Inflammatory Markers, Depression, and Cardiac Disease

TO THE EDITOR: We read with great interest the report by François Lespérance, M.D., and colleagues (1) about the relationship of inflammatory markers to major depression in patients with cardiac disease. They noted one previously published study that found an association between interleukin-1β and interleukin-6 levels and depression in patients about to undergo angioplasty (2). We wish to consider their results in the context of a previously published pilot study by our group (3), in which we found that serum interleukin-1β level was not associated with depressive symptoms or diagnosis in 37 patients age 50 years and older with coronary artery disease who were recruited from a cardiac rehabilitation program. Our negative results are consistent with those of Dr. Lespérance et al., who did not find an association between depression and interleukin-6 or C-reactive protein levels. They thoughtfully considered the possibility that statins might obscure any relationship between such inflammatory markers and depression. We add that a similar confound may be posed by the overall burden of medical illness, which was correlated with interleukin-1β level in our study group. The obscuration of any depression-inflammatory marker relationship may be particularly important in older patients, with their greater physical comorbidities. Also, times of acute cardiac exacerbation, with concomitant increases in levels of inflammatory markers, may make the association with depression most evident. This may help explain the positive findings of Appels et al. (2).

Given such complex potential confounds, the finding by Dr. Lespérance et al. of a cross-sectional association between soluble intercellular adhesion molecule 1 and depression are particularly noteworthy. We applaud their efforts and heartily second their call for careful longitudinal studies in light of the causal models they raised as well as other proposed models by which chronic age-associated inflammatory processes or immunodysregulation might contribute to the pathogeneses of depression (4, 5).

References

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Dr. Lespérance and Colleagues Reply

TO THE EDITOR: The interesting letter from Dr. Lyness et al. informs us of a study they carried out that paralleled our results in finding no association between an inflammatory marker, interleukin-1β, and depression in a group of cardiac patients. However, that study included only 27 subjects, and only four had a current major depression, making the meaning of a lack of relationship between depression and this inflammatory marker unclear. In addition, interleukin-1β is not the same as interleukin-6, which is the cytokine that has been found to predict cardiac events.

We agree with Dr. Lyness et al. that we may not have been able to find an association between interleukin-6 and depression because of the timing of our assessment. We interviewed our subjects approximately 2 months after hospitalization for an acute coronary syndrome. Because the release of interleukin-6 is more dynamic and short term than the release of soluble intercellular adhesion molecule 1 and C-reactive protein, it is conceivable that we missed the peak of the increase in interleukin-6 associated with the acute coronary artery events. Although we could hypothesize that this peak may have been greater among the depressed subjects, by 2 months after the event, it was no longer apparent in our study.

Dr. Lyness et al. are also correct in suggesting that inflammatory markers are likely to correlate with other measures of the severity of cardiac disease that reflect atherosclerotic processes. For example, in our study, interleukin-6 was significantly correlated (all $p<0.05$) with age; previous myocardial infarction, bypass surgery, or angioplasty; coronary bypass surgery at index; abdominal obesity; high body mass index; low high-density lipoprotein; high blood pressure; high fasting glucose level; high fasting insulin level; and the presence of metabolic syndrome. However, even after statistical control for these potential confounders, there was still no association between depression and interleukin-6 levels in our group.

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Astrocytic Activation as Evidence for Brain Damage

TO THE EDITOR: Andrew J. Dwork, M.D., et al. (1) found in their study that increased "cortical and hippocampal immunoreactivity for glial fibrillary acidic protein…was most intense in the group that received ECT" (p. 576). They wrote that these "statistically significant" increases in glial fibrillary acidic protein "probably" indicated "widespread astrocytic activation." In other words, 5 weeks after the last ECT, they found abnormal tissue changes under the microscope that were made visible by specialized staining techniques. This makes sense. Astrocytic activation is the brain's well-known pathological response to injury and disease of all kinds.

Astrocytic activation evidenced by increased glial fibrillary acidic protein has been found in multiple sclerosis (2), temporal lobe epilepsy (3), amyotrophic lateral sclerosis (4), systemic lupus erythematosus (5), human immunodeficiency virus dementia, Alzheimer's dementia, and, of course, traumatic injury.

Astrocytic activation, then called reactive astrocytic gliosis, was found after ECT as far back as 1948 (6). This latest finding