatory agencies (collaborate with industry partners and regulatory agencies to define research criteria for clinical outcome endpoints, ensuring that clinical trials are designed to meet regulatory requirements and address unmet clinical needs};

7) patient involvement (involve patients in the design of new diagnostic tools, therapeutic approaches, clinical trials, and definition of clinical outcome measurements; this ensures that research is patient-centered and addresses the needs of those affected by psychiatric disorders).

Those steps aim to improve the translation of scientific discoveries into clinical psychiatry. The challenges of translational research in mental health include the "translational chasm" between basic science discoveries and real-world clinical practice. Addressing this gap requires a multidisciplinary approach that is collaboration among researchers, clinicians, regulatory agencies and industry partners.

3.5. Biomarkers

The search for specific biomarkers for mental disorders and new directions in therapy, such as targeted therapy, is a promising area of research. An extraordinary effort has been made to identify biomarkers as potential tools for improving prevention, diagnosis, drug response and drug development in psychiatry. Identification of biomarkers for psychiatric disorders is essential to facilitate diagnosis through the developing of markers that allow to stratify groups within the syndrome. The advances in this field may be sorted into five categories: genetics, transcriptomics, proteomics, metabolomics, and epigenetics. The goal is to develop valid, reliable and broadlyusable biomarkers for psychiatric disorders. The identification of factors predicting treatment response will reduce tri-al-and-error switches of medications facilitating the discovery of new effective treatments, being a step towards the establishment of personalized medicine [74].

Biomarkers that are directly related to the pathophysiology of the disease and can track the severity of the disease process would be particularly valuable. Biomarkers can be used to form risk groups, predict the course of the disease, and assess the response to therapy. Biomarkers with a certain degree of syndrome specificity can help differentiate between different psychiatric disorders and identify specific subgroups within each disorder. It is also important to distinguish between "disease markers", "vulnerability markers", and "progression markers". "Disease markers" are biomarkers that are directly related to the pathophysiology of the disease and can be used to diagnose or monitor the disease. "Vulnerability markers" are biomarkers that are associated with an increased risk of developing a mental health disorder but are not necessarily specific to a particular disorder. "Progression markers" (epiphenomena) are biomarkers that reflect changes in the disease process over time and can be used to monitor the response to treatment or predict the progression of the disease [75].

Examples of biomarkers for psychiatric disorders include: genetic markers (genetic variants associated with increased risk of schizophrenia or bipolar disorder); neuroimaging markers (changes in brain structure or function on MRI or PET scans); neurotransmitter markers (levels of neurotransmitters like dopamine or serotonin); biomarkers of inflammation (C-reactive protein (CRP) or interleukin-6 (IL-6), etc.); biomarkers of oxidative stress (malondialdehyde (MDA) or 8-hydroxy-2'-deoxyguanosine (8-OHdG), etc.).

These biomarkers can be used in combination with other diagnostic tools, such as clinical assessments and behavioral observations, to improve the accuracy of diagnosis and treatment outcomes.

Our research was aimed to identify potential biomarkers for schizophrenia, with a focus on the possibility of using blood tests to diagnose the condition. The study found that:

1) the concentration of CRP is higher in patients with more severe psychosis ($r = 0.394$, $p = 0.031$), longer duration of illness ($r = 0.317$, $p = 0.003$), and more pronounced depressive symptoms ($p < 0.05$);

2) there are changes in the functioning of both glial cells and neurons at the early stages of the disease, including decreased levels of S100B and NSE compared to controls, which may serve as an additional diagnostic parameter;

3) elevated NSE levels can be considered a negative prognostic factor, as they correlate with memory impairments, cognitive disturbances, and a greater number of hospitalizations;

4) the level of S100B protein is a potential peripheral biomarker for differential diagnosis of negative and depressive symptoms in schizophrenia;

5) here is a correlation between S100B protein levels and post-schizophrenic depression ($r = 0.047$, $p < 0.001$), consistent with literature data on increased S100B protein levels in affective disorders of varying severity;

6) no correlation was found between S100B protein levels and the severity of negative symptoms, allowing for consideration of increased S100B protein levels as a parameter for differential diagnosis of negative symptoms and depression in schizophrenia;

7) decreased levels of brain-derived neurotrophic factor (BDNF) are associated with more severe cognitive deficits, making BDNF a potential target for therapeutic intervention to improve cognitive functioning in patients with schizophrenia.

