Associations of observational and genetically determined caffeine intake with coronary artery disease and diabetes

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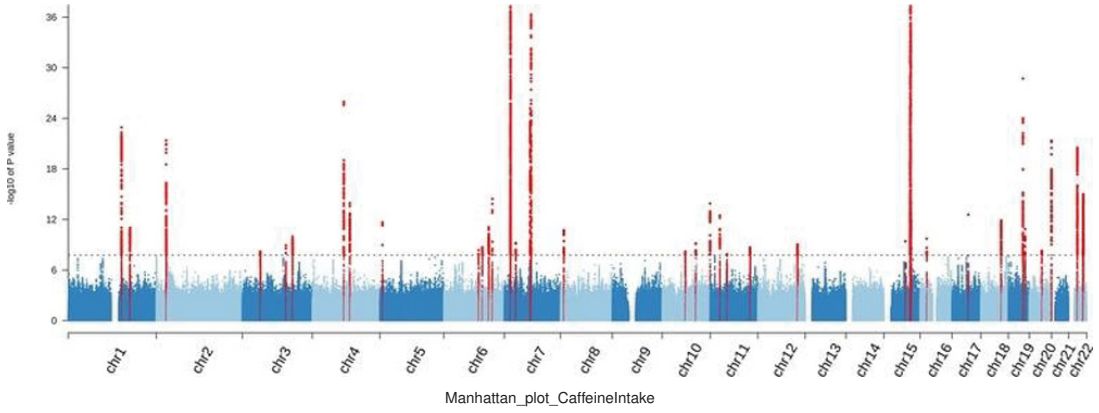
Background: Caffeine is the most widely consumed psychostimulant and is associated with lower risk of coronary artery disease (CAD) and type 2 diabetes (T2D). However, whether these associations are causal remains unknown.

Objectives: This study aimed to identify genetic variants associated with caffeine intake, and to investigate possible causal links between genetically determined caffeine intake and CAD or T2D. Additionally, we aimed to replicate previous observational findings between caffeine intake and CAD or T2D.

Methods: Genome wide associated studies (GWAS) were performed on caffeine intake from coffee, tea or both in 407,072 UK Biobank participants. Identified variants were used in a two-sample Mendelian randomization (MR) approach to investigate evidence for causal links between caffeine intake and CAD in CARDIoGRAMplusC4D (60,801 cases; 123,504 controls) or T2D in DIAGRAM (26,676 cases; 132,532 controls). Observational associations were tested within UK Biobank using Cox regression analyses.

Results: Moderate observational caffeine intakes from coffee or tea were associated with lower risks of CAD or T2D compared to no or high intake, with the lowest risks at intakes of 120–180 mg/day from coffee for CAD (HR=0.77 [95% CI: 0.73–0.82; P<1e-16]), and 300–360 mg/day for T2D (HR=0.76 [95% CI: 0.67–0.86]; P=1.57e-5). GWAS identified 51 novel genetic loci associated with caffeine intake, enriched for central nervous system genes. In contrast to observational analyses, MR analyses in CARDIoGRAMplusC4D and DIAGRAM yielded no evidence for causal links between caffeine intake and the development of CAD or T2D.

Conclusions: MR analyses indicate caffeine intake might not protect against CAD or T2D, despite protective associations in observational analyses.



Manhattan_plot_CaffeineIntake