Depression Ramps Up Inflammatory Response to Stress

ATLANTA, Sept. 1 -- Men with major depression have an exaggerated inflammatory response to stress, a finding that could partly explain some of the somatic diseases associated with the condition, according to researchers here.

They believe that the finding may shed some light on why conditions such as heart disease, cancer, and diabetes often go hand in hand with depression.

This small study is the first to demonstrate such an exaggerated response in major depression patients compared with controls, reported Andrew H. Miller, M.D., of Emory University School of Medicine, and colleagues, in the Sept. 1 issue of the *American Journal of Psychiatry*.

"Several examples of increased resting inflammation in depressed patients already exist in the literature, but this is the first time anyone has shown evidence to suggest that the inflammatory response to stress may be greater in depressed people," they said.

When medically health, depressed and non-depressed volunteers were subjected to stressful situations, the men with depression had elevated levels of inflammatory markers in peripheral blood, the investigators reported.

The effect was especially pronounced in depressed men who had experienced increased stress in early life.

The investigators recruited 28 medically healthy men, 14 of whom had been diagnosed with major depression, to participate in a study measuring physiologic responses to moderately stressful situations.

All volunteers were tested with the Childhood Trauma Questionnaire to quantify their relative degrees of early life stress. The mean score was significantly higher in depressed participants (69.0, SD=25.08) compared with controls (35.0, SD=15.68).

Men with either past or current psychotic symptoms, bipolar disorder, substance abuse/dependence within the previous year, current eating disorder, or those taking psychotropic medications were excluded.

The participants were subjected to the Trier Social Stress test, consisting of 10 minutes preparation for a five-minute public speech, followed immediately by a five-minute mental arithmetic test.

Investigators collected blood samples through an in-dwelling venous catheter every 15 minutes starting immediately before and then up to 90 minutes after the test.

The plasma samples were checked for levels of interleukin 6, a pro-inflammatory cytokine. In addition, peripheral blood mononuclear cells from nine depressed patients and 12 non-depressed patients were examined for activation of nuclear factor kappa B (NFκB), a transcription factor implicit in the inflammatory cascade.

The investigators found that depressed patients had increased levels of IL-6 relative to controls at baseline and at 90-minutes after completion of the stress challenge ($P<0.05$), but not at the 30-, 60- or 75-minute intervals tested.

Levels of NFκB binding were also elevated by about 12% over baseline in depressed patients, but decreased about 2% from baseline in the non-depressed patients.

"This difference was observable only at later time points following Trier Social Stress Test onset, and may explain why previous studies have failed to identify increased inflammatory responses after psychological stress," they wrote.

The increased inflammatory response seen in depressed patients could be due to changes in neuroendocrine function such as increased sympathetic nervous system responses and altered glucocorticoid feedback regulation, they suggested.

"Sympathetic nervous system activation has been shown to enhance inflammatory responses," they wrote, "and major depression patients with early life stress have been shown to exhibit enhanced sympathetic nervous system responses to stressor challenge."

The authors acknowledged that because of the small sample size and study design, they were unable to determine the relative contributions of depression or of early life stress to the ramped-up inflammatory

response they observed in the depressed patients.

Action Points

Explain to interested patients that this study suggests that inflammatory responses to stress are elevated in those who are depressed, a finding that could explain in part why depression is associated with diseases known to have an inflammatory component, such as heart disease, cancer and diabetes.

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