EDITORIAL

The research interface between psychiatry and medicine: Evolving paradigms and their implications

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INTRODUCTION

The interface between psychiatry and medicine has long been an area of interest, with the recognition that biological, psychological, and social factors influence mental health disorders. The emergence of the liaison psychiatry subspecialty and the development of integrated, collaborative models to address co-occurring physical and mental health problems are a testament to this enthusiasm. Over the years, our understanding of psychiatric conditions and their underlying aetiology has evolved, leading to a paradigm shift in the approach to diagnosis and treatment. This editorial aims to explore the changing paradigms at the research interface of psychiatry and medicine and discuss the implications of these changes for the practice of psychiatry.

Historically, psychiatric disorders were primarily viewed through a psychological lens, with little consideration given to their biological underpinnings. However, advancements in medical research and technology have allowed for a deeper understanding of the biological aspects of mental health. The discovery of genetic markers associated with psychiatric conditions and the development of neuroimaging techniques have shed light on the intricate interplay between the brain and mental health disorders. This integration of biological and psychological perspectives has fuelled the emergence of a more holistic approach to psychiatry. It recognizes that mental health is not solely a result of environmental or psychological factors but also has a biological basis. This paradigm shift has enabled clinicians to identify better and treat the root causes of psychiatric disorders, paving the way for precision medicine.

Precision medicine is an innovative approach that aims to personalize treatment strategies based on an individual's unique genetic, physiological, and environmental factors.1 By leveraging the knowledge gained from the interface between psychiatry and medicine, precision medicine seeks to move away from a one-size-fits-all approach and provide targeted interventions that yield better outcomes. The advent of precision medicine, which has already made significant strides in other medical specialities, provides a framework for precision psychiatry. Genetic testing, biomarker analysis, and machine learning algorithms can help identify specific subtypes of psychiatric disorders and predict treatment response. This information allows clinicians to choose interventions that are more likely to be effective, reducing trial-and-error approaches and improving patient outcomes.

On a related note, integrating wearable devices, such as activity trackers and physiological sensors, provides real-time data on patients' physical and mental states. This continuous monitoring allows for early identification of symptom exacerbation patterns unique for every individual, referred to as 'relapse signatures', enabling timely interventions to prevent relapse or crisis. Precision

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psychiatry also considers individual variations in drug metabolism, optimizing medication selection and dosing to minimize side effects and maximize efficacy.

To give a specific example of how efforts in other branches of medicine can guide tailored approaches to treatment in psychiatry, consider seizures in neurology, a speciality most closely allied with psychiatry. Seizures have been classified as psychogenic and non-psychogenic based on clinical and physiological features.2 Likewise, based on cognitive and physiological markers, psychosis has been stratified into biologically informed subtypes or 'biotypes'.3 Such stratification has two advantages: first, it allows exploration of specific aetiological factors, and second, it yields treatment targets that can be tested, which the current approach of classifying psychiatric disorders based on clinical course and outcome characteristics does not permit. To cite another example, the National Institute of Neurological Disorders and Stroke (NINDS) has developed the Parkinson's Disease (PD) biomarker project aimed at discovering clinical and laboratory-based biomarkers of PD that can accelerate the development and testing of targeted interventions.4 The field of psychiatry would benefit from investment in similar approaches to accelerate biomarker discovery that may improve care and outcomes.

However, many challenges impede the achievement of precision psychiatry. Major mental illnesses, such as schizophrenia, are multifaceted, with a complex interplay of genetic, developmental, and environmental factors as well as downstream pathophysiological mechanisms. Considerable heterogeneity in clinical phenotypes, absence of 'sine qua non' alterations, and difficulties in accessing appropriate samples have slowed down success rates in biomarker discovery approaches for mental illness. Further, one cause can lead to many outcomes (multifinality), and many causes can yield the same outcome (equifinality). Nowhere are these more evident than in psychiatric genetics: a range of internalizing, externalizing, and psychotic disorders have been associated with 22q11.2 deletion syndromes, while de novo mutations, copy number variants, and gene-environment interactions have all been centrally implicated in the pathogenesis of complex behaviour traits.5 In fact, complex, multifactorial genetic liability in major mental illnesses is now virtually indisputable.

These complementary concepts of equifinality and multifinality are also part of the Research Domain Criteria (RDoC) project of the National Institute of Mental Health (NIMH), which envisages a paradigm shift in the conceptualization of psychiatric disorders from a categorical to a dimensional perspective. More specifically, the 'outcomes' of interest are no longer diagnostic categories as defined by major classificatory systems but cross-cutting cognitive, affective, and social processes referred to as domains and constructs.6 Importantly, this multi-component research framework emphasizes multidisciplinary and interdisciplinary collaboration to develop new avenues for improving our understanding of the aetiology of mental illness and uncover novel treatment targets. The RDoC provides a conceptual platform for combining basic neuroscience, clinical neuroscience, and psychiatry. Research through such an integrative framework can help us better understand the genetic, molecular, neural, physiological, and biochemical basis of complex behaviour traits and manage them better. If sustained, such efforts could eventually contribute to a psychiatric nosology consistent with a precision medicine-based approach for evaluating and managing mental disorders.

Therefore, as research in precision psychiatry continues to evolve, it is crucial to foster interdisciplinary collaboration between psychiatry and other medical specialities. This will facilitate the exchange of knowledge and expertise, leading to the development of innovative approaches to mental healthcare. The integration of artificial intelligence and machine learning algorithms, essentially interdisciplinary, may also play a crucial role in identifying patterns and predictors of treatment response, further refining precision psychiatry approaches.

Lastly, and on a related note, there has been an increasing focus on understanding the complexity of mental illness by breaking them into individual subsystems, each of which interacts with each other to drive mental illness. These include genomics, transcriptomics, proteomics, metabolomics, and clinical data. Each of these represents interdisciplinary research streams that can be combined to discover biomarkers for the diagnosis, treatment, and prognosis of mental disorders. To cite another relevant example from neurology, such approaches have identified multiple pathophysiological causal pathways for Alzheimer's disease (AD) involving neuroinflammation, oxidative stress, and amyloid-Beta accumulation, necessitating a multitarget approach for drug development in AD. Further, combining biologically rich multi-omics data with state-of-the-art machine learning approaches could increase the translation of psychiatric research from bench to bedside.

To sum up, the interface between psychiatry and medicine is undergoing a transformative shift driven by advancements in genetics, neuroscience, and technology. The synergy between disciplines can improve our

understanding of the etiological basis of complex mental illnesses and uncover new treatment targets. An important offshoot of this development will be precision psychiatry, which revolutionizes how psychiatric disorders are diagnosed and treated. The cited examples from neurology in this article show how much other fields have advanced in terms of precision treatments and how much psychiatry can learn from other fields to advance itself in this area. Today, precision treatments are feasible for some rare diseases in neurology (e.g., GRIN2A-related epilepsy), but psychiatrists can claim no such advancements. By embracing this paradigm shift, psychiatrists can strive towards better patient outcomes, reduced treatment burden, and a more comprehensive understanding of mental health.

As a parting note, insights from precision medicine approaches in psychiatry must be positioned in a larger ecosocial view of symptom circuits, socio-cultural, and interpersonal contexts. This integration will enable individualization and partnership of care, combining precision and person-centred approaches to deliver interventions that are likely to have optimum uptake and impact. Both these approaches need to be embraced to improve clinical decision-making and patient outcomes.

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