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they experienced a higher state of anxiety. Significantly, regardless of their ethnic background, the women from either group who shared a particular genetic makeup, or genotype, identified as COMT Met158/Met158, were among those who tested highest for anxiety–higher than other women who lacked that particular genotype. In addition, the women with COMT Met158/Met 158 also exhibited a low-voltage alpha EEG, a specific brain-wave pattern associated with anxiety disorders, and alcoholism.

"Other studies have shown that women have lower COMT levels than men. In addition, the COMT Met158/Met158 genotype is associated with a threefold to fourfold decrease in COMT enzyme levels," says Dr. Enoch. "Therefore, our study suggests that women with this genotype may be more vulnerable to anxiety because their COMT levels fall below a minimum threshold."

The men in the study who had the COMT Met158/Met158 genotype did not rank as high on anxiety tests as the women, and their scores were similar to the test results of men with other genotypes. They also did not have the low-voltage alpha EEG. "Men naturally tend to have lower anxiety scores," says Dr. Enoch, "but it's possible that there may be a caveat here that a larger sample population may be necessary to study the association in men."

A recent study of COMT gene activity in both men and women conducted by the same laboratory was consistent with the findings of Dr. Enoch's study. David Goldman, MD, Chief of the Laboratory of Neurogenetics at NIAAA and colleagues from the University of Michigan found that the same genetic variant is associated with a higher level of brain response to pain and stress. (See *Science* 299: 1240, 2003, and the accompanying NIAAA news release of February 20, 2003).

Noting that other studies from NIAAA and elsewhere indicate a role for COMT in cognition, Dr. Goldman says, "The COMT polymorphism is a common genetic variant which leads to differences in both anxiety and cognition, both domains of normal behavior. The COMT variant's different effects also implicate it as a risk factor in diverse and clinically very distinct psychiatric diseases, including alcoholism, schizophrenia, and anxiety disorders. The evidence so far indicates that people with the Met158 variant, especially women, are more likely to be worriers, but, on the other hand, they benefit from effects of this variant on cognition."

For interviews with Dr. Enoch or Dr. Goldman, please call the NIAAA press office at 301-443-3860. The paper, "Genetic origins of anxiety in women: a role for a functional catechol-O-methyltransferase polymorphism," appears in the March 1, issue of *Psychiatric Genetics,* 2003: 13:33-41 (Web site: www.psychegenetics.com).

Additional alcohol research information, including publications from NIAAA's genetic research program, is available at www.niaaa.nih.gov.