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Opinion

The Era of Precision Psychiatry: Toward a New Paradigm in Diagnosis and Care

Antonio Del Casale [1,2,*], Liliana Bronzatti [1], Jan Francesco Arena [1], Giovanna Gentile [2,3], Carlo Lai [1], Paolo Girardi [1], Maurizio Simmaco [2,3] and Marina Borro [2,3]

[1] Department of Dynamic and Clinical Psychology and Health Studies, Faculty of Medicine and Psychology, Sapienza University of Rome, 00189 Rome, Italy
[2] Centre for Precision Medicine, Sant'Andrea University Hospital, 00189 Rome, Italy
[3] Department of Neuroscience, Mental Health and Sensory Organs (NESMOS), Faculty of Medicine and Psychology, Sapienza University of Rome, 00189 Rome, Italy
* Correspondence: antonio.delcasale@uniroma1.it

Abstract

Mental disorders affect nearly one billion persons worldwide, having a substantial burden on individuals, families, and healthcare systems. Current diagnostic and therapeutic approaches could fail to reach optimal outcomes, highlighting the need for more effective and personalized interventions. Precision psychiatry aims to address this challenge by integrating multidimensional data, ranging from genomics and epigenomics to neuroimaging and psychometric assessments, through advanced computational tools such as machine learning and artificial intelligence. This transdisciplinary approach could allow the study of biologically informed endophenotypes, improve diagnostic accuracy, and support individualized treatment strategies. Emerging technologies, including pharmaco-neuroimaging, virtual histology, and large-scale consortia, are advancing the field by elucidating the molecular and circuit-level correlates of mental disorders. Although significant progress has been made, the translational gap between research and clinical practice remains a critical issue. Effective implementation will require the systematic integration of bioinformatic tools, big data analytics, and clinician-guided interpretation, in a context in which the evolving landscape of precision psychiatry continues to prioritize therapeutic alliance and individualized patient care.

Keywords: precision medicine; mental disorders; psychiatry; biomarkers; genomics; neuroimaging; machine learning; artificial intelligence; translational medical research

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1. Introduction

The World Health Organization reports that nearly one billion people currently live with a mental disorder [1]. Moreover, approximately 50% of the global population might face a mental disorder by the age of 75 [2]. Despite the high prevalence, for a significant proportion of these individuals, the available treatments are not effective, leading to an increased treatment gap in mental health care [3]. Globally, mental disorders represent a major factor in disability, impacting individuals, families, and societies [4]. When it comes to treatment strategies, many patients face multiple therapeutic attempts before achieving relief, and a considerable portion might exhibit treatment resistance [5]. To optimize diagnostic accuracy and therapeutic decisions in terms of both efficacy and tolerability, the characterization of endophenotypes within psychiatric syndromes [6], along with the assessment of individual metabolic profiles, is becoming increasingly essential.

These developments are paving the way for more targeted and effective treatment strategies. In recent years, the unmet needs in psychiatric clinical practice have challenged the categorical nosological approach, and new transdiagnostic frameworks such as the Research Domain Criteria (RDoC) have been proposed [7]. Developing personalized treatments is a priority in addressing the public health impact of mental disorders, with new opportunities emerging from recent technological advances. Currently, the integration of exposome research (the comprehensive set of lifetime environmental exposures) with multi-omics approaches (including genomics, epigenomics, transcriptomics, proteomics, and metabolomics) through machine learning methods [8] is currently providing deeper insights into the biological mechanisms underlying mental disorders and represents a promising path for precision psychiatry.

