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GUEST EDITORIAL

Is the National Institute of Mental Health failing clinical psychiatry?

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The development of new treatments for mental illness (and a better understanding of how we should use these treatments) is facing a serious crisis. This crisis has been brewing over the last several decades for both pharmacologic and psychological treatments, despite years of promises and even the "Decade of the Brain," which was declared by President George H.W. Bush in the 1990s to enhance public awareness of the benefits to be derived from brain research.

Academic Medical Centers (AMCs), which have been in decline for some time,[1] are less invested in psychopharmacology research for several reasons. Studies examining treatments, which typically are funded by the pharmaceutical industry, are less valued in an academician's portfolio than are studies funded by agencies such as the National Institute of Mental Health (NIMH), and contacts with "Big Pharma" are now considered undesirable (if not forbidden) by some centers. There is no revenue stream for AMCs to fund treatment studies on their own. At the same time, the pharmaceutical industry has become less interested in the research conducted at AMCs because such research is considered slow and not as responsive to industry demands as are independent for-profit centers conducting psychopharmacology clinical trials.

However, these for-profit centers have their own problems. For instance, Thomas Laughren[2] points to the growing crisis in the development of treatments for schizophrenia. He notes the striking, unexpectedly high placebo response rates in schizophrenia drug trials and the decline in success of schizophrenia trials in North America (from an 81% success rate before 2009 to a 25% success rate post 2009). One of the factors contributing to this decline, Laughren writes, is that "clinical trial sites are incentivized to recruit patients, but without any particular reward for getting the right patient."[2] Another issue is the existence of fraudulent patients (for example, persons who pretend to be patients and enter clinical trials for financial gains). Laughren believes that many pharmaceutical companies will become reluctant to invest in North American sites, and he further

points out that many companies are leaving neuroscience research altogether. This example from the area of schizophrenia research is probably valid in other areas of clinical psychopharmacology research.

The situation in psychotherapy research is also concerning. Psychotherapy research is typically funded by the NIMH and other federal grant-making agencies. However, the NIMH only devotes a minuscule part of its budget on psychotherapy research.[3] For example, in 2015, only 5.4% of the total NIMH budget was spent on clinical research on psychotherapy.[3]

So, what should be done about the situation we find ourselves in? We have access to established but imperfect treatments and several new but problematic treatments, some of which raise more questions than answers (eg, esketamine). In addition, there are no significant new discoveries on the horizon, and there is lack of leadership and interest in academia and the pharmaceutical industry to develop new treatments. Ordinarily, the answer would be to turn to a premier research institution funded by the public, such as the NIMH, for help. Unfortunately, as we will see, the NIMH is part of the problem.

Three recent articles have highlighted the fact that the NIMH funds very little research on the treatment of mental illness. Torrey et al[4] analyzed 428 projects of the NIMH's schizophrenia-related research 2018 portfolio costing a total of $201 million (11.5% of the NIMH's total budget). Interestingly, this included "$25 million for schizophrenia-related intramural projects… $3.9 million for the Office of the Intramural Scientific Director and $10.2 million for 'NIMH space activation, maintenance and improvement.'" Torrey et al[4] rated how likely these projects were to improve the symptoms and/or quality of life of persons with schizophrenia. They found most of these studies were "very unlikely to provide clinical improvement within 20 years." Only 30 (7%) projects were rated by at least 1 reviewer as likely to provide clinical improvement within the next 2 decades. The cost of these 30 projects was 5.5% of the total schizophrenia-related portfolio, or 0.6% of the NIMH total budget. Only 1 trial examined a pharmacologic agent for the treatment of schizophrenia. One trial examined amphetamine in the enhancement of cognitive therapy, 1 trial examined a gluten-free diet, and 2 trials examined transcranial magnetic stimulation in schizophrenia. Interestingly, Torrey et al[4] cited a 1998 Institute of Medicine report[5] to highlight how some individuals believed that the "NIH cares more about curiosity than cure, more about fundamental science than clinical application."

In another article, Torrey et al[6] criticized the NIMH for not adequately funding schizophrenia treatment research and for suggesting that we should not expect new drugs from the NIMH. They noted, "There has been no significant pharmacologic advance for schizophrenia since clozapine was approved almost 30 years ago." NIMH Director Joshua Gordon issued a lame response[7] to this criticism that did not bring satisfactory answers or promises.

Markowitz and Friedman[3] also have been highly critical of the NIMH's lack of support for clinical research. They have observed a profoundly worrisome shift in psychiatric research funding and its consequences for patients and the future of psychiatry. They note, "Unlike other NIH institutes, the National Institute of Mental Health (NIMH) has taken a straight and neural path. Since 2002, the NIMH has increasingly funded neuroscience at the expense of clinical and services research, putting all its eggs in one biologic basket, envisioning a breakthrough that may not arrive for decades" and "Neuroscience has yielded scant clinical progress."[3] They cite former NIMH Director Thomas Insel, who in 2015 explained that 10% of NIMH research money was used to fund clinical trial research. They also put the focus on the NIMH and its basic science research into a broader perspective: "An even more ominous consequence [of the current NIMH policies] is brain drain. Young psychiatrists and psychologists recognize that NIMH will not support clinical research careers. These early-career professionals instead tackle laboratory neuroscience, or, if their hearts and brains are clinically focused, they leave research for practice. In surveying psychiatric researchers, we are finding what we feared: plenty of junior faculty neuroscientists, but a dearth of clinical researchers. A research generation is being lost. The specialized technical knowledge of senior clinical researchers risks extinction."[3]

These concerns, together with the emphasis AMCs and academic departments place on NIMH funding and the role of NIMH funding in promotion and tenure decisions, might result in departments of psychiatry being being manned by PhDs with no interest in clinical psychiatry and psychopharmacology or clinically oriented research and with no ability to teach clinical psychiatry. Is that what we expect from AMCs and academic departments of psychiatry?

Historically, the NIMH has funded large treatment trials, such as the Clinical Antipsychotic Trial of Intervention Effectiveness (CATIE) and Sequenced Treatment Alternatives to Relieve Depression (STAR*D). That was long ago. We need more studies on various treatments and on their combinations, not fewer. We need to fund research that can help answer important clinical questions, such as determining the adequate length of treatment, appropriate and maximum dosing of medications, and what long term-maintenance treatment constitutes (such as the study by Kupfer et al[8] that examined 5-year maintenance treatment using imipramine for major depressive disorder).

The NIMH strategy in the past 2 decades has been myopic and has outlived its usefulness. The preoccupation with genetics, biomarkers, and imaging has not helped us treat a single patient or helped us in any way to relieve a patient's suffering. Psychiatry cannot rely on the serendipity that brought us treatments in the past.[9] We need new paradigms. We also need to rethink the funding of psychiatric research. The 90/10 split between basic and clinical research funding is not working and is not acceptable. A 50/50 split seems more acceptable, although even that may not be enough for launching a true new national initiative to study and develop new and better psychopharmacologic and psychological treatments. The NIMH would benefit by having a clinician at its helm once again. Without these changes, the answer to my question in the title would be: Yes, the NIMH has failed us and our patients. ■

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