

Henry A. Nasrallah, MD Editor-in-Chief

A new 'brain-repai strategy aims to reverse neuroplastic changes that impair connectivity and **function**

Psychiatry's future is here Here are 6 trends to watch that will affect your practice

Do you sometimes wonder what psychiatry's future holds? Wonder no more: abundant clues point to exciting innovations in our field. Let me highlight 6 trends that will shape how we practice psychiatry.

- 1. Earlier diagnosis and early intervention. The past decade has witnessed a surge of progress in identifying individuals at high risk for psychosis or mood disorders. The "prodrome" has become a fertile area of research, with a focus on early "treatment" even before the clinical syndrome of schizophrenia or mania appears. The goal is to try to delay, modify, or ameliorate incipient serious mental illness by using both pharmacotherapy and psychotherapy.
- 2. A tsunami of genetic discoveries. Almost weekly, psychiatric geneticists are discovering genes associated with serious psychiatric disorders. Neuregulin 1, dysbindin, DISC1, DAOA (G72), PRODH, and COMT are among the many odd-sounding genes located on various chromosomes. These discoveries confirm the "complex genetics" of psychiatric disorders involving dozens-even hundreds-of susceptibility genes, in contrast to the "1 gene, 1 disease" Mendelian paradigm.

Ultimately, these genetic discoveries will provide clues to the molecular pathophysiology of major mental disorders, leading to the holy grail of psychiatric treatment: specific, biotechnology-driven, disease-modifying pharmacotherapeutics rather than merely symptom-control agents.

3. Neuroplasticity as treatment target. Over the past few years, structural atrophy of the brain at the cellular and molecular levels has been documented in psychosis, mania, depression, and anxiety. These findings have shifted our perspective of mental illness beyond the simplistic notions of "chemical imbalance." The new model is progressive neuroplasticity changes in neurons, dendritic spines, neurite extensions, and

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synapses, (ie, the neuropil), with both grey and white matter reductions impairing brain connectivity and functioning.

In response, researchers are developing a neuroprotective paradigm to reverse neuroplastic changes as a new brain-repair strategy. Thus, therapeutic agents and their targets may include:

- caspase inhibitors to stop apoptosis
- neurogenesis stimulators to replenish neurons
- · neurotropic enhancers to reverse deficits in various growth factors, such as nerve growth factor (NGF), brain-derived neurotropic factor (BDNF), vascular endothelial growth factor (VEGF), etc.
 - · antioxidants to neutralize excess free radicals
 - glia-proliferation enhancers to rebuild white matter
- tumor necrosis factor-alpha (TNF-α) inhibitors to combat the inflammatory process reflected by high cytokine levels in psychotic and mood disorders.

Interestingly, many existing psychotropic agents have one or more of these neurotropic effects.

- 4. Neurostimulation for brain repair. Electroconvulsive therapy has been an effective (though sparingly used) psychiatric treatment for decades. Now, a new era of brain stimulation for psychiatric disorders is evolving with the FDA-approved modalities of repetitive transcranial magnetic stimulation (rTMS) and vagal nerve stimulation (VNS). But the next "big thing" may be deep-brain stimulation (DBS), which is becoming a routine treatment for neurologic conditions such as Parkinson's disease. DBS has potential to provide major treatment breakthroughs, and DBS research is progressing rapidly.
- 5. Pharmacogenomics in clinical practice. Psychiatrists are aware that inherited genetic variations (such as in cytochrome enzymes) can influence the body's response to drugs. Thus, patients who are

poor metabolizers often experience side effects at usual clinical doses and may discontinue medications that could help them. Similarly, fast metabolizers may fail to respond to drugs that should work and are labeled as "treatment-resistant."

Pharmacogenetic screening in clinical practice soon will become routine—it already is at a few U.S. academic hospitals—and will enable psychiatrists to customize drug treatment to achieve better efficacy and tolerability for each patient. This will help us adapt therapies to address genetic variations within our ethnically diverse society.

6. Intertwining of physical and mental disorders.

A comparatively high mortality rate from cardiovascular disease has been documented in persons with serious psychiatric disorders, especially schizophrenia, bipolar disorder, major depression, and anxiety. Similarly, persons with obesity, diabetes, dyslipidemia, and hypertension suffer from higher rates of psychiatric disorders. Inflammatory factors, in part secreted from visceral adipose tissue, appear to be a common pathway.

The optimal psychiatric practice is becoming a collaborative model of care between psychiatrists and family physicians, so that patients receive integrated, comprehensive physical and mental treatments.

What this all means. The journey to the future of psychiatric practice is underway. In many respects, the future is already here. I encourage you to join the excitement.

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Welcome, Dr. Goldberg

Joseph F. Goldberg, MD, has joined CURRENT PSYCHIATRY's editorial board as Deputy Editor. Dr. Goldberg is associate clinical professor of psychiatry at Mount Sinai School of Medicine, New York, NY, and director of the affective disorders research program at Silver Hill Hospital, New Canaan, CT. He has published >100 peer-reviewed papers on bipolar disorder, his specialty in both research and clinical practice.



Dr. Goldberg