Our research provides valuable insights into the potential use of blood biomarkers for diagnosing and monitoring schizophrenia, as well as identifying potential therapeutic targets for improving cognitive functioning and treating depressive symptoms in patients with the condition [76, 77].

Genetic studies have identified hundreds of genes and protein coding variants involved in fundamental processes of neuronal synaptic biology, differentiation and transmission that may serve to discover new therapeutic targets. New technologies, including the use of artificial intelligence, digital health technologies that allow testing of new mechanisms, and biomarkers for stratification and staging of diseases, are leading to a better understanding of the mechanisms of mental disorders Precision psychiatry lever-ages advances in genetics, digital technologies, and multimodal biomarkers to develop early interventions, maximize clinical benefit, and reduce the burden of mental illness [78].

3.6. The gap between practical psychiatry and other areas of neurosciences

However, obstacles to the integration of neuroscientific perspectives remain. Most clinical psychiatrists today make evidence-based decisions based on a list of clinical symptoms, and all this can be done without taking into account the underlying pathophysiology. In other areas of medicine, such a practice is theoretically possible (for example, prescribing antiarrhythmic drugs for certain cardiac syndromes electrical circuits of the heart), but will be seen as a whimsical and scientific approach to practice. The gap between practical psychiatry and other areas of neurosciences can be attributed to several factors:

1) lack of knowledge in neurobiology (future psychiatrists may not have sufficient knowledge in the field of neurobiology, which is essential for understanding the biological basis of mental health and mental illness);

2) low motivation (psychiatrists may not be motivated to learn about neurobiology, which can be due to various reasons such as lack of time, lack of interest, or feeling that it is not relevant to their clinical practice);

3) negative attitude (some psychiatrists may have a negative attitude towards learning about neurobiology, which can be due to various reasons such as feeling overwhelmed by the complexity of the subject matter or perceiving it as unnecessary for their clinical work);

4) perception of irrelevance (some psychiatrists may believe that knowledge of neurobiology is not relevant to their clinical practice, which can lead to a lack of interest and motivation to learn about it).

These factors can contribute to a gap between the knowledge and skills required for effective psychiatric care and the actual practices and training received by psychiatrists [79].

There is a widespread belief that neuroscience represents a "next frontier" for psychiatry, and also widespread reluctance to adopt neuroscience principles in treatment, leading to enthusiasm for this discipline with often little clinical translation [80, 81].

We can create bridges across it by (a) surveying mental healthcare professionals' attitudes toward neuroscience and its clinical use and (b) describing a dialogue between a clinical practitioner and a translational neuroscientist as they consider the survey's results [82].

So, it begins with educational systems. Neuroscience perspectives integrate alongside other traditional psychiatric perspectives. Neuroscience education is most effective when it is case-based, clinically relevant, interactive, informed by adult learning theory, and fun. Neuroscience education must be individualized to the needs of the learners. Lessons from neuropsychiatry can help us to better understand our patients' brain function at the bedside. Integrating neuroscience perspectives means integrating the pathophysiology of our diseases, and thus, is essential for the field of psychiatry to take its proper place in modern medicine [83].

On the other hand, biological mechanisms of mental disorders, coping and response to treatment depend on social factors. Social processes have their own dynamics associated with causes, course and outcome of mental illness. Consideration of the issue from the perspective of the multilevel system will help to establish patterns of interaction be-tween social structure and individual biology. This cultural–ecosocial systems view can guide the development of tools for neuroscience-informed, person-centred clinical assessment, case formulation, and intervention in psychiatry. To implement this approach, training in systems thinking and social science needs to be a key feature of psychiatric education [84].

