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Interactions between *APOE* genotype and plasma fatty acids on cardiometabolic risk markers in individuals with the Metabolic Syndrome

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The $\epsilon 4$ allele of the *APOE* gene has been associated with higher TC, LDL-C and risk of cardiovascular disease (CVD)⁽¹⁾, and increased responsiveness to dietary saturated fat and cholesterol⁽²⁾. Given that individuals with the Metabolic Syndrome (MetS) have a four-fold increased risk of CVD⁽³⁾, they are an ideal target for gene-based nutrition interventions. However, the extent to which MetS traits are affected by interactions between the *APOE* genotype and plasma fatty acids (FA) is unknown.

The aim of the present analysis was to explore nutrient-gene interactions between the *APOE* polymorphism and plasma FA concentrations on metabolic markers in individuals with the MetS. To achieve this, plasma FA, blood pressure, insulin sensitivity, lipid concentrations and *APOE* genotype were determined in a cross-sectional analysis of 442 MetS individuals who participated in the LIPGENE study. Adjusted general linear models were used to assess nutrient-gene interactions at baseline.

A geographic cline was observed with respect to $\epsilon 4$ allele frequency, with 22.8 % frequency observed in Norway compared with 8.6 % in Spain. *E4* carriers had higher plasma concentrations of TC ($P = 0.004$), LDL-C ($P < 0.001$), and apo B ($P < 0.001$) compared with the *E2* carriers; and lower TC ($P = 0.013$), LDL-C ($P = 0.004$) and apoB ($P = < 0.001$) compared to the *E3/E3* group. High plasma n-3 PUFA was associated with a lower concentration of apoCIII in *E2* carriers ($P = 0.020$). High plasma C16:0 was associated with insulin resistance (HOMA-IR) in *E4* carriers ($P = 0.001$).

A detrimental impact of plasma SFA on insulin resistance was observed in *E4* carriers with MetS. In *E2* carriers, higher n-3 PUFA was associated with lower apoCIII concentrations. These findings suggest that individuals with MetS might benefit from personalised dietary advice targeted to *APOE* genotype, although further confirmatory intervention studies are required. This trial was registered at clinicaltrials.gov as NCT00429195.

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