



National Eating Disorders Association

NEDA Research Corner

A review of

“Bloss, C., Berrettini, W. Bergen, A., Magistretti, P., Duvvuri, V., Strober, M., Brandt, H., Crawford, S., Crow, S., Fichter, M., Halmi, K., Johnson, C., Kaplan, A., Keel, P., Klump, K., Mitchell, J., Treasure, J., Woodside, D.B., Marzola, E., Schork, N., & Kaye, W. (2011).

Genetic Association of Recovery from Eating Disorders:
The Role of GABA Receptor SNPs. *Neuropsychopharmacology*.”

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While many people with anorexia and bulimia nervosa recover by their mid 20's, approximately one quarter remain ill and are likely to have a chronic course. Effective treatments for this chronic group have remained elusive. Now, a new study from our group has asked the question as to whether there are genetic factors that explain the lengthy course of illness for some patients. This is an important question, because the successful identification of such genes might provide new targets for treatment.

We investigated almost 2000 women with eating disorders (EDs) as well as a group of comparison women who never had an ED from the Price Foundation Collaborative Genetic Dataset. We looked at approximately 350 genes and more than 5000 pairs of individual molecules (SNPs) that make up these genes. In genetic studies, single-nucleotide polymorphisms, or SNPs (pronounced “snips”), refer to genetic variations that exist within a population. We compared 361 women who were more than 25 years old and continued to be ill with an ED to 115 women who were also older than 25, but who had been recovered from an ED for more than a year. Importantly, we confirmed the findings in a separate group of women who were younger than 25 years old, but were either ill or recovered.

We found a group of SNP's within a number of GABA (γ -aminobutyric acid) genes that were particularly associated with discriminating good or poor outcome. Moreover, some of these GABA gene findings were associated with anxiety, an interesting finding since those ED individuals who had poor outcome were the most anxious. The 20 GABA genes code for molecules that form GABA subunits. The GABA receptor is made up of 5 of these subunits. Because there are about 20 subunits, they can combine in many different ways and form a series of GABA receptors that have different functions in different parts of the brain. GABA has long been thought to play a key role in anxiety. In fact, the benzodiazepines (e.g., valium) are a class of anti-anxiety drugs that work by interacting with the GABA receptor. Interestingly, the strongest finding in our study was for the GABA gamma 1 subunit, which has also been implicated in alcoholism. This gamma 1 subunit is present in only a small proportion of GABA receptors, but is known to play a key role in anxiety in regions of the brain that are known to modulate anxiety.

What does this mean clinically? As we learn more about genetics, it has become clear that there is not one gene that creates an ED. There is a considerable literature that shows that people who develop anorexia and bulimia tend to have certain temperament or personality traits. Importantly, these traits tend to first be present in childhood, years before the onset of an ED. Examples of these traits include



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anxiety, inhibition, obsessionality, and perfectionism. It does not mean that everybody has all these symptoms in childhood but people often have one or a few of these temperament and personality traits before they develop an ED. It is very likely that such traits are what one genetically inherits since these seem to also be present in families of people with an ED. These traits reflect the interactions of many genes, each having a relative small influence. Emerging evidence suggests that anxiety is a critical factor that creates a susceptibility to develop an ED. If someone has some of these GABA genes, perhaps they have an extra dose of anxiety and this may make it that much more difficult to recover. As Dr. Cinnamon Bloss, the first author noted, this may be the first study to find genes that may increase the risk of poor outcome. There are many medications that work on GABA receptors, but few of these have been tried in people who have a chronic ED.

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