Gene-Environment Interactions of Circadian-Related Genes for Cardiometabolic Traits

Common circadian-related gene variants associate with increased risk for metabolic alterations including type 2 diabetes mellitus.

Little is known about whether diet and sleep could modify associations between circadian-related gene variants and cardiometabolic traits to facilitate personalized recommendations.
Objectives

» To study whether diet and sleep can modify associations between circadian-related gene variants and cardiometabolic traits.
Methods (1)

» Inverse-variance weighted, fixed-effect meta-analyses were conducted of results of adjusted associations and interactions between dietary intake/sleep duration and selected gene variants on cardiometabolic traits.
Methods (2)

- Circadian-related gene variants were CLOCK-rs1801260, CRY2-rs11605924, MTNR1B-rs1387153, MTNR1B-rs10830963, NR1D1-rs2314339.

- Cardiometabolic traits were fasting glucose (FG), HOMA-insulin resistance, BMI, waist circumference, and HDL-cholesterol.
Results (1)

» Results are based on 15 cohort studies including up to 28,190 participants of European descent from the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium.
Results (2)

- Significant associations were found between
  - relative macronutrient intakes and glycemic traits.
  - short sleep duration (<7 h) and higher FG.
  - replicated known MTNR1B associations with glycemic traits.
- No interactions were evident after accounting for multiple comparisons.
Results (3)

- Nominally significant interactions (all P < 0.01) were observed between
  - carbohydrate intake and MTNR1B-rs1387153 for FG with a 0.003 mmol/L higher FG with each additional 1% carbohydrate intake in the presence of the T allele,
  - sleep duration and CRY2-rs11605924 for HDL-cholesterol with a 0.010 mmol/L higher HDL-cholesterol with each additional hour of sleep in the presence of the A allele,
  - long sleep duration (≥9 h) and MTNR1B-rs1387153 for BMI with a 0.60 kg/m² higher BMI with long sleep duration in the presence of the T allele relative to normal sleep duration (≥7 to <9 h).
Conclusions

» Our results suggest that lower carbohydrate intake and normal sleep duration may ameliorate cardiometabolic abnormalities conferred by common circadian-related genetic variants.
Implications

» Until further mechanistic examination of the nominally significant interactions is conducted, recommendations applicable to the general population regarding
  » diet (higher carbohydrate and lower fat composition) and
  » normal sleep duration

» should continue to be emphasized among individuals with the investigated circadian-related gene variants.

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