Energy and Macronutrient Metabolism

Prolonged Fasting Alters the Size, Function, and Glycoproteomic Profile of HDL Particles

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Objectives: To investigate the effects of a single 36-hour fast on HDL glycoproteomic composition on isolated HDL particles.

Methods: We obtained plasma from a previous study where 20 healthy subjects, age 20–40, fasted for 36 hours. HDL was isolated using density-based ultracentrifugation steps, followed by size-exclusion chromatography. Glycoproteomic was analyzed using a targeted LC-MS/MS method, and lipoprotein particle size distribution analysis using nuclear magnetic resonance (NMR) spectroscopy.

Results: HDL-associated apolipoprotein A-IV (ApoA-IV) content was significantly reduced (8918.39 +/− 3823.39 normalized ion counts vs 3690.82 +/− 2147.29 normalized ion count, p adjusted < 0.0001), suggesting a reduction in intestinally-derived HDL after a 36-hour fast. HDL associated apolipoprotein C-III (ApoC-III) di-sialylated glycopeptides decreased in HDL following a 36-hour fast compared to an overnight 12-hour fast (0.1680 +/− 0.0342 normalized ion counts vs 0.1315 +/− 0.0373 normalized ion counts, p adjusted = 0.041). Additionally, particle size distribution analysis showed an increase in abundance of calibrated large HDL of size 9.6–13nm (3.42 +/− 2.218 μmol/L vs 3.885 +/− 2.134 μmol/L, p adjusted = 0.011) and a decrease in abundance of medium HDL of size 8.1–9.5nm (6.88 +/− 1.86 μmol/L vs 5.82 +/− 2.048 μmol/L, p adjusted = 0.019) after a 36-hour fast. There were no significant changes in LDL particle size (21.115 +/− nm s 21.205 +/− 0.458 nm, p adjusted = 0.655) but there was a significant increase in overall calibrated LDL particle concentration (1138.05 +/− 357.94 μmol/L vs 1262.3 +/− 313.33 μmol/L, p adjusted = 0.011) and calibrated small LDL particle concentration (454.85 +/− 187.76 μmol/L vs 598.8 +/− 190.84 μmol/L, p adjusted = 0.025).

Conclusions: Our findings indicate that prolonged fasting alters lipoprotein profiles by affecting the proportions of large and small HDL and LDL particles, as well as altering the protein composition of HDL particles, specifically by reducing the abundance of ApoA-IV, which suggests a reduction in the contribution of intestinally-derived HDL particles to the circulating HDL pool. Future studies are needed to determine the long-term effects of multiple bouts of prolonged fasting.

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