4. CONCLUSIONS

The emergence of neuropsychiatry as a separate discipline acquired impetus in the mid-20th century, driven by the efforts of innovative researchers and practitioners [85]. Research into the central nervous system at various levels, from the molecular and cellular to the systemic, behavioral, and ultimately symptomatic, has led to the development of the concept of translational neuroscience, which aims to bridge the gap between fundamental research and clinical psychiatry, making the development of new methods for treating mental disorders possible. Understanding the normal and abnormal functioning of the central nervous system at several levels and knowledge of biological mechanisms allows us to identify potential "drug" targets that may form the basis for the treatment of mental disorders and the development of psychiatric drugs in the future. This progress opens up prospects for the diagnosis, prevention, and treatment of mental disorders. For many new goals based on neuroscience, it is still unclear how they relate to the clinical manifestation of mental disorders. The integration

of neurobiological approaches into psychiatry allows for a deeper understanding of the pathophysiology of mental illness. Drug discovery can be facilitated by the development of new classifications and sensitive assessment tools for mental disorders that are more closely related to advances in neuropharmacology and neurobiology. This is consistent with the concept of precision psychiatry, in which patients are grouped not just by symptoms, but primarily by biological phenotypes, which represent pathophysiologically relevant and "drugable" processes. Advances in neurology, genetics, and immunology are very important for improving our understanding of the mechanisms underlying mental illness. The identification of biomarkers and clinical profiling of mental disorders may lead to the development of new approaches to diagnosis, classification and treatment. Precision psychiatry represents a paradigm shift aimed at personalizing psychiatric treatments based on individual characteristics and has the potential to reduce the burden of mental disorders. It is possible to improve the implementation of research results into clinical practice by creating specialized research centers for translational psychiatry, promoting funding initiatives, and improving research infrastructure.

Funding: This research received no external funding.

Conflicts of Interest: The author declares no conflict of interest.

REFERENCES:

