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Analysis does not support association between genetic marker, stress and risk of depression

June 17 2009

Contrary to a previous report, an analysis of 14 previous studies does not find an association between a serotonin transporter gene variation, stressful life events, and an increased risk of major depression, according to an article in the June 17 issue of *JAMA*. The authors did find that the number of stressful life events is associated with depression.

Despite progress in risk gene identification for several complex diseases, few disorders have proven as resistant to gene identification as psychiatric illnesses. Although these disorders have long been assumed to result from some combination of genetic vulnerability and environmental exposure, direct evidence from a specific example has not been forthcoming. "Few if any of the genes identified in candidate gene association studies of psychiatric disorders have withstood the test of replication and to date, genome-wide association studies of psychiatric disorders have also had limited success," the authors write. One previous study (Caspi et al) concluded that, in interaction with stressful life events, genetic variation of the serotonin transporter gene (5-HTTLPR) plays a role in predisposition to major depression.

Neil Risch, Ph.D., of the University of California at San Francisco and Kaiser Permanente Northern California Division of Research, Oakland, and colleagues conducted a meta-analysis of the interaction between the serotonin transporter gene and stressful life events on depression. The

researchers identified 14 studies that met criteria for inclusion in the analysis. Of a total of 14,250 participants, 1,769 were classified as having depression; 12,481 as not having depression.

The researchers found there was no association between 5-HTTLPR genotype and depression in any of the individual studies nor in the weighted average and no interaction effect between genotype and stressful life events on depression was observed. Comparable results were found in the sex-specific meta-analysis of individual-level data. The meta-analysis did show that the number of stressful life events was significantly associated with depression.

The authors suggest that these results indicate why it is important that studies that find genetic associations be replicated.

"A more serious concern … is that the findings of this [Caspi et al] and other nonreplicated genetic associations are now being translated to a range of clinical, legal, research, and social settings such as forensics, diagnostic testing, study participants, and the general public. It is critical that health practitioners and scientists in other disciplines recognize the importance of replication of such findings before they can serve as valid indicators of disease risk or have utility for translation into clinical and public health practice."

Source: JAMA and Archives Journals (news : web)