From basic research to personalized medicine

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Abstract

In the future, precision medicine will enable every clinician to tailor treatment and even prevention strategies to an individual's unique characteristics. In order to reach this goal, we need to collect and analyze many different types of data, from many different sources, including symptoms, genomics, and brain circuitry, as well as family dynamics, environmental exposures, and cultural background.

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Precision medicine appears to be the new hot topic in the research world. The White House Website has a practical and useful definition of it: "Getting the right treatment at the right time to the right person." In the near future, precision medicine will enable every clinician to tailor treatment and prevention strategies to an individual's unique characteristics. To reach this goal, we need to collect and analyze many different types of data, from many different sources, including symptoms, genomics and brain circuitry, as well as family dynamics, environmental exposures, and cultural background. In fact, enormous amounts of clinical data can already be easily collected by health care providers and the patients themselves using new technologies (see our previous issue on this topic: *Dialogues in Clinical Neuroscience*. 2016;18[2]). Yet, the classical aspects of precision medicine, relating genotype to diagnosis and treatment, are not yet ready in psychiatry.

The director of the prestigious National Institute of Mental Health, Tom Insel, explained: "What does precision medicine mean for mental health? […] It is certainly possible that we may find specific mutations in relevant brain circuits that explain some cases of schizophrenia, bipolar disorder, or autism, just as mutations in the tumor explain cancer. […] But more likely, precision medicine for mental disorders will not come from a single genomic glitch."[6]

Rather, many common (and, in a few cases, rare) genes may contribute only a small amount of vulnerability as part of an overall risk profile that includes life experiences that may modify the gene expression through epigenetic mechanisms. In the research field, new techniques such as next-generation sequencing, enabling rapid and economic whole exome or genome sequencing are promising.[7] The study of gene-environment interactions and epigenetics also seems promising. However, gene/environment research still faces several conceptual and methodological challenges. As a consequence of these methodologies of genetic research, psychiatrists will collect "big data," and novel research and statistical methods will be needed to analyze and understand them.

In clinical practice, significant interindividual variability exists in psychotropic drug response, therapeutic dosage, and adverse effect profiles. Moreover, prolonged times to response or remission represent a period of suffering associated with an increased risk for morbidity and mortality. Genetic factors influencing pharmacokinetics and pharmacodynamics may contribute to this variability. Some genetic markers are now available as clinical tests. Clinical validation and reliability of genotyping, uniformity and clarity in test interpretation, and clinician and patient education are critical at this stage. In the near future, the improvement of our knowledge of the causes of certain psychiatric disorders will lead to the identification of reliable biological markers, which have been lacking to date. In turn, these biomarkers could help make psychiatric diagnoses, or predict the prognosis at the single-subject level. Recent reviews of potential biomarkers already available have been published for schizophrenia, depressive disorders, or bipolar disorders (for review see refs 3-7).In parallel, the identification of biomarkers in psychiatry will help us refine the diagnostic criteria, which is crucial. In particular, genetic overlap has now been demonstrated between several major mental diseases, suggesting a common neurodevelopmental spectrum rather than specific and different diseases. ❑

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