



For Information Contact:

Lydia Sermons-Ward, 703-907-8640

press@psych.org

Jim Rosack, 703-907-7862

jrosack@psych.org

FOR IMMEDIATE RELEASE:

September 27, 2007

Release No. 07-69

Risk of New Suicidal Thoughts During Antidepressant Treatment Has Genetic Component, New *AJP* Study Shows

Arlington, Va. - DNA samples from patients in the federally funded Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial have revealed two genetic markers that appear to be associated with the emergence of suicidal thoughts during treatment with citalopram, a selective serotonin reuptake inhibitor (SSRI) antidepressant. The findings strongly suggest a genetic basis underlying the rare emergence of suicidal thoughts associated with taking an SSRI.

The new findings are reported in the article "Genetic Markers of Suicidal Ideation Emerging During Citalopram Treatment of Major Depression," by Gonzalo Laje, M.D., and colleagues, which appears in the October 2007 issue of *The American Journal of Psychiatry (AJP)*, the official journal of the American Psychiatric Association (APA).

Since the introduction of SSRIs in the 1980s, there has been controversy over whether the medications can trigger suicidal thoughts or behaviors. The STAR*D trial, funded by the National Institute of Mental Health, provided a unique opportunity to study the phenomenon of treatment-emergent suicidal ideation in a large cohort of patients treated with an SSRI.

DNA samples were collected from 1,915 patients in the first phase of the STAR*D trial. Laje and his colleagues examined 768 genetic markers within 68 different genes. The target genes were selected to look at five broad signaling pathways of potential importance in antidepressant effects—serotonin, glutamate, dopamine, norepinephrine, and neurotrophins.

Suicidal ideation was assessed by patient self-report, using item 12 on the Quick Inventory of Depressive Symptomatology—Self Report (QIDS-SR), which asks the patient about "thoughts of death or suicide." Patients who scored zero before taking citalopram, but later scored 1, 2, or 3 at least once during treatment, were categorized as experiencing treatment-emergent suicidal ideation.

The two genetic markers identified, rs4825476 and rs2518224 (known as single nucleotide polymorphisms), are located on the GRIA3 and GRIK2 genes, respectively. Both GRIK2 and GRIA3 encode nerve cell receptors for glutamate, one of the brain's chemical messengers.

In the study, the highest odds of suicidal thoughts were for patients who had both of the identified markers. None of the patients with suicidal ideation actually attempted suicide. However, two other participants did attempt suicide, and one of these provided DNA and was found to have both of the high-risk genetic markers.

- more -

AJP editor-in-chief Robert Freedman, M.D., stated, “While this is a provocative first step towards individualization of the treatment of depression based on unique genetic and neurobiological differences between people, the data are still preliminary and require further investigation.”

The identified markers do not appear to be related to a general tendency toward suicide, but rather to suicidal thoughts specifically emerging during antidepressant treatment. Neither of the identified genes appears to have been previously associated with suicidal ideation.

“These data suggest that not everyone is at the same risk of suicidal thinking during antidepressant treatment. For most people the risk is low, but some may be at higher risk, due in part to their genetic makeup. Can genetic markers help identify those at high risk? It’s possible, but we’d like to see the results replicated in another sample before we reach any firm conclusions,” said Dr. Francis J. McMahon, who is one of the authors and chief of the Genetic Basis of Mood and Anxiety Disorders Unit at the National Institute of Mental Health.

This study was funded by the National Institutes of Health, the National Institute of Mental Health, the National Institute on Alcohol Abuse and Alcoholism, the National Human Genome Research Institute, and the Swedish Research Council. Forest Laboratories provided citalopram for the STAR*D study. Additional funding disclosures appear at the end of the article.

(Am J Psychiatry 2007; 164:1530-1538)

Note to Editors: Contact Jim Rosack at 703-907-7862 / jrosack@psych.org or the APA Office of Communications and Public Affairs at 703-907-8640 / press@psych.org for an embargoed copy of the article and accompanying editorial.

About the American Journal of Psychiatry:

The *American Journal of Psychiatry*, the official journal of the American Psychiatric Association, publishes a monthly issue with scientific articles submitted by psychiatrists and other scientists worldwide. The peer review and editing process is conducted independently of any other American Psychiatric Association components. Therefore, statements in this press release or the articles in the Journal are not official policy statements of the American Psychiatric Association. The Journal's editorial policies conform to the Uniform Requirements of the International Committee of Medical Journal Editors, of which it is a member. For further information about the Journal visit www.ajp.psychiatryonline.org.

About the American Psychiatric Association:

The American Psychiatric Association is a national medical specialty society whose more than 38,000 physician members specialize in diagnosis, treatment, prevention and research of mental illnesses including substance use disorders. Visit the APA at www.psych.org and www.HealthyMinds.org.

###