Postprandial and Fasting Metabolic Signatures: Insights From the ZOE PREDICT 1 Study

Inbar Linenberg,[1] Kate Bermingham,[1] Mohsen Mazidi,[1] Ana Valdes,[2] Paul Franks,[3] Andrew Chan,[4] Jonathan Wolf,[5] Tim Spector,[1] Jose Ordovas,[6] Wendy Hall,[1] and Sarah Berry[1]

[1]Kings College London; [2]School of Medicine; [3]Lund University; [4]Massachusetts General Hospital; [5]Zoe Ltd; and [6]CEI UAM + CSIC, Madrid, Spain

Objectives: Postprandial metabolomic signatures, although not well characterized, may provide greater insight into individuals' responses to food and subsequent cardiometabolic disease risk compared to fasting and routine clinical measures. Using the PREDICT 1 cohort, we assessed postprandial changes and inter-individual variability in metabolites sequenced by NMR.

Methods: The ZOE PREDICT 1 study (n = 1,002 healthy UK adults; NCT03479866) measured 250 metabolite parameters (Nightingale Health NMR panel, related to lipids, amino acids, glycolysis, ketones, and glycoprotein acetyls (GlycA)) by venous cannulation at fasting and postprandially after a mixed nutrient sequential test meal (4 and 6 h after meal 1, 3.7 MJ; meal 2 given at 4 h, 2.2 MJ). Postprandial changes in metabolites and their inter-individual variability (median absolute difference from the median (MADM)/median (%)) were evaluated. Associations (Spearman's correlations) and differences in variances (Fligner-Killeen test) were assessed between fasting and postprandial (6 h) measures.

Results: A significant 6 h postprandial change from fasting was seen in 85% of metabolites; of which, 47% increased, and 53% decreased (Kruskal-Wallis $p < 0.05$ for all). Ketone bodies and very-large lipoprotein particles showed the greatest changes. Fasting and postprandial measures had large, yet similar, inter-individual variability (MADM/median; 15% at 0, 4 and 6 h (mean for all)) and were strongly correlated ($r > 0.8$; 71% of measures), although ketone bodies, glucose, branched chain amino acids and LDL diameter were only weakly correlated ($r < 0.5$). Inter-individual patterns of response differed postprandially compared to fasting (Fligner-Killeen test of variance, $p < 0.05$).

Conclusions: In this large and generally healthy cohort, we demonstrate significant changes in circulating metabolites between the fasting and postprandial phase, as expected, within lipoprotein size and composition remodelling, glycolysis, essential amino acid and ketone body pathways. The large inter-individual variability in postprandial metabolite levels, suggests dietary challenges offer an opportunity for stratifying metabolic responses.

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