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Phenotypic and genotypic determinants of postprandial lipaemic response variation in healthy adults

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Response to dietary fat plays a key role in metabolic and cardiovascular health[(1)]. While this response can vary widely between individuals, variation within an individual and the associated contribution of phenotypic and genotypic factors is less well defined[(2,3)]. Understanding these issues is fundamental to the goal of achieving personalised nutrition. This work aimed to describe within- and between-person variation in lipaemic response to a repeated oral lipid tolerance test (OLTT) in 51 healthy adults as part of a larger randomised controlled trial. Fasting and postprandial plasma were collected hourly over 5 hours, from which SNP genotype and detailed biochemistry data, including triglyceride (TAG), non-esterified fatty acid, glucose and hormonal, were collected. Body composition (DXA, BodPod®), strength (isokinetic dynamometry), metabolic rate (indirect calorimetry) and fitness (sub-VO_{2max}) among other variables were also assessed. A TAG variability score (S_v), derived from the cumulative difference in TAG level at each time point across OLTTs, was assigned to each person as a proxy measure of lipaemic response. Those with the lowest variation in TAG concentration across OLTTs (LOW *n* 17) were compared to those of the highest variation (HIGH *n* 17). Analysis showed postprandial TAG response did not differ ($p = 0.64$) between visits for the group as a whole, with 82% exhibiting low variation ($S_v < 3.48$) in TAG response. When LOW and HIGH individuals were compared however, significant phenotypic and genotypic differences were observed. *Phenotype association:* HIGH individuals were significantly ($p < 0.05$) younger, heavier, taller, had a larger waist circumference, higher truncal bone mineral density and metabolic rate (kJ/kg FFM) and displayed higher TAG and lower NEFA levels at fasting. *Genotype association:* Exploratory analysis revealed associations between high Sv and SNPs in genes associated with satiety, lipoprotein metabolism, adipogenesis and type 2 diabetes risk after correction for phenotypic variables. In conclusion this work (1) confirms preliminary findings that postprandial lipaemic response is highly constant within the majority of healthy adults, and (2) strongly suggests that people who do exhibit the most variable response have a defined set of phenotypic and genotypic characteristics that warrant further research.

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