



## Integrating Psychiatry and Medical Biotechnology as a Way to Achieve Scientific, Precision, and Personalized Psychiatry

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### Abstract

Besides concerns about the increasing prevalence of psychiatric disorders and the significant burdens and costs, there are concerns about its validity. The dilemma of validity went so far that studies described the diagnoses in psychiatry as scientifically worthless. We suggest integrating psychiatry and medical biotechnology and using biotechnological products in psychiatric aspects help psychiatry become more precise, strengthen its position among other sciences, and increase its scientific credibility by giving examples. For this matter, we need different inputs to choose between the vast outputs. The most common inputs are clinical symptoms, cognitive function, individual and environmental risk factors, molecular markers, genetic markers, neuroimaging signs, and big data. Some molecular markers have been shown to have a relationship with psychiatric disorders such as Interleukin-6 (IL-6) and Tumor Necrosis Factor- $\alpha$  (TNF- $\alpha$ ). Genetic studies might evolve the most accurate part of precision psychiatry. Currently, and through the developments in technology, genome-wide association studies have become available. In neuroimaging signs, psychiatric disorders are associated with generalized rather than focal brain network dysfunction, and functional magnetic resonance imaging could be performed to study them. It would exhibit different aberrancies in various psychiatric disorders. In big data, the constitution of predictive models and movement toward precision psychiatry can be led by using artificial intelligence and machine learning.

*Avicenna J Med Biotech 2021; 13(4): 172-175*

**Keywords:** Behavioral sciences, Cytokines, Integrative medicine, Knowledge, Technology

### Introduction

Today, the importance of psychiatry in the mental health of individuals and public health is evident. Psychiatric disorders that are highly prevalent and increasing cause patients' dysfunction, adverse effects on people in contact, isolation, reduced quality of life, the tendency to drugs and alcohol, and suicide, thereby imposing significant burdens and costs <sup>1,2</sup>.

Validity is generally defined to the extent that a concept reflects the nature of reality and is measured precisely in quantitative studies. In assessing the validity of a theory, the definition of a concept is not enough, and the appropriate methodology for testing the concept should also be considered. This problem, which has clinical, moral, financial, and legal implications, has always been a significant concern in psychiatry <sup>3</sup>.

This dilemma went so far that studies described the accuracy of diagnosing most psychiatric disorders at about half and the diagnoses as scientifically meaningless and worthless <sup>4,5</sup>. We aim to suggest biotechnology

assistance to psychiatry and the integration of psychiatry and medical biotechnology as a way out of this dilemma and achieve precision personalized psychiatry by giving examples.

### Precision and personalized psychiatry

Precision psychiatry is an almost equal term for personalized psychiatry and is consists of using all health-related aspects of a patient to reach the best possible outcome <sup>6</sup>. For this matter, we need different inputs to choose between the vast therapeutic options. The most common types of these inputs are clinical symptoms, cognitive function, individual and environmental risk factors, molecular markers, genetic markers, neuroimaging signs, and big data <sup>7,8</sup>. The combination could help the diagnosis, disease susceptibility, treatment (selection and dosage), and prognosis.

### Clinical and environmental markers

The Diagnostic and Statistical Manual Mental Dis-

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**Received:** 1 Sept 2021  
**Accepted:** 7 sept 2021

orders 5 (DSM-5) and the International Classification of Diseases 10 (ICD-10) are the most useful classification tools to diagnose psychiatric disorders. They provide an acceptable system to formulize the clinical presentations; however, the lack of specificity makes it challenging to identify the definite diagnosis. Several risk factors contribute to the evolution of a psychological disorder. History of trauma or serious illness and related medication, occupational and marital status, habits and lifestyle, presence of previous mental health disorders (especially during childhood and adolescence), genetic vulnerability, and family history of mental disorders (especially bipolar and psychotic disorders) could be a trigger for psychological disorders and might predict the prognosis<sup>9-14</sup>.

