CLOCK genetic variation and metabolic syndrome risk: modulation by monounsaturated fatty acids.

BACKGROUND: Disruption of the circadian system may be causal for manifestations of the metabolic syndrome (MetS).

OBJECTIVE: The objective was to study the associations of 5 CLOCK polymorphisms with MetS features by analyzing fatty acid (FA) composition from dietary and red blood cell (RBC) membrane sources.

DESIGN: Participants (n = 1100) in the Genetics of Lipid Lowering Drugs and Diet Network (GOLDN) study were included. Dietary intake was estimated with a validated questionnaire. Anthropometric and biochemical measurements and genotypes were determined. Postprandial lipids and the FA composition of RBC membranes were analyzed.

RESULTS: CLOCK single nucleotide polymorphisms were significantly associated with obesity and individual components of MetS. For single nucleotide polymorphism rs4580704, minor allele carriers had a 46% lower risk of hypertension than did noncarriers. The monounsaturated fatty acid (MUFA) content of RBC membranes, particularly oleic acid, changed according to CLOCK genetic variants (P < 0.05). We identified significant gene-diet interactions associated with MetS at the CLOCK locus. By dichotomizing MUFA intake, we found different effects across rs4580704 genotypes for glucose (P = 0.020) and insulin resistance (P = 0.026). The protective effect of the minor allele on insulin...
sensitivity was only present when MUFA intake was >13.2% of energy. We also found different effects across CLOCK 3111T-->C genotypes for saturated fatty acid intake (% of energy) (P = 0.017). The deleterious effect of gene variants on waist circumference was only found with high saturated fatty acid intakes (>11.8%).

CONCLUSIONS: CLOCK polymorphisms interact with FAs to modulate MetS traits. The dietary source and membrane content of MUFAs are implicated in the relations between alterations in the circadian system and MetS.

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