

NCDEU Plenary Session: The Art and Science of Personalizing Treatments for Mental Disorders
May 28, 2008

NCDEU Co-chairs Matt Rudorfer, M.D., of the National Institute of Mental Health (NIMH) and John Kane, M.D., of the American Society of Clinical Psychopharmacology opened the plenary session by welcoming everyone to the 2008 NCDEU meeting. Philip Wang, M.D., Dr. P.H., of NIMH and chair of the plenary session, introduced the five speakers:

- Thomas R. Insel, M.D., Director, NIMH
- Steve M. Paul, M.D., Executive Vice President for Science and Technology, President of Lilly Research Laboratories, Eli Lilly and Company
- Francis McMahon, M.D., Chief, Genetic Basis of Mood and Anxiety Disorders Unit, Mood and Anxiety Program, NIMH
- Silvana Borges, M.D., Medical Officer, Genomics Group, Center for Drug Evaluation and Research, Food and Drug Administration
- Robert M. Kolodner, M.D., National Coordinator for Health Information Technology, U.S. Department of Health and Human Services

Each of the five speakers provided different perspectives on progress and opportunities toward personalizing medicine for mental disorders.

Personalized Medicine for Mental Disorders: What Do We Know? What Do We Need?

Dr. Insel discussed progress toward personalizing medicine for mental disorders from an NIMH perspective. According to Dr. Insel, personalizing the treatment of mental disorders requires a paradigm shift in thinking. We must move from an acute disease model to a chronic disease model, from a focus on the idea of a single gene being responsible for a disease to multiple gene alleles contributing to complex disease, and from making treatment decisions based on group averages to making decisions based on the genetic makeup of the individual.

Dr. Insel described the pathway to personalized medicine as moving through three phases: (1) Discovery through exploratory studies and comparative clinical trials; (2) Development of moderators for stratifying and testing populations through prospective clinical trials; and (3) Use of the predictor data to create and disseminate personalized practice guidelines. By taking this path, we should be able to move from identifying simple biomarkers to developing panels of individual biomarkers that will accurately inform treatment patterns.

Tailoring Therapies for Common Complex Diseases: Pharmacogenomic (and Other) Lessons from Non-Psychiatric Disorders—An Industry Perspective

Dr. Paul provided a pharmaceutical industry perspective. He discussed tailoring therapies for complex mental disorders within the context of lessons learned from treatments for non-psychiatric illnesses. The best examples of tailoring drug therapies are from other fields of medicine, particularly oncology. Through research, some cancer drugs have been found to be effective only in people with certain genetic mutations or biomarkers.

Tailoring pharmacotherapy to individual needs is not a new concept—doctors already work to choose the right medicine for the right disease at the right dose and for the right duration. But advances in pharmacogenomics will allow researchers to identify people most at risk for a disease, predict how they may respond to a therapy and determine their likelihood for experiencing side effects. Such advances will also reduce costs associated with clinical trials because patients can be included or excluded based on their individual genotypes. Patients whose genotypes are known will also enjoy greater protection from exposure to drugs that may harm them.

Pharmacogenetics of Antidepressants: What We've Learned from the STAR*D Study

Dr. McMahon discussed pharmacogenetic lessons learned from analysis of genetic data from the NIMH-funded Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study. In his research, Dr. McMahon and his team found that people who carry certain alleles have different rates of response or remission when taking an antidepressant. Other genotypes are associated with a greater likelihood for adverse events, side effects and treatment-emergent suicidal thinking.

Dr. McMahon noted that to get a clinically meaningful effect size, a large sample, like that of STAR*D, is needed to develop accurate panels of multiple biomarkers. Larger samples also allow for identifying tolerability levels and who may experience adverse events. By developing clinically meaningful biomarkers, we will be able to develop a fuller clinical picture of individual patients, and better predict how they may respond to a treatment.

Personalizing Treatments: What Can We Do at the Food and Drug Administration?

Dr. Borges discussed the role of the FDA in personalized medicine. The FDA is striving to advance the field of pharmacogenomics by sponsoring several incentive programs. For example, the new Genomic Initiative is a voluntary program encouraging drug companies to share data from exploratory genomic studies. The initiative allows for exchanges between industry and the regulatory agency to develop better understanding of tools, data analysis and critical applications. It can also help identify regulatory gaps. So far, the program has been fairly successful, with more than 40 submissions. The FDA is also undergoing a pilot process to determine what qualifiers are needed for consistent biomarker identification. As pharmacogenomics becomes more established, the FDA will need to consider how to adjust drug labeling language, health care professional training, patient education, and other related challenges.

EHRs and PHRs in the Era of NHIN: Ensuring the Alphabet Soup for Health Information Technology Includes and Benefits the Treatment of Mental and Substance Use Disorders

Dr. Kolodner concluded the plenary by discussing the national health information technology agenda and how health IT benefits the treatment of mental disorders. The agenda is meant to enable the process of improving the quality and value of health care services. It aims to ensure individual and population health and well being through IT solutions such as ehealth systems, personal health records, and population-level health information. As we move toward an operational national health IT system, Dr. Kolodner and his office are working toward ensuring that five critical components are in place for a nationwide operable network—a clear governance protocol; established privacy, security and licensure policies; solid IT standards for health products; and a reliable network to connect them all. More information about the national health IT agenda is available at www.hhs.gov/healthit.

More information about the NCDEU meeting is available at www.ncdeumeeting.org