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Effect modification by metabotype in an EWAS of usual dietary food consumption

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Background and Objectives: Different metabolic states may effect associations between diet and DNA methylation. This can be captured by metabotypes, clustered subgroups with metabolically homogenous profiles. Our aim was to examine the effect modification by metabotype between habitual consumption of various food groups and white blood cell DNA methylation.

Methods: Habitual dietary intake was estimated based on repeated 24-hour diet recalls and a food frequency questionnaire in participants of the population-based KORA FF4 study. Residuals of energy-adjusted food group intake data were used in this epigenome-wide association study [EWAS]. DNA methylation was measured using the Infinium MethylationEPIC BeadChip providing data on >850 000 loci. Using four standard clinical parameters and BMI, three metabotype clusters were identified by the K-means clustering procedure. The final study sample comprised 1261 participants. Confounder-adjusted linear regression models were used to test for effect modification by metabotype between diet and DNA methylation.

Results: Many significant hits were observed in models including food group-metabotype interaction terms, e.g. >80 hits for cheese and margarine consumption, respectively. Most findings refer to effect modification of food intake (e.g., cheese, whole-grain products, margarine) by metabotype 3, which is the metabotype with the most unfavorable metabolic profile. Many of the significant CpG's in this EWAS could be annotated to genes, which will be interpreted in the context of the study aims.

Conclusion: This research emphasizes the importance of including metabolic information of subjects when identifying associations between diet and white blood cell DNA methylation in EWAS. However, replication in future studies is needed.

Keywords: EWAS, Metabotype, Effect Modification, Food groups

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