

## **Mental Health Research: Into the Future**

by

Thomas. R. Insel, M.D., Director  
National Institute of Mental Health  
National Institutes of Health

In the six decades that NIMH has led the nation's research effort in mental health, advancement has been dramatic. We understand now that the major mental disorders are brain disorders, with specific symptoms rooted in abnormal patterns of brain activity. We realize that the devastation of autism and schizophrenia are not the result of bad parenting or early psychic conflict. We recognize that mental disorders, unlike most chronic medical disorders, generally begin in childhood, with 50 percent of affected adults reporting onset of symptoms before age 14. We now have reliable diagnostic tools as well as effective medications and psychological therapies for depression and anxiety disorders; we have treatments that can predictably reduce the hallucinations and delusions of schizophrenia, as well as psychosocial interventions that enable people with schizophrenia to remain in their communities, to work and lead productive lives. The number of patients in state hospitals has decreased from 600,000 to less than 60,000.

While research funded by the National Institute of Mental Health (NIMH), part of the National Institutes of Health, has resulted in profound advancement in most of the major mental illnesses, in 2006 we recognize that not all treatments work for everyone. After six decades of progress, mental disorders remain unacceptably common, causing more disability in people under age 45 than any other class of non-communicable medical illness.

How can we do better? The NIMH has raised the bar on the nation's research effort to reduce the public health burden of mental disorders by going for cures and strategic preventions. Since mental disorders are brain disorders, the path forward is to exploit the power of genomics and neuroscience to solve these mysteries of the mind. Genetics can now help us to understand how one person is susceptible to an illness and another is resilient. Neuroscience now allows us to study the brain in children and adults with mental disorders just as we study the heart in those with cardiac disease. Genetics and neuroscience together are giving us the tools for predicting risk, validating diagnosis, and identifying targets for new, more effective treatments.

Of course, environmental factors – such as loss of a loved one, traumatic events, or physical attributes of the fetal environment – exert a powerful influence on the development of mental disorders, possibly triggering the leap from genetic predisposition to illness. Researchers are now asking how environmental factors during critical phases of development exert long-term effects on how and when genes are activated. Exploring how genes interact with the environment to result in depression is not much different from understanding how environmental toxins contribute to cancer or how diet influences cardiovascular disease. However, for mental disorders, the trigger may be stressful

experiences, the exposure may only have an impact at specific stages of development, and the effects may be limited to a narrow range of cells in the brain.

But doing better must mean more than discovering biological markers for diagnosis or new targets for treatment to help people in the future. We must use current treatments more effectively, identifying those who will respond best to the treatments available now. Over the past seven years, NIMH has completed several practical clinical trials that are the largest and longest of their kind, involving more than 10,000 patients at more than 200 sites. These “effectiveness studies” were designed to examine not only changes in symptoms but changes in functioning, to determine whether a treatment improves quality of life, care giving burden, or use of health services.

These studies have already demonstrated the effectiveness of antidepressant medication for adolescents with depression and the value of an off-patent, inexpensive antipsychotic medication for adults with chronic schizophrenia. These clinical trials are part of a rigorous effort to discover what therapies work best, and for whom. Current research is discovering how individual differences in biology could determine how that person reacts to a certain medication. Discovering these individual differences will help improve both diagnosis and treatment. For a person with mental illness, one can imagine that in the future a physician would perhaps use a memory task together with brain imaging and a genetics test to diagnose and select a specific treatment -- just as a contemporary cardiologist uses a stress test and echocardiogram to diagnose heart disease and select the proper treatment.

It is critical to realize that this vision of personalized care does not mean designing exotic therapies for a few privileged patients. The ultimate goal is personalized or individualized care for the full spectrum of people with mental disorders. As researchers learn more about the brain mechanisms of mental disorders and related behavioral and environmental factors, treatments will become more specific.

These are some of the issues that will be addressed by the newest generation of NIMH researchers. In the 60 years of NIMH’s history, there has never been a more exciting time. Payoffs are imminent. For instance, years of basic research on depression have led to development of a new class of medication that, in initial trials, works in hours rather than weeks. We are on the verge of significant advances that will move us closer to predictive, preventive, and personalized mental health care grounded in research.

One of the most elusive elements of improving mental health, however, will be the integration of psychiatry with the rest of medicine. Stress and depression, for example, are among the risk factors for heart disease and other serious medical conditions. The mechanisms underlying these relationships aren’t yet clear, but integration will be a significant step toward improved care of the whole person by an effective treatment team, while also reducing the stigma felt by those with these devastating diseases.

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