1. Whiteford, H.A.; Degenhardt, L.; Rehm, J.; et al. Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. *Lancet*. **2013,** 382(9904):1575-1586. https://doi.org/10.1016/S0140-6736(13)61611-6.
2. World Health Organization. Depression: Fact Sheet (updated Feb 2017). *WHO*, **2018**. (http://www.who.int/mediacentre/factsheets/fs369/en/).
3. Chang, C.K.; Hayes, R.D.; Perera, G.; et al. Life expectancy at birth for people with serious mental illness and other major disorders from a secondary mental health care case register in London. *PLoS One*. **2011**, 6(5):e19590. https://doi.org/10.1371/journal.pone.0019590.
4. Teng, A.; Taylor, Z.; Pfeffer, J.; Williams, L.M. Using longitudinal prescription data to examine the incidence of other chronic diseases following antidepressant use. *J Psychiatric Research*. **2020**, 125:7-12. https://doi.org/10.1016/j.jpsychires.2020.02.030.
5. Huhn, M.; Tardy, M.; Spineli, L.M.; et al. Efficacy of pharmacotherapy and psychotherapy for adult psychiatric disorders: a systematic overview of meta-analyses. *JAMA Psychiatry*. **2014**, 71(6):706-15. https://doi.org/10.1001/jamapsychiatry.2014.112.
6. Kahn, R.S.; Sommer, I.E.; Murray, R.M.; Meyer-Lindenberg, A.; Weinberger, D.R.; Cannon, T.D.; O'Donovan, M.; Correll, C.U.; Kane, J.M.; van, Os. J.; Insel, T.R. Schizophrenia. *Nat Rev Dis Primers*. **2015,** 1:15067. doi: 10.1038/nrdp.2015.67.
7. Berton, O.; Nestler, E.J. New approaches to antidepressant drug discovery: beyond monoamines. *Nat Rev Neurosci*. **2006**, 7(2):137-51. https://doi.org/10.1038/nrn1846.
8. Agid, Y.; Buzsáki, G.; Diamond, D.M.; et al. How can drug discovery for psychiatric disorders be improved? *Nat Rev Drug Discov.* **2007,** 6(3):189-201. https://doi.org/10.1038/nrd2217.
9. Stephan, K.E.; Bach, D.R.; Fletcher, P.C.; et al. Charting the landscape of priority problems in psychiatry, part 1: classification and diagnosis. *Lancet Psychiatry*. **2016**, 3(1):77-83. https://doi.org/10.1016/S2215-0366(15)00361-2.
10. Stephan, K.E.; Binder, E.B.; Breakspear, M.; et al. Charting the landscape of priority problems in psychiatry, part 2: pathogenesis and aetiology. *Lancet Psychiatry.* **2016,** 3(1):84-90. https://doi.org/10.1016/S2215-0366(15)00360-0.
11. Marazziti, D. Biomarkers and Emerging Drug Targets in Neuropsychiatry (Part I). *Curr Med Chem*. **2022**, 29(35):5583. https://doi.org/10.2174/0929867329352209071504l2.
12. Shulman, R.G. Neuroscience: A multidisciplinary, multilevel field. In: Shulman RG editor. Brain Imaging: What it Can (and Cannot) Tell Us About Consciousness. *New York: Oxford University Press*. **2013**, 59-74.
13. Ogawa, H.; Oka, K. Methods in Neuroethological Research. *Tokyo: Springer*. **2013**.
14. Tanner, K.D. Issues in Neuroscience Education: Making Connections. *CBE Life Sci Educ*. **2006**, 5(2):85. https://doi.org/10.1187/cbe.06-04-0156.
15. Kandel, E.; Koester, J.D.; Mack, S.H.; Siegelbaum, S. Principles of Neural Science. 6th ed. *New York: McGraw-Hill Education*, **2021**.

