Inflammation and cognition in schizophrenia

November 1 2012

There are a growing number of clues that immune and inflammatory mechanisms are important for the biology of schizophrenia. In a new study in *Biological Psychiatry*, Dr. Mar Fatjó-Vilas and colleagues explored the impact of the interleukin-1β gene (IL1β) on brain function alterations associated with schizophrenia.

Fatjó-Vilas said that "this study is a contribution to the relatively new field of 'functional imaging genetics' which appears to be potentially powerful for the study of schizophrenia, where genetic factors are of established importance and cognitive impairment – affecting particularly executive function and long-term memory – is increasingly recognized as a core feature of the disorder."

To conduct this study, they recruited patients with schizophrenia and healthy volunteers, all of whom completed a working memory task while undergoing a functional magnetic resonance imaging scan in the laboratory. This allowed the researchers to determine which areas of the brain became activated during the task. Each participant was also genotyped to determine which allelic combination of the -511C/T polymorphism at the promoter region of the IL1β gene they carry: CC, TT, or CT.

Patients who were homozygous for the C allele (CC) showed reduced prefrontal cortex activation associated with working memory than patients who had at least one copy of the T allele. Among the healthy volunteers, frontal brain activation did not differ according to genotype.

"The analyzed genetic variant exerts an influence on prefrontal cortex function and this influence is different in healthy subjects and patients with schizophrenia," summarized Fatjó-Vilas.

An important issue is that the -511C/T seems to have a role in regulating the levels of IL1B expression, in which case it would influence neuronal activity dependent on the protein availability. This means that the T allele has been reported to be more active than the C allele, suggesting that a tendency for greater expression of IL1β is associated with greater compromise of frontal cortical functions underlying cognition.

Interleukin-1β is released in the blood under stressful conditions and its release is one of the ways that stress promotes inflammation. IL-1β levels in the blood are altered, for example, in patients with depression and other neuropsychiatric disorders.

Apart from having a role in the immune system, interleukins are also involved in a variety of developmental and functioning processes of the central nervous system. Thus, this study provides further clues for identifying specific biological mechanisms of the disorder associated with both neurodevelopmental processes and immunological and stress response functions.

Dr. John Krystal, Editor of *Biological Psychiatry*, commented, "We are just beginning to explore the functional impact of inflammatory mechanisms in schizophrenia and the current findings increase our curiosity about these novel mechanisms."

The article is "Effect of the Interleukin-1β Gene on Dorsolateral Prefrontal Cortex Function in Schizophrenia: A Genetic Neuroimaging Study" by Mar Fatjó-Vilas, Edith Pomarol-Clotet, Raymond Salvador, Gemma C. Monté, Jesús J. Gomar, Salvador Sarró, Jordi Ortiz-Gil, Candibel Aguirre, Ramón Landín-Romero, Amalia Guerrero-Pedraza,

Sergi Papiol, Josep Blanch, Peter J. McKenna, and Lourdes Fañanás (doi: 10.1016/j.biopsych.2012.04.035). The article appears in Biological Psychiatry, Volume 72, Issue 9 (November 1, 2012), published by Elsevier.