Plasma and Urine Metabolomic Response to an Ultra-Processed Dietary Pattern: A Biomarker Discovery Analysis in a Domiciled Randomized Controlled Crossover Feeding Trial

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Objectives: To identify metabolomic markers that differed between dietary patterns (DP) that are either high in or void of ultra-processed foods (UPFs) according to NOVA.

Methods: A secondary analysis of a randomized, crossover, controlled feeding trial in which 20 domiciled, healthy participants (mean ± SD: 31 ± 7 years, BMI 22 ± 11.6, 50% female) consumed a UPF-DP (80% UPFs) and an unprocessed DP (UN-DP; 0% UPFs) for two weeks with no washout. DPs were matched for energy, macronutrients, total fiber, total sugar, and sodium; presented at 200% of energy requirements; and consumed ad libitum. Metabolite levels were measured in EDTA plasma at the end of each DP (wk 2) and in 24-hr and spot urine at wk 1 and 2, using untargeted liquid chromatography with high resolution/tandem mass spectrometry and annotated using Metabolon's reference library and authentic standards. Metabolites (n = 1000 plasma, n = 1272 24-hr urine, and n = 1281 spot urine) with <80% missing data and coefficients of variation <30% were assigned minimum detected values, scaled to median of 1, and log2-transformed. Linear mixed models in SAS identified metabolites that differed between UPF-DP and UN-DP adjusted for trial, DP sequence, timepoint, and body weight changes, with a subject-specific random intercept and Benjamini-Hochberg multiple comparison correction.

Results: For plasma, 183 metabolites differed between UPF-DP and UN-DP at wk 2. For 24-hr urine, 461 metabolites differed between UPF-DP and UN-DP at wk 1 and 2, 68 of which also differed at wk 1 and 2 for spot urine. Twenty metabolites consistently differed between UPF-DP and UN-DP at each timepoint and for each sample type. The sub pathways for these 20 metabolites included glutamate metabolism (n = 1 metabolite); ascorbate and aldarate metabolism (n = 1); benzoate metabolism (n = 2); methionine, cysteine, SAM and taurine metabolism (n = 2); secondary bile acid metabolism (n = 2); fatty acid dicarboxylate (n = 1); and plant-food components (n = 2); 9 could not be annotated.

Conclusions: We identified exogenous and endogenous metabolites, representing a range of metabolic pathways, that consistently differed between a UPF-DP and UN-DP. These candidate biomarkers of UPF intake require investigation in larger samples with dietary data sufficient for NOVA classification.

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