



Testimony
Before the Subcommittee on Health
Committee on Energy and Commerce
United States House of Representatives

**Research Progress in Understanding
Mental Disorders**

Statement of

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Chairman Deal, Ranking Member Brown, Mrs. Myrick and members of the Subcommittee: I am Thomas R. Insel, M.D., Director of the National Institute of Mental Health (NIMH), the component of the National Institutes of Health (NIH) of the Department of Health and Human Service (HHS) tasked with responsibility for developing improved methods of diagnosing, treating, and preventing mental disorders, including schizophrenia, autism, and mood and anxiety disorders. Thank you for giving us this opportunity to share our excitement about progress in understanding mental illnesses.

Mental illnesses are brain disorders, with specific symptoms rooted in abnormal patterns of brain activity; like other medical disorders, they are diagnosable, and they are treatable. This is critical, given the tremendous burden mental illnesses exert personally, socially and economically. Unlike most chronic medical disorders, mental disorders most often begin in adolescence and young adulthood. Without proper treatment they can devastate individuals and their families. Despite this dour background, there has been significant advancement in the science of mental illness. We have reliable diagnostic tools and 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 disorder to remain in their communities, to work and lead productive lives.

We referred to the 1990s as the “Decade of the Brain,” based on a Congressional Resolution signed by President George H.W. Bush on July 17, 1990. It was a period of major growth in neuroscience, revolutionizing the way we think about the brain. We were able to demonstrate that mind and body cannot be separated, that mental activity

can be represented as brain activity, and that a clear distinction cannot be made between mental events and neural events. One implication of this revolution is the recognition of mental disorders as brain disorders.

For example, studies of children who have the onset of a rare form of schizophrenia before age 14 show a marked change in brain structure. When they were initially seen in the clinic in the NIMH intramural program at about age eight or nine, they had already shown some thinning of the part of the brain called the cerebral cortex, compared to the cortical thickness of other eight- and nine-year-olds. Scans of their brains over the next five years demonstrated a profound loss of cerebral cortex relative to the brain scans of normal children of the same age. This provided strong evidence that childhood-onset schizophrenia involves loss of brain matter in a manner similar to other neurological or neurodegenerative disorders. The difference is that in most neurological disorders, such as Parkinson's disease, there is a specific site of damage. But, schizophrenia, bipolar disorder, depression and autism seem to be disorders of networks, or circuits, rather than of specific cells identifiable by brain scan.

NEW FINDINGS

Genes and Neuroscience

Since mental disorders are brain disorders, we have been exploiting the power of genomics and neuroscience to solve the mysteries of the mind. The Human Genome Project in 2003 provided a full map of the 23,000 genes common to all humans. The next vital map, which has just become available in the past few months, comes from the International HapMap Project, whose goal is to chart all of the common points of variation in the human genome. This new map of variation should give us the clues for

understanding how one person is susceptible to a mental disorder and another is resilient. Genetics and neuroscience together give us the tools for predicting risk, validating diagnosis, and identifying targets for new, more effective treatments.

Gene-Environment Interactions

We have learned that genes confer susceptibility; but environmental factors, such as the loss of a loved one, traumatic events, or physical attributes of the fetal environment, also exert a powerful influence on the development of mental illness. The complexity of this interaction is apparent in a serotonin gene that has been associated with depression. A particular segment of the gene comes in two forms; people with the “short” form are about two to three times more likely to get depressed when also faced with severe life stressors, such as death of a family member or loss of a job. Conversely, if a person has the other “long” form, they appear to be protected, even when faced with four or more severe life stressors. With the protective form, a person is actually no more likely to develop depression than if he had experienced none of those events.

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 a mental disorder such as depression is not much different from understanding how environmental toxins contribute to illness. 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.

Brain Systems

With the advent of neuroimaging, we can, for the first time, look at the activity of brain circuits during illness and map how activity changes during recovery. Advances in neuroimaging in the past 5 years have provided more detailed pictures and the ability to see events almost in real time. For instance, imaging has recently revealed that a brain region called Area 25 is important in depression. In depressed people, both volume and metabolic activity in this region are abnormal. As people recover from depression, activity in Area 25 undergoes significant changes. Whether the treatment is an antidepressant medication, behavioral therapy, or deep brain stimulation, recovery is associated with a reduction in the activity of this brain circuit.

Clinical trials

In addition to searching for new targets for treatments to help people in the future, we have been working to 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 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 and personalize 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.

THE FUTURE

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 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 not been a more exciting time. We are on the verge of significant advances that will move us closer to predictive, preventive, and personalized mental health care grounded in research.

We are also striving to assure that evidence-based practices can be disseminated and delivered, so that people have access to treatment and services that are coordinated and effective. We are working within NIH to better integrate psychiatry with the rest of medicine, for they are inextricably linked: stress and depression are major risk factors for heart disease and other serious medical conditions. The mechanisms underlying these

relationships are not yet clear, but integration will be a significant step toward improved care of the whole person by an effective treatment team.

I firmly believe we have made a great start in understanding mental illnesses and that in our lifetimes we will be able to treat and even prevent mental illnesses with much greater certainty and speed. This will restore productivity, make families whole, and eliminate many of the 30,000 suicide deaths each year.

Thank you for providing me the opportunity to discuss these issues with you. I will be happy to answer any questions you may have.