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Impact of the CYP7A1 single nucleotide polymorphism rs3808607 on postprandial lipids and gut hormones in response to functional interventions -findings from the CABALA study

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Changes in gut microbiota composition following supplementation with dietary fibres, polyphenols, and probiotics (referred to as functional interventions) may impact on cardiometabolic health via effects on bile acid (BA) metabolism[(1)]. A single nucleotide polymorphism (SNP) in the cholesterol 7-a hydroxylase (*CYP7A1*) gene (rs3808607), a rate limiting enzyme in the classic BA pathway, has been linked with the responsiveness of fasting lipid levels to dietary fibre (oat beta-glucan) intake[(2)]. The CABALA study aimed to investigate the association of this *CYP7A1* SNP with postprandial cardiometabolic disease risk markers following chronic consumption of functional interventions known to impact on the gut microbiota. In this single-blind, acute within chronic, parallel-trial, forty-six healthy volunteers (mean ± SD, age 52±11y and BMI 24.9±3.1kg/m^2), were randomised based on age, sex, BMI and serum total cholesterol to one of three interventions: two placebo capsules and i) 40g/day of porridge oats (n = 15) or ii) two Renetta Canada apples/day (n = 16), or iii) two *Lactobacillus reuteri* capsules with 40g/day of cornflakes (n = 15) for 8 weeks. At weeks 0 and 8, lipids, insulin and gut peptides were measured prior to and for 360 min after consumption of a high-fat meal representative of the assigned functional intervention. Retrospective genotyping data for the three interventions were combined to determine the impact of the *CYP7A1* SNP [TT 'wild-type' (n = 16) and G allele carriers (GT and GG, n = 30)] on the cardiometabolic outcomes. Significant visit*genotype interactions were evident for non-esterified fatty acid (NEFA) postprandial summary measures area (AUC) and incremental area under the curve (IAUC)($p \leq 0.035$). Compared to baseline, there were differential effects of genotype on the AUC and IAUC, with 11% and 18% increases in the TT group compared with 10% and 13% decreases in the G allele carriers, respectively. However, there was only a trend for a significant visit*genotype interaction for the TAG IAUC ($p = 0.054$), with a tendency for a greater postprandial TAG response at both study visits for the TT group compared with the G allele carriers. There were significant visit*genotype interactions for the AUC ($p = 0.016$) and IAUC ($p = 0.013$) for the postprandial insulin response. Compared with baseline, the TT group showed a decrease in the AUC and IAUC (8% and 21%, respectively) whereas there was an increase in G allele carriers (13% and 17%, respectively) after the functional interventions. There was no effect of genotype on any other gut hormones measured. Preliminary findings indicate the *CYP7A1* genotype had an impact on postprandial NEFA and insulin in response to daily consumption of the functional interventions.

Further analysis from this study will determine the impact on plasma and faecal BA profiles and cardiometabolic health.

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