Different Gene Ensembles, Different Schizophrenias

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- Schizophrenia comprises eight genetically different diseases, each of which presents its own symptoms. Whether schizophrenia is characterized by hallucinations and delirium, or by incongruent speech and disorganized behavior, for example, is not a matter of individual genes gone awry, but rather groups of genes that interact in particular ways, disturbing the structures and functions of the brain.

  This finding emerged from a study conducted by scientists at the Washington University School of Medicine in St. Louis. These scientists examined data from genome-wide association studies to demonstrate that in schizophrenia, “different genotypic networks ... cause distinct clinical syndromes."

  The details appeared in the February print issue of the American Journal of Psychiatry, in an article entitled, “Uncovering the Hidden Risk Architecture of the Schizophrenias: Confirmation in Three Independent Genome-Wide Association Studies.” The article describes how the authors began by identifying sets of interacting single-nucleotide polymorphisms (SNPs) that cluster within particular individuals (SNP sets) regardless of clinical status, and ultimately tested whether SNP sets were associated with distinct phenotypic sets in a replicable manner.

  “[We] identified 42 SNP sets associated with a 70% or greater risk of schizophrenia, and confirmed 34 (81%) or more with similar high risk of schizophrenia in two independent samples,” the authors wrote. “Seventeen networks of SNP sets did not share any SNP or subject. These disjoint genotypic networks were associated with distinct gene products and clinical syndromes (i.e., the schizophrenias) varying in symptoms and severity.”

  “Genes don’t operate by themselves,” said C. Robert Cloninger, M.D., Ph.D., a professor of psychiatry at Washington University and one of the study’s senior investigators. “They function in concert much like an orchestra, and to understand how they’re working, you have to know not just who the members of the orchestra are but how they interact.”

  “What we’ve done here, after a decade of frustration in the field of psychiatric genetics, is identify the way genes interact with each other, how the ‘orchestra’ is either harmonious and leads to health, or disorganized in ways that lead to distinct classes of schizophrenia,” Dr. Cloninger added.

  Although individual genes only present weak, inconsistent associations with schizophrenia, the interaction networks of gene groups pose a high risk of suffering from the disease, between 70 and 100%, which makes it almost impossible that individuals with those genetic variation networks will avoid schizophrenia, noted a release issued by Washington University.

  This new research, in which 4,196 patients diagnosed with schizophrenia and 3,200 healthy control patients participated, has for the first time identified the different genes networks that contribute to the existence of eight different types of schizophrenia. This discovery could lead to better diagnosis and treatment of schizophrenia, which affects about 1% of the world population.

  By identifying the genes networks and their relationship to the symptoms in individual patients, “it will soon be possible to determine a possible localized treatment for the specific paths that cause schizophrenia,” explained Igor Zwir, Ph.D., a study coauthor. Dr. Zwir is a research associate in psychiatry at Washington University and an associate professor in the Department of Computer Science and Artificial Intelligence at the University of Granada, Spain.

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