16. Samancı, B.M.; Yıldızhan, E.; Tüzün, E. Neuropsychiatry in the Century of Neuroscience. *Noro Psikiyatr Ars.* **2022,** 59(1):S1-S2. https://doi.org/10.29399/npa.28375.
17. Sullivan, P.F.; Geschwind, D.H. Defining the genetic, genomic, cellular, and diagnostic architectures of psychiatric disorders. *Cell*. **2019**, 177(1):162-183. https://doi.org/10.1016/j.cell.2019.01.015.
18. Gutiérrez-Rodríguez, A.; Cruz-Fuentes, C.S.; Genis-Mendoza, A.D.; Nicolini, H. CRISPR/Cas9 Genome Editing Approaches for Psychiatric Research. *Braz J Psychiatry*. **2023,** 45(2):137-145. https://doi.org/10.47626/1516-4446-2022-2913.
19. Buckholtz, J.W.; Meyer-Lindenberg, A. Psychopathology and the human connectome: toward a transdiagnostic model of risk for mental illness. *Neuron.* **2012**, 74(6):990-1004. https://doi.org/10.1016/j.neuron.2012.06.002.
20. Nestler, E.J.; Peña, C.J.; Kundakovic, M.; Mitchell, A.; Akbarian, S. Epigenetic basis of mental illness. *Neuroscientist*. **2016,** 22(5):447-63. https://doi.org/10.1177/1073858415608147.
21. Orrù, G.; Pettersson-Yeo, W.; Marquand, A.F.; et al. Using Support Vector Machine to identify imaging biomarkers of neurological and psychiatric disease: a critical review. *Neurosci Biobehav Rev***. 2012**, 36(4):1140-52. https://doi.org/10.1016/j.neubiorev.2012.01.004.
22. Grezenko, H.; Ekhator, C.; Nwabugwu, N.U.; et al. Epigenetics in neurological and psychiatric disorders: a comprehensive review of current understanding and future perspectives. *Cureus.* **2023**, 15(8):e43960. https://doi.org/10.7759/cureus.43960.
23. Insel, T.R.; Cuthbert, B.N. Medicine. Brain disorders? Precisely. *Science.* **2015,** 348(6234):499-500. https://doi.org/10.1126/science.aab2358.
24. Taslim, S.; Shadmani, S.; Saleem, A.R.; et al. Neuropsychiatric disorders: bridging the gap between neurology and psychiatry. *Cureus*. *2024*, 16(1):e51655. https://doi.org/10.7759/cureus.51655.
25. Koliatsos, V.E.; Wisner-Carlson, R.; Watkins, C. Neuropsychiatry: definitions, concepts, and patient types. *Psychiatr Clin North Am*. **2020**, 43:213-27. https://doi.org/10.1016/j.psc.2020.02.007.
26. Medina-Rodríguez, J.C. Exploring neuropsychiatry: contemporary challenges, breakthroughs, and philosophical perspectives. *Cureus*. **2023**, 15(11):e49404. https://doi.org/10.7759/cureus.49404.
27. Yatham, L.N.; Thibaut, F. Translational chasm and dialogues in clinical neuroscience. *Dialogues Clin Neurosci*. **2022**, 23(1):1-2. https://doi.org/10.1080/19585969.2022.2073566.
28. Torres, E.B.; Isenhower, R.W.; Nguyen, J.; et al. Toward Precision Psychiatry: statistical platform for the personalized characterization of natural behaviors. *Front. Neurol*. **2016**, 7, 8. https://doi.org/10.3389/fneur.2016.00008.
29. Gandal, M.J.; Leppa, V.; Won, H.; et al. The road to precision psychiatry: translating genetics into disease mechanisms. *Nat Neurosci*. **2016**, 19(11):1397-1407. https://doi.org/10.1038/nn.4409.
