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Associations among dietary intake, gene polymorphisms and adipose fatty acid in TwinsUK study

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Fatty acids are essential molecules, which function as structural components, energy sources, and signaling mediators[(1)]. Subcutaneous adipose tissue (SAT) is the largest fat depot and plays a crucial role in maintaining health and homeostasis[(2,3)]. While regulation and health impacts of circulating fatty acid levels are well established, less is known about the regulation of fatty acid levels within adipose tissue itself. The aim of this study was to investigate the effect of dietary and genetic contribution to fatty acid contents in adipose tissue and identify the interaction between single nucleotide polymorphism (SNP) and diet on adipose fatty acids.

In 427 healthy female twins from TwinsUK, 18 types of fatty acids were measured in SAT biopsies alongside genotype, RNA-Seq and clinical phenotypes. Dietary intake was collected by food frequency questionnaire. The associations between dietary intake and adipose fatty acids were tested with linear mixed models, adjusting for age, smoking, physical activity, index of multiple deprivation, energy intake, and relatedness. Genome-wide association studies (GWAS) were performed adjusting for age.

The association between dietary scores, food intake, nutrient intake and fatty acid levels in adipose tissue were examined. Most dietary scores were positively correlated with polyunsaturated fatty acid (PUFA) but negatively correlated with trans-unsaturated fatty acid (TFA) ($P_{FDR} < 0.05$). We highlighted the positive association between polyunsaturated margarine and fish intake and PUFA levels, as well as butter and cream intake and saturated fatty acid (SFA) levels ($P_{FDR} < 0.05$). Negative associations between fresh red meat including lamb and beef, butter, and cream intake and PUFA levels in adipose tissue were observed ($P_{FDR} < 0.05$). Regarding nutrient intake, PUFA, SFA, TFA, cholesterol, vitamin D, and vitamin E were correlated with fatty acid levels in adipose tissue ($P_{FDR} < 0.05$). To reveal local genetic regulation of fatty acids in adipose tissue, we performed GWAS and identified 10 fatty acid-associated genetic *loci* across 13 fatty acids (i.e. palmitic acid/palmitoleic acid – at the *SCD locus*, dihomo-γ-linolenic acid/arachidonic acid at the *FADS1 locus*, $P < 5 \times 10^{-8}$). The integration of adipose gene expression data revealed the mediation effects of *SCD* and *FADS1* expressions in the associations between *FADS1* SNP and the conversion of unsaturated fatty acids. We took forward two GWAS lead SNPs (*SCD* SNP and *FADS1* SNP) to test the SNP-by-diet interaction on adipose fatty acids. Milk intake showed SNP-by-diet interaction with *FADS1* SNP for linoleic acid and docosapentaenoic acid levels ($P < 0.001$). The interactions between roasted potatoes/chips and *FADS1* SNP were significant for dihomo-γ-linolenic acid/linoleic acid ($P < 0.001$).

Adipose fatty acid levels were regulated by both genetic variants and dietary intake. We found suggestive evidence for the interaction of genetic variant and diet.

References

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