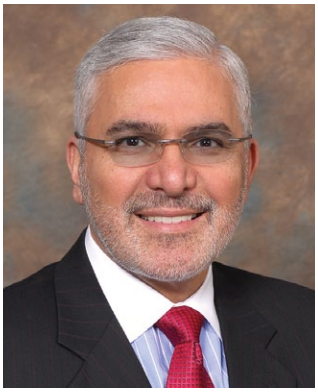
Can philanthropy fill the unmet needs of psychiatry?



Henry A. Nasrallah, MD
Editor-in-Chief

I'm heartened whenever a philanthropist gives generously to research that is targeted to unravel the myriad mysteries of the human brain and its disorders.

Recent examples come quickly to mind:

- **$100 million** from the Lieber family to fund the Lieber Institute for Brain Development at Johns Hopkins University
- **$300 million** from Microsoft cofounder Paul G. Allen to create the Allen Institute for Brain Science
- **$650 million** from Ted Stanley for the Stanley Center at the Broad Institute.

Such generosity is cause for celebration by psychiatrists and their long-suffering patients who are disabled by a brain disorder. Private money supplements research funding by the National Institutes of Health and will bolster the war against mental illness,[1] which costs >$300 billion annually (***Box,***[2] ***page 12***).

Although philanthropy will help, many needs in psychiatry are unmet, and not all can be addressed with money. Consider a number of areas of need.

Unmet clinical needs

Models of disease. Psychiatry is in desperate need of an objective, valid diagnostic system that transcends the DSM model of symptom clusters. The Research Domain Criteria[3] represents the effort to find an alternative. To achieve that goal, it's necessary to identify biomarkers and establish their utility—a task that requires a huge amount of funding.

Therapeutics. Clinicians are hungry for innovative, safe pharmaceuticals and non-drug treatments that modify disease, not just alleviate symptoms. Obsessive-compulsive disorder always has lacked such therapies; so have dementia, schizophrenia, personality disorders, dissociative disorders, and sexual pathologies. In fact, >80% of DSM disorders do not have an FDA-approved, evidence-based treatment,[4] and many available medications are only partially efficacious, poorly tolerated, or unsafe.

There are more unmet needs in therapeutics:

- Development of promising non-drug therapies, such as neuromodulation, proceeds slowly.
- Research into neurobiological mechanisms of psychotherapy is in its infancy.
- A foolproof method to monitor adherence does not exist, and countless patients relapse needlessly and deteriorate functionally.
- Effective, evidence-based rehabilitation for serious psychiatric disorders is used narrowly and vastly underfunded.
- Insurers continue to thumb their nose at laws that require parity for treating mental illness—thus impeding access to, delaying, or truncating psychiatric care.

continued

Some of the unmet needs of psychiatry require more discoveries, a change of attitude, broader training, and forceful political activism—not just money

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Box

Private-public partnerships

Joint funding of research by government and charitable foundations can succeed: Consider the landmark study of the Schizophrenia Working Group of the Psychiatric Genomics Consortium, published a few weeks ago,[2] which describes discovery of a mother lode of 108 independent genetic loci for schizophrenia risk. This is a massive collaboration of 350 scientists from 26 countries who pooled an unprecedented collection of >150,000 case and control DNA specimens. The Group's work undoubtedly will lead to unprecedented insights about the molecular pathophysiology of schizophrenia and related disorders that share genes, such as autism, bipolar disorder, and major depressive disorder.

Unmet scientific needs

Translational investigators. Despite increased funding for basic neuroscientific study and breathtaking discoveries in animal molecular neurobiology, a trickle of findings has been applied to clinical medicine. This translational gap has many causes, including a shortage of translational neuroscientists (MD-PhD psychiatrists and neurologists), insufficient long-term funding to develop such clinician-researchers, and complex regulatory oversight of human research.

Stalled progress in drug development. Development of novel-mechanism therapeutics for brain disorders is languishing. Some pharmaceutical manufacturers have abandoned the development of drugs that act on the CNS in favor of less complex, more lucrative areas such as oncology and cardiology; others have reduced their investment in CNS products. Developing treatments for knotty disorders of the most complex structure in the known universe requires mammoth investment. Why are stakeholders bailing out on the greatest challenge for science and medicine for easier endeavors?

Discovering new genes for every devastating neuropsychiatric syndrome, such as schizophrenia, is cause for celebration, but the champagne won't flow until the coding of every gene is unscrambled so that specific biological interventions can be developed. The cost of the chase might be orders of magnitude greater than what is invested in research today.

Conceptualizing new models of brain disorders is a critical part of scientific progress and an antidote to the inertia of perpetual group-think. Depression, for example, is being reconceptualized as a disorder of impaired neuroplasticity and neurotropic deficiency, rather than a shortage of serotonin and norepinephrine. Rapid reversal of severe depression to euthymia—in 1 or 2 hours—with IV ketamine shattered the dogma that depression takes weeks to lift, and is ushering in unprecedented new thinking and models likely to revolutionize treatment of severe depression. We need such breakthroughs for other psychiatric brain disorders.

Unmet professional and sociopolitical needs

Broadening of training. Psychiatrists have focused on the mind but insufficiently attended to the biology of the brain. For psychiatry to rise to the next level as a medical specialty and brain discipline, training must incorporate more neurology than it does now. The converse is true in neurology.

Hospitalization not incarceration. It is unconscionable that people suffering from a medical illness that impairs

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8.7 Hepatic Impairment

No dose adjustment to FANAPT is needed in patients with mild hepatic impairment. Exercise caution when administering it to patients with moderate hepatic impairment. FANAPT is not recommended for patients with severe hepatic impairment *[see Dosage in Special Populations (2.2)]*.