2. Precision Psychiatry Through Multidisciplinary Neuroscience Integration

Mental disorders are classically understood as multifactorial conditions involving multiple biological systems, underpinned by complex nonlinear interactions among genes, individual biological factors, and environmental influences. This complexity results in significant individual variability, with clinically similar phenotypes and overlapping symptoms concealing important underlying biological differences [9,10]. This aspect limits the effectiveness of diagnostic, clinical, and therapeutic interventions [11]. Current models, such as the Diagnostic and Statistical Manual of Mental Disorders (DSM) and the International Classification of Diseases (ICD), are based on symptomatic classifications of advanced-stage mental illnesses. While these frameworks have greatly contributed to the standardization of psychiatric nosography, they are currently unable to incorporate biological aspects into the diagnostic assessment, resulting in clinically heterogeneous and biologically non-homogeneous groups [12]. Ultimately, his symptom-centric approach has significant limitations when considering a personalized approach to diagnosis and therapy [7].

Progress in molecular biology has paved the way for the identification of 'biological endophenotypes', heritable, state-independent biomarkers associated with mental disorders that co-segregate within families, thereby broadening our understanding of these conditions, such as immuno-metabolic depression within major depressive disorders [13]. This form of depression, characterized by atypical symptoms, systemic inflammation, and metabolic dysfunctions, is emerging as a promising, though still evolving, target for personalized therapeutic interventions consistent with the principles of precision psychiatry [13]. Building on this line of research, recent studies have linked inflammatory markers to depressive, anxiety, and stress-related disorders, forming an evidence base for the possible use of inflammatory markers as biomarkers of high-risk states for the development of these mental disorders [14]. This provides valuable integrative evidence to expand psychiatric nosography and potentially better guide therapeutic interventions. Further investigation of the biological aspects characterizing mental disorders could open avenues for integrating neurofunctional and cognitive information, with the compelling possibility of bridging the gap between psyche and brain [15]. Integrating genetic, neuroanatomical, neurofunctional, clinical, psychometric, and cognitive data into predictive models can significantly improve outcome prediction in psychosis, with crucial implications for both treatment and prevention [16]. Looking ahead, as far as we can foresee, the notion of 'integration' may well emerge as a key concept in the evolving field of precision psychiatry.

When it comes to technological advancements, on the one hand we are now able to process large volumes of data, such as genetic data from genome-wide association studies (GWAS) and clinical information from Electronic Health Records. Furthermore, increasingly sophisticated technologies, such as Machine Learning and Artificial Intelligence (AI), are

among the approaches suitable for integration into precision psychiatry. Their ability to incorporate evidence from diverse fields, including nuclear medicine, neuroradiology, and the full spectrum of omics sciences, offers promising opportunities for predictive modeling and clinical application. The growing use of machine learning, particularly deep learning, is having a significant impact on clinical research and drug development, enhancing computational power and enabling the processing of large volumes of data [10]. These technologies enable the analysis of complex data such as clinical records, genetic information, brain imaging, and biomarkers, to identify disease subtypes and predict individual clinical trajectories. This allows patients to be grouped into more neurobiologically homogeneous categories, improving diagnosis, prognosis, and personalized treatments [6,17,18]. Notably, interesting contributions are coming from pharmaco-neuroimaging, where the integration of functional neuroimaging data (e.g., fMRI, PET) can enhance our understanding of interindividual responses to drugs [19], expanding our understanding of neurofunctional correlates of exposure to exogenous psychoactive substances.

The more we learn about biology, the more we can rethink mental disorders. One noteworthy example is the Research Domain Criteria (RDoC) framework, an empirically derived approach that integrates multiple levels of analysis, including neural circuits, behavior, physiology, and genetics. This approach represents an effort to overcome the limitations of traditional diagnostic classifications, which are based on purely descriptive taxonomies and provide often limited guidance for treatment decisions [20].

In the field of treatment, research is progressively orienting toward innovative therapeutic strategies based on brain circuit–targeted interventions, aimed at personalizing care and predicting clinical outcomes. Preliminary evidence in mood, anxiety, and obsessive–compulsive disorders suggests that these approaches may open new avenues beyond conventional pharmacological treatments [21]. At the same time, genetic studies and large-scale genomic analyses have identified variants associated with specific subtypes of neurological and mental disorders. Moreover, fluid biomarkers are emerging as essential tools for the assessment and monitoring of these conditions, as they bypass anatomical barriers of the brain and offer novel opportunities for prevention and early diagnosis [15]. The probabilistic integration of multi-domain biomarkers, including cognitive, inflammatory, and peripheral immune factors, through machine learning represents a promising strategy for the differential diagnosis between bipolar disorder and schizophrenia, with potential application in clinical diagnosis. In fact, machine learning approaches have shown potential in distinguishing between bipolar disorder and schizophrenia, with promising sensitivity and specificity values, while also emphasizing the need for further validation across broader and more diverse populations [22].

