

## Low levels of good cholesterol linked to memory loss, dementia risk

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Low levels of high-density lipoproteins (HDL) — the "good" cholesterol — in middle age may increase the risk of memory loss and lead to dementia later in life, researchers reported in *Arteriosclerosis, Thrombosis and Vascular Biology*: Journal of the American Heart Association.

Observing 3,673 participants (26.8 percent women) from the Whitehall II study, researchers found that falling levels of HDL cholesterol were predictors of declining memory by age 60. Whitehall II, which began in 1985, is long-term health examination of more than 10,000 British civil servants working in London.

"Memory problems are key in the diagnosis of dementia," said Archana Singh-Manoux, Ph.D., lead author of the study and Senior Research Fellow with the French National Institute for Health and Medical Research (INSERM, France) and the University College London in England. "We found that a low level of HDL may be a risk factor for memory loss in late midlife. This suggests that low HDL cholesterol might also be a risk factor for dementia."

Researchers defined low HDL as less than 40 mg/dL and high HDL as 60 mg/dL or higher. The team compared blood-fat and memory data collected in phases 5 (1995?) and 7 (2002?) of Whitehall II, when the average ages of the study members were 55 and 61 years, respectively.

Researchers measured lipid concentrations in blood samples collected

after an eight-hour fast, or at least four hours after a light, fat-free breakfast. They assessed short-term verbal memory using 20 one- or two-syllable words read aloud at two-second intervals. Study participants then had two minutes to write down as many of the words as they could remember.

Their main findings are:

- At age 55, participants with low HDL cholesterol showed a 27 percent increased risk of memory loss when compared to those with high HDL.
- At age 60, participants with low HDL had a 53 percent increased risk of memory loss compared to the high HDL group.
- During the five years between phases 5 and 7, study members with decreasing HDL had a 61 percent increased risk of decline in their ability to remember words versus those with high HDL.
- Men and women did not differ significantly in the link between lipids and memory loss, so researchers combined data from both sexes for analysis.
- Total cholesterol and triglycerides did not show a link with memory decline.
- Using statin drugs to raise HDL and/or lower low-density lipoprotein (LDL or "bad" cholesterol) showed no association with memory loss.

HDL cholesterol, which at high levels decreases the risk of heart attacks, serves several vital biological functions. It helps clear excess cholesterol from the blood; assists nerve-cell synapses to mature; and helps control the formation of beta-amyloid, the major component of the protein plaques found in the brains of Alzheimer's patients. Dementia most often occurs in people 65 years or older, the fastest growing age group in the industrialized world.

The precise mechanism linking HDL cholesterol to dementia remains unclear. "But it is possible that HDL cholesterol prevents formation of

beta-amyloid," Singh-Manoux said. "HDL could also affect memory through its influence on atherosclerotic disease and stroke, or vascular injury. Finally, HDL cholesterol may influence memory through its anti-inflammatory and antioxidant effects.

"Many previous investigations into the association between lipids and memory in the elderly have focused on total or LDL cholesterol because of their status as proven risk factors for cardiovascular disease," Singh-Manoux said. "Our results show HDL cholesterol to be important for memory. Thus, physicians and patients should be encouraged to monitor levels of HDL cholesterol."

In an accompanying editorial, Anatol Kontush, Ph.D. and M. John Chapman, Ph.D., D.Sc., at INSERM and University Pierre and Marie Curie in Paris, France, note, "It is tempting to speculate that increasing levels of HDL-C, or "good cholesterol" might protect our memories. However, unfortunate results in large interventional trials with dietary antioxidants suggest that we should remain cautious when proposing therapeutic intervention on the basis of observational studies which do not allow causation to be inferred. Nonetheless, these studies demand that we focus more effort on research at the interface between HDL and brain function."

To raise HDL and lower LDL cholesterol, the American Heart Association recommends exercising regularly; eliminating trans fats from the diet; reducing the intake of all fats, especially saturated fats; and consuming monounsaturated fats, such as olive, canola and peanut oils. Statins can also improve HDL and LDL cholesterol levels, when they pose a heart risk.

Source: American Heart Association

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