

Henry A. Nasrallah, MD Editor-in-Chief

These advances will alter psychiatric practice for the better, leading to more objective diagnoses and precise treatment options

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Transformative advances are unfolding in psychiatry

The future of psychiatry is bright, even scintillating. Disruptive changes are gradually unfolding and will proceed at a brisk pace. Psychiatric practice will be transformed into a clinical neuroscience that will heal the mind by repairing the brain. The ingredients of change are already in place, and the trend will accelerate.

Consider the following scientific, technical, and therapeutic advances that will continue to transform the psychiatric practice landscape.

Scientific advances

- Pluripotent cells. By dedifferentiating fibroblasts or skin cells and re-differentiating them into neurons and glia, the study of the structure and function of psychiatric patients' brains can be conducted in a test tube. That will exponentially expand the knowledge of the neural circuitry that underpin psychiatric disorders and will lead to novel strategies for brain repair.1
- **CRISPR.** This revolutionary advance in excising and inserting genes will eventually lead to the prevention of a psychiatric disease by replacing risk genes or mutations.1
- Molecular genetics. The flurry of identifying risk genes, copy number variants (CNV), and de novo mutations

using gene-wide association studies (GWAS) will facilitate gene therapy in psychiatric disorders.

- Neuroimmunology. The discovery of the role of neuroinflammation and oxidative stress (free radicals exceeding glutathione and other antioxidants) in neuropsychiatric disorders will ultimately lead to new insights into preventing the neurodegeneration associated with acute psychotic or mood disorders. Inhibiting the activation of microglia (the immune cells of the brain) is one example of innovative therapeutic targets in the future.2
- Recognizing the role of mitochondrial dysfunction as a pathogenic pathway to neuropsychiatric disorders such as depression, schizophrenia, bipolar disorder, and even the comorbid diabetes that is common among those psychiatric disorders will chart an entirely new approach to diagnosis and treatment.2
- The role of the microbiota and microbiome in psychiatric disorders has emerged as a fertile new frontier in psychiatry, both for etiology and as therapeutic targets.3
- The enteric brain in the gut, in close proximity with the microbiome, is now known to be a major source of neurotransmitters that modulate brain functions (dopamine, serotonin, and others). Consequently, it is implicated in psychopathology, rendering this "second brain" a target for therapeutic



interventions in the future, in addition to the "cephalic brain."4

• Biomarkers and endophenotypes. The rapid discoveries of biomarkers are setting the stage for the recognition of hundreds of biologic subtypes of complex neuropsychiatric syndromes such as schizophrenia, autism, depression, anxiety, and dementia. Biomarkers will steadily pave the road to precision psychiatry.5,6

Technical advances

- Artificial intelligence is beginning to revolutionize psychiatric practice by identifying psychopathology via voice patterns, facial features, motor activity, sleep patterns, and analysis of writing and language. It will significantly enhance the early detection and diagnosis of neuropsychiatric disorders.⁷
- Machine learning. As with other medical specialties, this radical and important new technology is likely to generate currently unrecognized information and decision options for psychiatric practitioners in the future.8
- Neuromodulation. The future is already here when it comes to employing neuromodulation as a therapeutic technique in psychiatry. The past was prologue with the discovery of electroconvulsive therapy (ECT) 30 years ago, evolving into vagus nerve stimulation (VNS), and transcranial magnetic stimulation (TMS) over the past 2 decades. Their application will go beyond depression into several other psychiatric conditions. A flurry of other neuromodulation techniques are being developed, including cranial electrical stimulation (CES), deep brain stimulation (DBS), epidural cortical stimulation (ECS), focused ultrasound (FUS), low-field magnetic stimulation (LFMS), magnetic seizure therapy (MST), near infrared light therapy (NIR), and transcranial direct current stimulation (TDCS).9

Therapeutic advances

- Rapid-acting parenteral antidepressants are one of the most exciting paradigm shifts for the treatment of severe depression and suicidal urges. In controlled clinical trials, ketamine, scopolamine, and nitrous oxide were shown to reverse chronic depression that had failed to respond to multiple oral antidepressants in a matter of hours instead of weeks or months.10 This remarkable new frontier of psychiatric therapeutics has revolutionized our concept of the neurobiology of depression and its reversibility into rapid remission. The use of IV, intranasal, and inhalable delivery of pharmacotherapies is bound to become an integral component of the future of psychiatry.
- Telepsychiatry is an example of how the future has already arrived for psychiatric practice. Clinicians' virtual access to patients living in remote areas for evaluation and treatment is certainly a totally new model of health care delivery when compared with traditional face-to-face psychiatry, where patients must travel to see a psychiatrist.
- New terminology for psychotropic agents is also an impending part of the future. The neuroscience-based nomenclature (NbN) will rename more than 100 psychotropic medications by their mechanisms of action rather than by their clinical indication.¹¹ Not only will this new lexicon be more scientifically accurate, but it also will avoid pigeon-holing drugs such as selective serotonin reuptake inhibitor antidepressants, which also are used to treat obsessive-compulsive disorder (OCD), anxiety, bulimia nervosa, and pain, or second-generation "atypical" antipsychotics, which are indicated not only for schizophrenia but also for bipolar mania and bipolar depression, and have been reported to improve

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This will be a fascinating journey of creative destruction of traditional psychiatry

treatment-resistant major depression, treatment-resistant OCD, borderline personality disorder, posttraumatic stress disorder (PTSD), and delirium.¹²

- Early intervention during the prodromal phase of serious psychiatric disorders is already here and will advance rapidly in the future. This will spare patients the anguish and suffering of acute psychosis or mania, hospitalization, or disability. It will likely reduce the huge direct and indirect costs to society of serious psychiatric disorders.¹³
- Repurposing hallucinogens into therapeutic agents is one of the most interesting discoveries in psychiatry. As with ketamine, a dissociative hallucinogen that has been rebranded as a rapid antidepressant, other hallucinogens such as psilocybin, lysergic acid diethylamide (LSD), and 3,4-methylenedioxy-methamphetamine (MDMA) are being investigated as therapeutic agents for depression, anxiety, and PTSD. They will become part of our expanding future pharmacotherapeutic armamentarium.14

It is obvious that parts of the future of psychiatry are already in place today, but other trends will emerge and thrill us clinicians. These advances will gradually but certainly alter psychiatric practice for the better, as the neuroscience of the mind expands and guides psychiatrists to more objective diagnoses and precise treatment options. The pace of advances in psychiatry is one of the most rapid in medicine.

So hold on: This will be a fascinating journey of creative destruction of traditional psychiatry.15 But as Emily Dickinson wrote: "Truth must dazzle gradually, or every man be blind."

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