In adult subjects with mild hepatic impairment no relevant difference in pharmacokinetics of iloperidone, P88 or P95 (total or unbound) was observed compared to healthy adult controls. In subjects with moderate hepatic impairment a higher (2-fold) and more variable free exposure to the active metabolites P88 was observed compared to healthy controls, whereas exposure to iloperidone and P95 was generally similar (less than 50% change compared to control). Since a study in severe liver impaired subjects has not been conducted, FANAPT is not recommended for patients with severe hepatic impairment.

8.8 Smoking Status

Based on *in vitro* studies utilizing human liver enzymes, FANAPT is not a substrate for CYP1A2; smoking should therefore not have an effect on the pharmacokinetics of FANAPT.

10 OVERDOSAGE

10.1 Human Experience

In premarketing trials involving over 3210 patients, accidental or intentional overdose of FANAPT was documented in 8 patients ranging from 48 mg to 576 mg taken at once and 292 mg taken over a 3-day period. No fatalities were reported from these cases. The largest confirmed single ingestion of FANAPT was 576 mg; no adverse physical effects were noted for this patient. The next largest confirmed ingestion of FANAPT was 438 mg over a 4-day period; extrapyramidal symptoms and a QTc interval of 507 msec were reported for this patient with no cardiac sequelae. This patient resumed FANAPT treatment for an additional 11 months. In general, reported signs and symptoms were those resulting from an exaggeration of the known pharmacological effects (e.g., drowsiness and sedation, tachycardia and hypotension) of FANAPT.

10.2 Management of Overdose

There is no specific antidote for FANAPT. Therefore appropriate supportive measures should be instituted. In case of acute overdose, the physician should establish and maintain an airway and ensure adequate oxygenation and ventilation. Gastric lavage (after intubation, if patient is unconscious) and administration of activated charcoal together with a laxative should be considered. The possibility of obtundation, seizures or dystonic reaction of the head and neck following overdose may create a risk of aspiration with induced emesis. Cardiovascular monitoring should commence immediately and should include continuous ECG monitoring to detect possible arrhythmias. If antiarrhythmic therapy is administered, disopyramide, procainamide and quinidine should not be used, as they have the potential for QT-prolonging effects that might be additive to those of FANAPT. Similarly, it is reasonable to expect that the alpha-blocking properties of bretylium might be additive to those of FANAPT, resulting in problematic hypotension. Hypotension and circulatory collapse should be treated with appropriate measures such as intravenous fluids or sympathomimetic agents (epinephrine and dopamine should not be used, since beta stimulation may worsen hypotension in the setting of FANAPT-induced alpha blockade). In cases of severe extrapyramidal symptoms, anticholinergic medication should be administered. Close medical supervision should continue until the patient recovers.

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their judgment and behavior are locked up as criminals. Psychiatry must forcefully lobby so that the seriously mentally ill are treated in secure hospitals staffed by physicians, nurses, and mental health professionals.

That's right: Bring back the asylum to address this unmet medical, political, and ethical need for psychiatric patients.[a] A serious mental disorder must be accepted as a fault-free illness.

Full integration of psychiatry into the rest of medicine remains an unmet need, despite good progress. Because almost every medical illness can cause psychiatric symptoms, DSM-5 mandates that general medical conditions be ruled out before a primary psychiatric diagnosis is made.

Along the same lines, most severely mentally ill persons suffer from medical and neurologic ailments before their first episode,[5] and many die prematurely from cardiovascular causes that often are the result of unhealthy lifestyle; iatrogenic complications; and lack of primary care interventions.[6] Psychiatric patients must always receive standard general medical evaluation and management, side by side with their psychiatric care.

[a]To read more about this, I recommend my March 2008 editorial, "Bring back the asylums?," at CurrentPsychiatry.com, and Dr. George Paulson's excellent book, Closing the asylums: Causes and consequences of the deinstitutionalization movement (Jefferson, NC: McFarland & Co. Inc; 2012).

Philanthropy for psychiatry

Philanthropic support of psychiatry is a salutary trend. Some unmet needs in psychiatry, however, require not only money but a change in attitude (such as eliminating the absurd and discriminatory stigma of mental illness), better training, and forceful political activism by all of us.

Henry A. Nasrallah, MD
Editor-in-Chief

References

1. Licinio J, Wong ML. Launching the 'war on mental illness'. Mol Psychiatry. 2014;19(1):1-5.
2. Schizophrenia Working Group of the Psychiatric Genomics Consortium. Biological insights from 108 schizophrenia-associated genetic loci. Nature. 2014;511(7510):421-427.
3. Devulapalli KK, Nasrallah HA. An analysis of the high psychotropic off-label use in psychiatric disorders. The majority of psychiatric diagnoses have no approved drug. Asian J Psychiatr. 2009;2(1):29-36.
4. Cuthbert BN. The RDoC framework: facilitating transition from ICD/OSM to dimensional approaches that integrate neuroscience and psychopathology. World Psychiatry. 2014;13(1):28-35.
5. Sørensen HJ, Nielsen PR, Benros ME, et al. Somatic diseases and conditions before the first diagnosis of schizophrenia: a nationwide population-based cohort study in more than 900000 individuals [published online July 25, 2014]. Schizophr Bull. doi: 10.1093/schbul/sbu110.
6. Nasrallah HA, Meyer JM, Goff DC, et al. Low rates of treatment for hypertension, dyslipidemia and diabetes in schizophrenia: data from the CATIE schizophrenia trial sample at baseline. Schizophr Res. 2006;86(1-3):15-22.