New Study Sheds Light on Role of Genetics in Recovering from Eating Disorders

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A substantial number of people with eating disorders, such as anorexia nervosa have a chronic course. They are severely underweight and have a high likelihood of dying from malnutrition. No treatment has been found that helps people who are chronically ill. Now, a new study sheds light on the reason that some people have poor outcome.

An international team of scientists, led by researchers at the University of California, San Diego (UCSD) School of Medicine and the Scripps Translational Science Institute (STSI) in La Jolla, CA, has identified possible genetic variations that could influence a patient's recovery from an eating disorder such as anorexia or bulimia. Their findings, reported online in the journal *Neuropsychopharmcology*, may provide new insights into development of effective interventions for the most treatment-resistant patients with these disorders.

"This study sheds light on important 'SNPs' or genetic variations within an individual's DNA, associated with long-term, chronic eating disorders," said Walter H. Kaye, MD, professor of psychiatry and director of UCSD's Eating Disorder Treatment and Research Program, who was senior author with Nicholas J. Schork, PhD, director of bioinformatics and biostatistics at STSI and professor at The Scripps Research Institute. "These variations suggest genetic predictors for patients who may be particularly susceptible to eating disorders and whose illnesses are most difficult to treat effectively."

Kaye said such genetic traits are also linked to individuals with higher anxiety and higher concern over mistakes – traits associated with anorexia and bulimia.

Researchers from the Price Foundation Collaborative Study were responsible for the study's data collection, while scientists at STSI and UCSD led the design of the study and the analysis of its results.

According to the study's lead author, Cinnamon Bloss, PhD, assistant professor at STSI, the findings could eventually help pave the way toward a more individualized approach to treating patients with eating disorders. "Anorexia and bulimia likely stem from many different causes, such as culture, family, life changes and personality traits," said Bloss. "But we know biology and

genetics are highly relevant in terms of cause and can also play a role in how people respond to treatment. Understanding the genetics behind these conditions is important, because it could eventually help us tailor treatment based on the person's genetic makeup, with the goal of more personalized and effective treatments."

Anorexia and bulimia are serious and complex psychiatric disorders. Anorexia nervosa is characterized by an inability to maintain normal body weight and a relentless pursuit of thinness; bulimia is characterized by recurrent episodes of binge eating. In recent studies, researchers including Kaye have theorized that anorexia and bulimia likely share some risk factors, and that patients may be genetically predetermined to possess personality traits and temperaments that make them susceptible to the eating disorders.

"Individuals with anorexia in particular are often resistant to treatment and lack awareness of the medical consequences of their behavior, which can result in chronic, protracted illness and even death," said Kaye. "The question for us became, 'Are there prognostic factors that might help clinicians identify good versus poor outcomes for treatments including medication or psychotherapies?'"

The research team studied a total of 1,878 women in the large-scale candidate gene association study, which was designed based on hypotheses regarding the genes, pathways and biological systems involved in susceptibility to eating disorders. Most were individuals with a lifetime diagnosis of either anorexia or both anorexia and bulimia, who also exhibited lower body mass index, higher anxiety and higher concern over mistakes than control subjects.

The scientists then identified the top 25 most statistically significant SNPs (single-nucleotide polymorphisms), after evaluating a total of 5,151 SNPs in about 350 genes. According to Bloss, 10 of the 25 most strongly associated "haplotypes" (combinations of alleles for different genes that are located closely together on the same chromosome and that tend to be inherited together) involved SNPs in GABA genes. An intronic SNP on chromosome 4 of the gene GABRGI showed the strongest correlation to chronic symptoms. "The study suggests genes that may pre-dispose individuals to a chronic course of an eating disorder," Bloss said, adding that additional studies are needed to confirm such associations.

In addition to Kaye, Schork, and Bloss, contributors to the study include Wade Berrettini, University of Pennsylvania, Philadelphia; Andrew W. Bergen, Center for Health Sciences, SRI International, Menlo Park; Pierre Magistretti, University of Lausanne Medical School, Switzerland; Vikas Duvvuri and Enrica Marzola, UC San Diego School of Medicine; Michael Strober, UCLA David Geffen School of Medicine; Harry Brandt and Steve Crawford, University of Maryland School of Medicine, Baltimore; Scott Crow, University of Minnesota, Minneapolis; Manfred M. Fichter, Roseneck Hospital for Behavioral Medicine, Prien, Germany and University of Munich; Katherine A. Halmi, New York Presbyterian Hospital, Weill Medical College of Cornell University; Craig Johnson, Laureate Psychiatric Clinic and Hospital, Tulsa, OK; Allan S. Kaplan and D. Blake

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