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Inflammatory Cause of Bipolar Disorder Suggests New Treatments

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PARIS – Recently reported evidence implicating inflammatory mediators in the pathophysiology of bipolar disorder and major depression have opened the door to testing new agents for treating these psychiatric disorders or slowing their progression.

"Bipolar disorder is associated with neuro-progression, and oxidative stress, neurotrophins, and inflammation may underpin this process, Dr. Michael Berk said at the annual Congress of the European College of Neuropsychopharmacology. "Early interventions can potentially improve the outcome" of bipolar disorder, and the new findings give new opportunities to find effective neuroprotective agents, said Dr. Berk, professor and chairman of psychiatry at Deakin University in Geelong, Australia.

"We increasingly think there is a systemic biology that underpins" bipolar disorder and potentially other inflammatory diseases. "The brain does not exist in isolation, and we need to understand that pathways similar to those that underpin risks for cardiovascular disorders, stroke, and osteoporosis might also underpin the risk for psychiatric disorders, and that other treatments might be helpful," he said in an interview.

Based on this concept, and supported by suggestive results from epidemiologic studies, Dr. Berk said he and his associates are running a prospective, randomized study assessing a role for aspirin in treating bipolar disorder, and that they are seeking funding for a second study to test combined treatment with a statin and aspirin in bipolar disorder patients. "We are only starting to understand the core elements of neuroprogression" in bipolar disorder patients, including the roles of neurogenesis, apoptosis, oxidative stress, and mitochondrial energy generation. "If we accept that these are determining long-term outcomes, it gives us a diversity of novel treatments we can begin to look at that might have a potential impact on these underlying processes. I think this is one of the most hopeful areas of psychiatry."

Evidence of a role for inflammation in bipolar disorder and major depression includes the finding by Dr. Berk and his associates that women who received statin treatment had about a 2% incidence of newly diagnosed major depressive disorder during 10 years of follow- up, significantly less than the 10% incidence rate among women who did not receive a statin, in a nonrandomized study that controlled for age (Psychother. Psychosom. 2010;79:323-5).

In another study, Dr. Berk and his associates found a link between elevated serum levels of high sensitivity C-reactive protein (hsCRP) and the incidence of major depressive disorder. They followed 644 randomly selected women aged 20-84 and with no history of depression at baseline for 10 years. During follow-up, the rate of new- onset major depressive disorder rose by a statistically significant 44% for each one standard deviation increase in the log-transformed level |of serum hsCRP, after adjustment for baseline differences in weight, smoking history, and use of nonsteroidal anti-inflammatory drugs (Br. J. Psychiatry 2010;197:372-7).

Also, a 2006 report from Irish researchers had results from a study of the plasma levels of five different cytokines in 42 people aged 1-68, including nine with bipolar affective disorder in the depressive phase, 12 with bipolar affective disorder in the manic phase, and 21 control people with no personal or family history of a mood disorder. The results showed significantly elevated plasma levels of interleukin-8 and tumor necrosis factor-! in both subgroups of bipolar disorder patients studied compared with the controls (J. Affective Disorders 2006;90:263-7).