In research, integration has led to significant advancements in the understanding of mental disorders. As is the case with the Enhancing NeuroImaging Genetics through Meta-Analysis (ENIGMA) consortium, which has made substantial advancements in integrating multimodal neuroimaging data with genetic information, contributing to the identification of both structural and functional correlates of mental disorders. ENIGMA working groups have developed and disseminated multiscale analytical pipelines based on big data, enabling internationally harmonized analyses that integrate genetic, epigenetic, multimodal magnetic resonance imaging (MRI), magnetic resonance spectroscopy (MRS), and electroencephalography (EEG) data. This initiative represents a notable example of international collaboration and methodological integration in the field [23]. Following this direction, genomics and metabolomics provided valuable insights into the biological underpinnings of conditions such as bipolar disorder, obsessive–compulsive disorder, schizophrenia, and major depressive disorder [24–26]. These findings offer promising perspectives for improving current models of risk prediction and stratification within the

general population [25]. Among the most innovative approaches is virtual histology, which arises from the integration of MRI-derived structural profiles with regional genetic profiles, both disorder-specific and cell-type-specific, such as those provided by the Allen Brain Atlas. Using a meta-analytic approach focused on the association between interregional differences in cortical thickness and interregional patterns of cell-specific gene expression, shared neurobiological substrates across mental disorders have been identified [27]. This has led to the hypothesis of a specific role for pyramidal CA1 cells, astrocytes, and microglia, suggesting potential shared processes related to both prenatal and postnatal neurodevelopment, thereby expanding our understanding of the neurobiology of mental disorders [27]. Considering the applicability of research methodology, these approaches the integration of multi-omics data can overcome the ethical and economic limitations that hinder the large-scale application of PET studies [28]. At the same time, it has provided new insights into the relationships between structural and functional correlates of the central nervous system and neurotransmitter systems, laying the groundwork for the potential discovery of new biomarkers and targeted therapeutic approaches [28]. The growing availability of data, together with advances in analytical strategies, is driving increasingly personalized approaches in precision psychiatry and has fostered the development of new domains, including computational psychiatry [29]. Data-driven methodologies are gaining prominence, allowing data to guide research trajectories and, in some cases, challenge existing clinical and nosography frameworks. A case in point is the potential use of EEG recordings as a predictor of antidepressant treatment response, as hypothesized in a recent machine learning meta-analysis [30]. Finally, in the future, sociodemographic, biological (e.g., blood lipids, inflammatory markers, genomics), clinical/psychological, and instrumental data (e.g., neuroimaging, EEG) could be integrated for clinical use, providing information capable of guiding treatment selection and the intensity of therapeutic interventions.

Nevertheless, despite the abundance of information, the practical implementation of precision techniques remains a critical challenge, underscoring the future need to effectively select, synthesize, and integrate such data within established diagnostic systems. The integration of multi-omics data still lacks a standardized framework that would facilitate uniform analyses. Furthermore, there is a pressing need to improve interoperability between omics and non-omics data, such as clinical information, to enhance the translational potential of research findings [31]. In the context of advances in AI, models applied to precision psychiatry offer promising opportunities, yet several challenges remain. Regarding validity and reproducibility, it is essential to ensure that algorithms are tested on representative datasets. Many current models lack external validation, limiting their generalizability across clinical settings [32]. Additionally, the interpretability of results remains a significant challenge, particularly due to the "black box" nature of deep learning algorithms, which raises ethical concerns about their use in potential AI-based clinical decision-making protocols [32]. These issues underscore the importance of translational research aimed at applying such techniques in clinical practice to improve patient stratification, identify biomarkers, and personalize treatments. Moreover, the sharing of genomic data in psychiatric research requires strict attention to data privacy, ensuring that sharing protocols adequately safeguard patient confidentiality [32]. In this field, concerns have also been raised regarding the prediction of phenotypic traits, particularly in the context of prenatal testing, and the need for policies that provide adequate protection against potential discrimination, given that these models are designed to generate predictive medical information [33,34]. Comprehensively, two main areas of concern can be identified. The first relates to conceptual challenges, including the limited understanding of the biological mechanisms underlying mental disorders, the translation of omics-derived information into practical decisions, the evaluation of the clinical relevance of newly identified genomic

