Depression Boosts Blood-Vessel Disease

Mild to moderate depression may substantially increase the impact of several known contributors to a blood-vessel disease that can lead to a heart attack or stroke, according to findings released last week at a meeting of the American Heart Association in Memphis.

"Treating depression, even in cases without severe impairment, may be important in both the prevention and treatment of cardiovascular disease," contends epidemiologist George A. Kaplan of the California Department of Health Services in Berkeley.

Kaplan and his co-workers – including scientists at the University of Kuopio, Finland – studied 1,225 Finnish men, age 42 to 60, taking part in a larger, ongoing investigation of risk factors for heart disease. The men live in eastern Finland, an area known for high rates of heart and blood-vessel disease.

The researchers looked at the link between depression and atherosclerosis, a disease in which cholesterol-filled plaques collect in arteries. Ultrasound tests indicated that each man suffered from some degree of atherosclerosis in the carotid artery, which carries blood to the brain through its two tributaries in the neck. Thickening of the carotid reflects plaque buildup, which increases the likelihood of stroke. The condition of the carotid artery often mirrors that of the coronary arteries, which cannot be viewed with ultrasound, Kaplan says.

Participants also completed the Minnesota Multiphasic Personality Inventory (MMPI), which includes a scale for depression. Kaplan's group divided the sample into approximately equal numbers of "depressed" and "nondepressed" individuals using MMPI scores. Most of the former group suffered mild to moderate symptoms of depression, including general apathy, denial of personal worth and sleep problems.

Depression showed no direct relationship to the extent of carotid atherosclerosis, Kaplan points out. But depression did amplify the link between atherosclerosis and two of its risk factors, cigarette smoking and fibrinogen, a blood-clotting protein that encourages plaque formation.

Depressed men who smoked displayed three times as much plaque buildup in the carotid as nondepressed men who smoked, with years of smoking and cigarettes smoked per day held constant. Depressed men with elevated fibrinogen levels suffered nearly four times as much carotid atherosclerosis as nondepressed men with the same levels of the protein.

Twice as much plaque formation occurred among depressed men with increased blood levels of LDL cholesterol (the "bad" cholesterol), compared with nondepressed men with the same LDL levels. Kaplan calls this a "marginally significant" finding.

Since living with poor health caused by heart and blood-vessel disease may produce depression, the researchers separately examined 695 men in the sample with no prior diagnosis or treatment for such problems. Depression exerted comparable effects on the three risk factors.

"These findings provide one more reason for physicians to pay close attention to depression in patients with heart disease," comments Robert Anda, a physician and epidemiologist at the Centers for Disease Control in Atlanta. "[Severe] depression may have an even stronger effect on risk factors for atherosclerosis."

However, Anda considers the implications of the new data speculative until additional studies confirm the results.

Kaplan's team plans to follow the Finnish men, tracking the course of their depression and atherosclerosis. For now, however, the findings suggest that depression accentuates the influence of risk factors for the disease through biological pathways that remain unknown, Kaplan says. Blood platelets contain receptors for some chemical messengers in the central nervous system, such as epinephrine and serotonin, which may increase with depression, he points out.

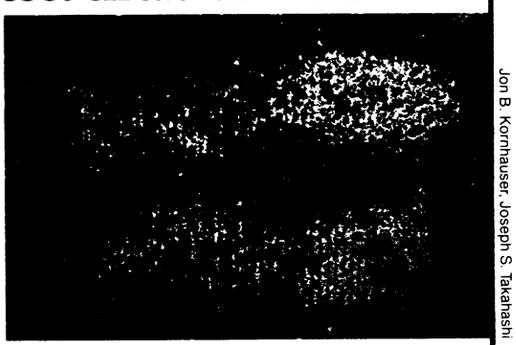
"But we don't know if blood platelets are more activated in depressed people," Anda notes. "Speculation is wide open on physiological mechanisms at work here."

– B. Bower

Genes may help reset circadian clock

Researchers know from past experiments that morning light calibrates the biological clock in the brain to keep it running on a 24-hour schedule. But scientists have only a dim understanding of how this process works. Now a group of researchers suggests that two light-sensitive genes tell a cockeyed clock to reset itself.

The biological clock – a group of nerve cells clustered in the hypothalamus, at the base of the brain – regulates daily cycles such as sleepiness, hormone levels and body temperature in mammals.



Jon B. Kornhauser, Joseph S. Takahashi

Rise and shine: In this photo of a hamster's hypothalamus, computer enhancement highlights hundreds of jun-B genes (colored areas) responding to a light burst.

In the new study, Joseph S. Takahashi and his co-workers at Northwestern University in Evanston, Ill., kept hamsters in complete darkness for seven days and then exposed them to a brief, predawn light burst. The flash activated a gene called jun-B in the brain, they report in the March 20 SCIENCE. In 1990, Takahashi's group discovered that a gene called c-fos responded similarly to light.

The researchers now believe that these two genes work in concert to stimulate the production of a protein called AP-1 transcription factor, which may spark other genes within the brain to reset the biological clock.

"There is an extremely tight correlation between the effects of light on the clock and its resetting, and the effects of light on the genes and AP-1," Takahashi says.

Although c-fos and jun-B serve many different purposes in cells throughout the brain, they appear to have a specific role in the resetting process, he says. "When you expose these animals to light, c-fos and jun-B don't change in any other part of the brain," he explains. "They only change in that one place [the circadian clock]."

Interestingly, the circadian clock appears to control when c-fos and jun-B will respond. "The clock only allowed the gene to go on in the nighttime, not in the daytime," Takahashi says.

The new findings represent an important step toward a better understanding of the resetting mechanism, although many mysteries remain. "AP-1 is just half of the story," says neurobiologist Stephen P. Hunt of the University of Cambridge Medical School in England. Hunt speculates that many proteins like AP-1 may help reset the clock. "It's going to be enormously complicated to work out," he says.

– M. Stroh