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

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The ε4 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 ε4 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.