variables, and the integration of these data within healthcare organizations [34]. The second involves practical challenges, such as the size and quality of databases, the management of AI-related biases, data security, and the risk of dehumanization in clinical care. Addressing these issues requires investment in the training of expert clinicians, who must ultimately assume responsibility for clinical decisions, particularly when supported by clinical decision support systems [34]. Nevertheless, personalized treatments and the ability to prevent adverse drug reactions, such as the cutaneous effects of antiepileptic drugs [35], represent a critical area of research with broad potential for bedside clinical applications [34] and as shown in several studies, a potential for cost savings [36]. Pharmacogenomics currently represents the main field suitable for effective clinical application. Nevertheless, no universally accepted reference guidelines are available to date. The literature indicates that testing should be offered when there is clear clinical evidence of atypical treatment inefficacy or significant adverse effects in patients who have already undergone clinical evaluation and adequately dosed, appropriately timed treatment regimens [37]. This is particularly recommended for CYP2D6 and CYP2C19 genotypes, given their well-established role in the metabolism of antidepressants [38] and antipsychotics, as well as for other drugs with strong supporting evidence [37]. In this context, preliminary clinical assessment is crucial to identify patients eligible for pharmacogenetic investigations.

Among future perspectives, the implementation of bioinformatic decision-support systems is envisioned to assist clinicians from the initial patient evaluation, particularly since genetic testing is currently recommended in selected cases. Another area of application for precision psychiatry is forensic psychopathology, where precision techniques such as therapeutic drug monitoring [39] and genomically guided treatments may have significant clinical implications, particularly in the field of suicide prevention, a recognized and pressing issue [40,41].

Therefore, to enable the implementation of pharmacogenomics and precision psychiatry, future research should promote the dissemination of knowledge on precision medicine, provide training for clinicians, further investigate the clinical efficacy and cost-effectiveness of pharmacogenomics-guided genotyping, standardize procedures, develop clinical guidelines that incorporate the application of precision medicine, and establish new regulations for pharmacogenomics-related drug development and labeling [42,43].

3. Conclusions

Precision psychiatry represents a promising avenue for improving the diagnosis, treatment, and prevention of mental disorders. The field of neuroscience is currently undergoing remarkable technological advancements, from modern whole-genome sequencing techniques in molecular biology to the growing interplay between psychiatry and computational neuroscience, including the expanding discipline of computational psychiatry. However, the still somewhat limited applicability of these innovations in routine clinical practice underscores the complexity and challenges inherent in the translational pathway, particularly regarding the integration of advanced technologies into routine clinical workflows, which remains a significant hurdle for the widespread adoption of precision psychiatry. Current research increasingly underscores the importance of incorporating data analysis methodologies, bioinformatic tools, and machine learning techniques among the core resources available to investigators. In parallel with the implementation of data analysis techniques, it is essential to update and refine regulatory systems and to provide methodological guidelines, ensuring that the use of new technologies is standardized, accurate, and reliable, and that it can be effectively integrated into clinical practice while adhering to appropriate ethical boundaries. Finally, maintaining a strong focus on the therapeutic relationship remains essential to effectively guide and interpret the expanding

body of knowledge on mental disorders, ensuring that the individual remains at the center of precision psychiatric care.

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