30. Lin, E.; Tsai, S.J. Genome-wide microarray analysis of gene expression profiling in major depression and antidepressant therapy. *Prog. Neuropsychopharmacol. Biol. Psychiatry* **2016**, 64:334–340. https://doi.org/10.3389/fneur.2016.00008.
31. Lin, E.; Lane, H.Y. Machine learning and systems genomics approaches for multi-omics data. *Biomark Res.* **2017**, 5, 2. https://doi.org/10.1186/s40364-017-0082-y.
32. Bzdok, D.; Meyer-Lindenberg, A. Machine learning for precision psychiatry: opportunities and challenges. *Biol. Psychiatry Cogn. Neurosci. Neuroimaging* **2018**, 3:223–230. https://doi.org/10.1016/j.bpsc.2017.11.007.
33. Davatzikos, C. Machine learning in neuroimaging: Progress and challenges. *Neuroimage*. **2019**, 197:652-656. https://doi.org/10.1016/j.neuroimage.2018.10.003.
34. Sullivan, P.F.; Agrawal, A.; Bulik, C.M.; et al. Psychiatric Genomics Consortium. Psychiatric Genomics: an update and an agenda. *Am J Psychiatry*. **2018**, 175(1):15-27. https://doi.org/10.1176/appi.ajp.2017.17030283.
35. Singh, A.B.; Bousman, C.A.; Ng, C.H.; Berk, M. Antidepressant pharmacogenetics. *The Australian and New Zealand Journal of Psychiatry*. **2017**, 51(8):776-87. https://doi.org/10.1097/YCO.0000000000000023.
36. Woo, C.W.; Wager, T.D. Neuroimaging-based biomarker discovery and validation. *PAIN*. **2015**, 156(8): 1379-1381. https://doi.org/10.1097/j.pain.0000000000000223.
37. Miller BJ, Buckley P. Precision medicine in psychiatry. *Journal of Clinical Psychopharmacology*. **2017**, 37(6):703-707.
38. Dwyer, D.B.; Falkai, P.; Koutsouleris, N. Machine learning approaches for clinical psychology and psychiatry. *Annu Rev Clin Psychol.* **2018**, 14:91-118. https://doi.org/10.1146/annurev-clinpsy-032816-045037.
39. Lin, E.; Kuo, P.-H.; Liu, Y.-L.; et al. Polymorphisms of the DNA repair gene EXO1 modulate cognitive aging in old adults in a Taiwanese population. *DNA Repair (Amst).* **2019**, 78:1-6. https://doi.org/10.1016/j.dnarep.2019.03.013.
40. Stein, M.B.; Smoller, J.W. Precision psychiatry-will genomic medicine lead the way? *JAMA Psychiatry*. **2018**, 75(7):663-664. https://doi.org/10.1001/jamapsychiatry.2018.0375.
41. Lin, C.H.; Lin, E.; Lane, H.Y. Genetic biomarkers on age-related cognitive decline. *Front Psychiatry.* **2017**, 8:247. https://doi.org/10.3389/fpsyt.2017.00247.
42. Iniesta, R.; Stahl, D.; McGuffin, P. Machine learning, statistical learning and the future of biological research in psychiatry. *Psychol. Med.* **2016**, 46:2455–2465.
43. Mukherjee, S.; Asnani, H.; Lin, E.; Kannan, S. ClusterGAN: Latent space clustering in generative adversarial networks. *Proc. AAAI Conf. Artif. Intell*. **2019**, 33. https://doi.org/10.1609/aaai.v33i01.33014610
44. Hu, Y.; Hase, T.; Li, H.P.; et al. A machine learning approach for the identification of key markers involved in brain development from single-cell transcriptomic data. *BMC Genom*. **2016**, 17(13):1025. https://doi.org/10.1186/s12864-016-3317-7

