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The Influence of Cholesterol on Resting Brain Blood Flow and Cognition in Mid-Life Adults

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Low-density lipoprotein (LDL) cholesterol tends to increase, while high-density lipoprotein (HDL) cholesterol tends to decrease with age. Cognition can begin to decline with aging past mid-life (50-64 years old). Alterations in resting brain blood flow have been linked to this impaired cognitive function. **PURPOSE**: To determine the influence of cholesterol on resting brain blood flow and cognition in mid-life adults. **METHODS**: LDL and HDL cholesterol were measued in 18 participants (57 ± 4 years old). Resting whole brain and hippocampal blood flow were assessed using a pseudo-continuous arterial spin labeling (pCASL) sequence from the Human Connectome Project with a 64-channel head coil inside a Siemens Prisma 3T MRI scanner. Cognition was assessed using the Hopkins Verbal Learning Test (HVLT) and the National Institute of Health (NIH) Toolbox's Flanker Inhibitory Control and Attention Test and Pattern Comparison Processing Speed Test. The influence of cholesterol on resting brain blood flow and cognition was analyzed using Pearson correlations. **RESULTS**: LDL cholesterol (123 ± 23 mg/dL) was negatively correlated with resting whole brain (70.1 ± 12.5 $ml.100g^{-1}.min^{-1}$; r = -0.78, p = 0.0001) and hippocampal (67.6 ± 13.1 $ml.100g^{-1}.min^{-1}$; r = -0.74, p = 0.0005) blood flow. There were no associations for HDL cholesterol (67 ± 17 mg/dL) on resting whole brain (r = -0.03, p = 0.9) or hippocampal (r = -0.04, p = 0.9) blood flow. From the cognitive testing, only hippocampal-dependent memory retention using the HVLT was positively associated with HDL cholesterol (r = 0.51, p = 0.03). A follow-up analysis revealed participants with a higher resting brain blood flow presented a tendency for higher scores in the Pattern Comparison Processing Speed Test (r = 0.44, p = 0.06). **CONCLUSION**: LDL cholesterol, a cardiometabolic risk factor, was negatively associated with resting whole brain and hippocampal blood flow whereas the potentially cardioprotective factor HDL cholesterol was not. HDL cholesterol was positively associated with memory related outcomes. Our results suggest cholesterol may impact resting brain blood flow and cognitive function in mid-life adults, but additional data is required to elucidate the underlying mechanisms. **SIGNIFICANCE / NOVELTY:** The cardiometabolic effects of cholesterol may have further implications on cerebrovascular and brain health.

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