Associations of plasma and urine TMAO with actual diet of healthy individuals in KarMeN

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Trimethylammonium-N-oxide (TMAO) and related methylated amino compounds have been widely discussed in the context of nutrition and health. On the one hand, TMAO has been linked to consumption of specific food such as fish, meat and eggs. On the other hand, TMAO was found to be associated with clinical aspects such as cardiovascular disease risk or renal impairment. Moreover, TMAO is significantly associated with age. In fact, the specificity of TMAO for either clinical or nutritional aspects is still not clear.

Several food sources may influence plasma or urine TMAO concentrations in different ways. Natural TMAO and trimethylamine are present in fish and seafood. Precursor compounds such as choline or carnitine origin mainly from animal food, e.g. meat and eggs, and microbial degradation in the intestine and subsequent oxidation by flavin containing monooxygenase finally leads to formation of TMAO.

However, it is not clear how far plasma and urinary TMAO are determined by current diet or other parameters such as age or lean body mass, and how significant such associations are in a healthy study population without dietary intervention. Therefore, we investigated to what extent concentrations of TMAO and related compounds can be traced back to current food intake, using data from the well-characterized cross-sectional study KarMeN (Karlsruhe Metabolomics and Nutrition).

TMAO was analysed by LC-MS in plasma and by 1H-NMR in urine. Food consumption was assessed by 24h recall. In a first step, parameters were screened by partial Spearman correlation controlling for age, sex, lean body mass index and glomerular filtration rate (GFR) to identify food groups that are correlated with plasma and urinary TMAO. In a second step, associations with identified food groups as independent variables were investigated in multivariate linear regression models for parameters with Spearman's $\rho > |0.15|$. The effect size of different parameters on TMAO variation was estimated based on individual regression coefficients in the multivariate model.

In general, the investigated parameters could explain less than 25% of the TMAO variations. The influence of age was below 9% in plasma and below 5% in urine. Lean body mass and GFR contributed to less than 3%. Several food groups were significantly associated with TMAO, including fish and meat. Interestingly, association with fish was much higher in 24h urine compared to plasma, whereas a significant association with meat was found only in plasma, but not in urine. From our preliminary data, we propose distinct differences between direct TMAO intake from fish and indirect TMAO intake from other animal sources containing the metabolic precursors choline and carnitine.