45. Lin, E.; Tsai, S.-J. Diagnostic prediction based on gene expression profiles and artificial neural networks. soft computing for biological systems. *Springer: Berlin, Germany*, **2018**, 13–22.
46. Williams, L.M. Special report: precision psychiatry—Are we getting closer? *Psychiatric News.* **2022,** 57(9). https://doi.org/10.1176/appi.pn.2022.09.9.23
47. Dalvie, S.; Koen, N.; McGregor, N.; et al. Toward a global roadmap for precision medicine in psychiatry: challenges and opportunities. *OMICS.* **2016**, 20(10):557-564. https://doi.org/10.1089/omi.2016.0110.
48. Williams, L.M. Precision psychiatry: A neural circuit taxonomy for depression and anxiety. *Lancet Psychiatry* **2016**, 3, 472–480. https://doi.org/10.1016/S2215-0366(15)00579-9.
49. Lin, E.; Lin, C.H.; Lane, H.Y. Precision psychiatry applications with pharmacogenomics: artificial intelligence and machine learning approaches. *Int J Mol Sci.* **2020,** 21(3):969. https://doi.org/10.3390/ijms21030969.
50. Lin, E.; Tsai, S.-J. Multi-omics and machine learning applications in precision medicine. *Curr. Pharm. Pers. Med. (Former. Curr. Pharm.)* **2017**, 15, 97–104. https://doi.org/10.2174/1875692115666170616093844.
51. Serretti, A. The present and future of precision medicine in psychiatry: focus on clinical psychopharmacology of antidepressants. *Clin Psychopharmacol Neurosci*. **2018**, 16(1):1-6. https://doi.org/10.9758/cpn.2018.16.1.1.
52. Scala, J.J.; Ganz, A.B.; Snyder, M.P. Precision medicine approaches to mental health care. *Physiology (Bethesda)*. **2023**, 38(2):0. https://doi.org/10.1152/physiol.00013.2022.
53. Hutson, P.H.; Clark, J.A.; Cross, A.J. CNS target identification and validation: avoiding the valley of death or naive optimism? *Annu Rev Pharmacol Toxicol.* **2017**, 57:171-187. https://doi.org/10.1146/annurev-pharmtox-010716-104624.
54. Blokland, A. Drug Discovery in CNS: Finding a target for what? In: Schreiber, R. (eds) *Modern CNS Drug Discovery. Springer, Cham*. https://doi.org/10.1007/978-3-030-62351-7_2
55. Halene, T.B.; Vahdat, L.T. Molecular mechanisms of psychiatric disease. *Wiley Interdisciplinary Reviews: Systems Biology and Medicine*. **2018**, 10(3):e1424.
56. Sanacora, G.; Frye, M.A.; McDonald, W.; et al. American Psychiatric Association (APA) Council of Research Task Force on Novel Biomarkers and Treatments. A Consensus Statement on the Use of Ketamine in the Treatment of Mood Disorders. *JAMA Psychiatry*. **2017,** 74(4):399-405. https://doi.org/10.1001/jamapsychiatry.2017.0080.
57. Popik, P.; Kozela, E.; Krawczyk, M. Gliptins: a novel therapeutic approach in the treatment of depression? *CNS & Neurological Disorders Drug Targets.* **2014**, 13(10):1630-41. 27.
58. Jurek, B.; Neumann, I.D.; Theodorsson, E. How to study sex differences in addiction using animal models. *Addiction Biology*. **2015**, 20(5):911-937.
59. Goldsmith, D.R.; Haroon, E.; Miller, AH. Major depressive disorder in youths: clinical and treatment implications. *Pediatric drugs.* **2017**, 19(4):329-42.
60. Javitt. D.C.; Zukin, S.R. Recent advances in the phencyclidine model of schizophrenia. *Am J Psychiatry.* **1991,** 148(10):1301-8. https://doi.org/10.1176/ajp.148.10.1301.
61. Mueller, L.G.; Slusher, B.S.; Tsukamoto, T. Empirical analysis of drug targets for nervous system disorders. *ACS Chem Neurosci*. **2024**, 15(3):394-399. https://doi.org/10.1021/acschemneuro.3c00676.
62. van der Doef, T.F.; Zaragoza, D.S.; Jacobs, G.E.; et al. New approaches in psychiatric drug development. *Eur Neuropsychopharmacol*. **2018,** 28(9):983-993. https://doi.org/10.1016/j.euroneuro.2018.06.006.
63. Littman, B.H.; Di Mario, L.; Plebani, M.; Marincola, F.M. What's next in translational medicine? *Clin Sci (Lond).* **2007**, 112(4):217-227. https://doi.org/10.1042/CS20060108.
64. Hurko, O. The uses of biomarkers in drug development. *Ann N Y Acad Sci.* **2009**, 1180:1-10. https://doi.org/10.1111/j.1749-6632.2009.04946.x.
65. Hurko, O. Future drug discovery and development. *Mol Genet Metab*. **2010**, 100 (1):92-96. https://doi.org/10.1016/j.ymgme.2010.01.010.
66. Insel, T.R. Translating scientific opportunity into public health impact: a strategic plan for research on mental illness. *Arch Gen Psychiatry*. **2017**, 68(1):14-20.
67. Machado-Vieira, R. Tracking the impact of translational research in psychiatry: state of the art and perspectives. *J Transl Med.* **2012**, 10:175. https://doi.org/10.1186/1479-5876-10-175.
68. Hyman, S.E. Revolution stalled. *Sci Transl Med.* **2012**, 4(155):155cm11. https://doi.org/10.1126/scitranslmed.3003142.
69. Nosek, B.A.; Alter, G.; Banks, G.C.; et al. Promoting an open research culture. *Science.* **2015**, 348(6242):1422-5. https://doi.org/10.1126/science.aab2374.
70. Miller, G. Mental health funding: closing the gap between research and practice. *Science.* **2010**, 327(5969):1193-4.
71. DeJong, C.; Aguilar, T.; Tseng, C.; et al. Pharmaceutical Industry–Sponsored Meals and Physician Prescribing Patterns for Medicare Beneficiaries. *JAMA Intern Med.* **2016**, 176(8):1114–1122. https://doi.org/10.1001/jamainternmed.2016.2765
72. Tanaka, M.; Battaglia, S.; Giménez-Llort, L.; et al. Innovation at the intersection: emerging translational research in neurology and psychiatry. *Cells.* **2024**, 13(10):790. https://doi.org/10.3390/cells13100790.
73. Meijboom, F.L.B.; Kostrzewa. E.; Leenaars, C.H.C. Joining forces: the need to combine science and ethics to address problems of validity and translation in neuropsychiatry research using animal models. *Philos Ethics Humanit Med*. **2020**, 15(1):1. https://doi.org/10.1186/s13010-019-0085-4.
74. García-Gutiérrez, M.S.; Navarrete, F.; Sala, F.; et al. Biomarkers in psychiatry: concept, definition, types and relevance to the clinical reality. *Front Psychiatry*. **2020**, 11:432. https://doi.org/10.3389/fpsyt.2020.00432.