#### **Molecular markers**

More quantifiable data are necessary for precision psychiatry, and here we note some. The neurocognitive function could be assessed with tests measuring multiple domains, such as attention, memory, and cognitive control. Each of these domains might be altered in distinct diseases and may predict the illness severity<sup>15</sup>. Some molecular markers have been shown to have a relationship with psychiatric disorders. In a meta-analysis performed by Goldsmith *et al*, it was demonstrated that the levels of interleukin-6, tumor necrosis factor- $\alpha$ , serum soluble interleukine-2 receptor, and interleukine-1 receptor antagonist were significantly elevated in patients afflicted with acute presentation of schizophrenia, bipolar disorders, or major depressive disorder, in comparison with healthy controls. However, these results differed in chronically ill patients and those who received proper treatment, but significant changes in these markers were seen<sup>16</sup>. Wang *et al* also revealed that in patients with schizophrenia and bipolar disorders, the CSF interleukine-1 $\beta$  and kynurenic acid levels increased, and in those with schizophrenia and major depressive disorder, interleukine-6 and interleukine-8 levels become higher. They also noted that many of these changes were in concordance with serum samples<sup>17</sup>. Some other biomarkers have been studied and shown to have a possible relationship with psychiatric disorders such as CRP levels, interleukine-3, interleukine-10, interleukine-12, interleukine-17, interleukine-18, interleukine-23, transforming growth factor- $\beta$ , interferon- $\gamma$ , serum glucose, lipid profile<sup>18-20</sup>. These markers need further investigation to evaluate their efficacy and applicability before implementing in clinical practice.

#### **Genetic markers**

Genetic studies might evolve the most accurate part of precision psychiatry. At first, family studies and then twin studies scrutinized the hereditary phenotypes of mental health diseases; currently and through the developments in technology, genome-wide association studies have become available. These studies showed a correlation between genetic alterations in CACNA1C,

NCAN, and ODZ4 and bipolar disorder. They also revealed nucleotide polymorphism in schizophrenia<sup>21, 22</sup>. It seems that depression and suicidal ideation could also be affected with some genes alteration such as CRHR1 and FKBP5<sup>23,24</sup>. In a recently published study, Li *et al* used methylation microarray and pyrosequencing to detect methylation. They found that the DNA methylation of two CpG sites in LIME1 and one in SPTBN2 methylation could lead to attention deficit in children<sup>25</sup>. Other suggested methylation sites related to attention deficit hyperactivity disorder (ADHD) are TRABP1, COMT, ANKK1, BDNF, NGFR, DPP10, and TPH2<sup>26,27</sup>. Patients with some genetic syndromes like DiGeorge syndrome (micro-deletion on chromosome 22p11.2) could develop mental health issues (in this case: schizophrenia)<sup>28</sup>.

#### **Structural markers**

Psychiatric disorders are supposed to be associated with generalized rather than focal brain network dysfunction<sup>29</sup>. To study these networks, functional Magnetic Resonance Imaging (fMRI) could be performed. It would exhibit different aberrancies in various psychiatric disorders. Besides, distinct brain areas and networks could be afflicted in a specific presentation of a single disease. For example, schizophrenia can cause numerous symptoms, each probably related to a particular part<sup>30</sup>. However, these changes do not have an exact diagnostic role yet but can predict the possible signs and prognosis<sup>31</sup>. Previous studies also used volumetric MRIs showing enlargement of the ventricles, specifically in schizophrenia, and reduction in hippocampus size, mainly in severe cases of depression, schizophrenia which are related to drug resistance and poorer outcome<sup>32-34</sup>. Yu *et al* conducted an MRI-based study on depressed patients and concluded that cortical thickness and subcortical volumes in the frontal lobe and limbic system negatively correlated with the level of anxious misery measures. Patients with more positive scores had more amygdala and hippocampal volumes and thickness of precuneus and cingulate cortex.

#### **Pharmacogenetics**

Pharmacogenetics (by studying CYP metabolism rate, target receptor polymorphisms, *etc.*) has been shown to be advantageous in patients respecting choosing the best medication and dosage and predicting the prognosis and adverse effects<sup>35-38</sup>.

#### **Big data**

Big data employ large databanks, electronic health records, and mobile devices data other than all of this information. Then by using artificial intelligence and machine learning, they can lead to the constitution of predictive models and movement toward precision psychiatry<sup>39</sup>.

All of the mentioned data are representative cases of the more precise implications of patient's information; even if they are currently not fixed or feasible enough to be used worldwide, there is a possible future for

them to benefit patients with psychiatric disorders.

### Conclusion

Besides concerns about the increasing prevalence of psychiatric disorders and the significant burdens and costs associated with them, there are concerns about its validity. We suggested that integrating psychiatry and medical biotechnology and using biotechnological products in various aspects of psychiatry help psychiatry become more precise, strengthen its position among other sciences, and increase its scientific credibility.

### Acknowledgement

None.

### Conflict of Interest

The authors have no conflict of interest.

### Funding Statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

### Ethical Statement

Not applicable.

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