75. Emerson, E.; Einfeld, S.L. Challenging Behavior. *Cambridge University Press, Cambridge, UK*, **2014**. https://doi.org/10.1017/CBO9780511861178
76. Chumakov, E.; Dorofeikova, M.; Tsyrenova, K.; Petrova, N. A cross-sectional study on associations between BDNF, CRP, IL-6 and clinical symptoms, cognitive and personal performance in patients with paranoid schizophrenia. *Front. Psychiatry* **2022**, 13:943869. https://doi.org/10.3389/fpsyt.2022.943869
77. Dorofeikova, M.; Neznanov, N.; Petrova, N. Cognitive deficit in patients with paranoid schizophrenia: Its clinical and laboratory correlates. *Psychiatry Research* **2018**, 262:542-548. https://doi.org/10.1016/j.psychres.2017.09.041
78. Brady, L.S.; Lisanby, S.H.; Gordon, J.A. New directions in psychiatric drug development: promising therapeutics in the pipeline. *Expert Opin Drug Discov.* **2023**, 18(8):835-850. https://doi.org/10.1080/17460441.2023.2224555.
79. Petrova, N .; Dorofeikova, M. Psychiatry as clinical neuroscience: present and future. *Neurology bulletin named after V.M. Bekhterev*. **2020**, LII(4):12–19. https://doi.org/10.17816/nb52656
80. Arbuckle, M.R.; Travis, M.J.; Ross, D.A. Integrating a neuroscience perspective into clinical psychiatry today. *JAMA Psychiatry*. **2017,** 74(4):313-314. doi: 10.1001/jamapsychiatry.2016.3849.
81. Cooper, J.J.; Korb, A.S.; Akil, M. Bringing neuroscience to the bedside. *Focus (Am Psychiatr Publ).* **2019**, 17(1):2-7. https://doi.org/10.1176/appi.focus.20180033.
82. Strege, M.V.; Persons, J.B.; Ressler, K.J.; et al. Integrating neuroscience into clinical practice: current opinions and dialogue between drs. Jacqueline Persons and Kerry Ressler. *Behav Ther (N Y N Y).* **2021**, 44(7):326-334.
83. Cooper, J.; Walke, A.E. Neuroscience education: making it relevant to psychiatric training. *Psychiatr Clin North Am*. **2021**, 44(2):295-307. https://doi.org/10.1016/j.psc.2020.12.008
84. Gómez-Carrillo, A.; Kirmayer, L.J.; Aggarwal, N.K.; et al. Integrating neuroscience in psychiatry: a cultural-ecosocial systemic approach. *Lancet Psychiatry.* **2023,** 10(4):296-304. https://doi.org/10.1016/S2215-0366(23)00006-8.
85. Griffiths, R.R.; Johnson, M.W.; Carducci, M.A.; et al. Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial. *J Psychopharmacol.* **2016**, 30(12):1181-1197. https://doi.org/10.1177/0269881116675513.