Associations between plasma metabolite profiles and blood pressure: the HELIUS study

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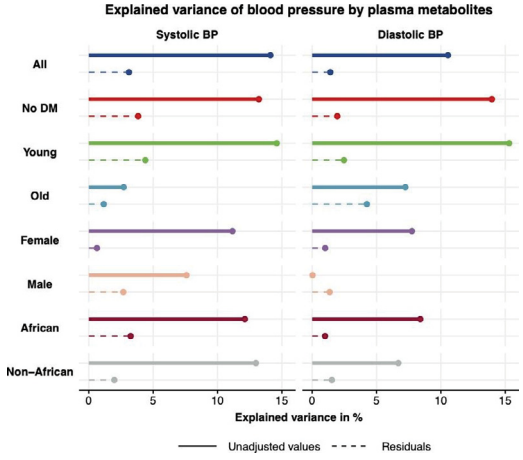
Background: Blood pressure (BP) is regulated by plasma metabolites from different neurohumoral and cardiometabolic systems. Since there are established differences in hypertension pathogenesis and treatment response between ethnicities, we hypothesized that plasma metabolites may be differently associated with BP across ethnic groups.

Purpose: To investigate associations between plasma metabolite profiles and BP in a multi-ethnic population-based cohort.

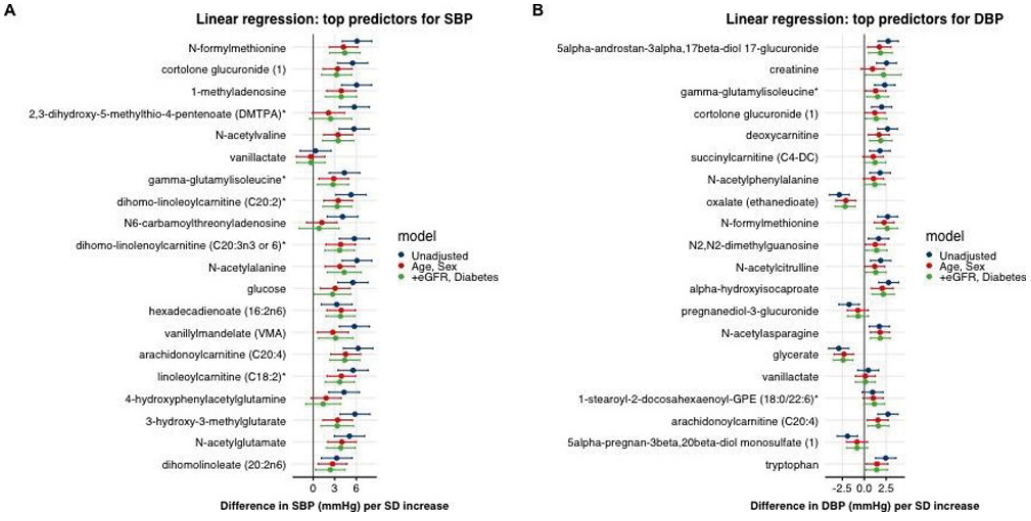
Methods: From the Healthy Living In an Urban Setting (HELIUS) study, 369 subjects (mean age 52±11 years, 51%F) of African and non-African descent were included. Office systolic (136±21 mmHg) and diastolic (83±12 mmHg) BP levels were recorded. Plasma metabolites were measured semi-quantitively with LC-MS (Metabolon) from fasting plasma samples. Associations between metabolite profiles and BP were assessed with machine learning prediction models using the XGBoost algorithm with nested cross-validation. Associations between the resulting best predictors and BP were assessed with linear regression models while adjusting for age, sex, estimated glomerular filtration rate and diabetes.

Results: Plasma metabolite profiles explained 14.1% of systolic BP variance and 10.6% of diastolic BP variance. These were attenuated to 3.1% and 1.4% respectively, when using residuals of BP after adjusting for age and sex. Top predictors for both systolic and diastolic BP included N-formylmethionine, several acylcarnitines and polyunsaturated fatty acids such as hexadecadienoate. These metabolites were significantly associated with higher systolic BP with estimates ranging from 3.0 to 4.5 mmHg per 1 SD increase in the adjusted models. Associations with hexadecadienoate, dihomolinoleate and catecholamine metabolites, including vanillactate had significant interactions ($p<0.05$) with ethnicity, and were only significant in subjects of non-African descent.

Conclusions: Plasma metabolome composition explained a large proportion of BP variance, but this association was attenuated when adjusting for confounders. Polyunsaturated fatty acids and catecholamine metabolites were only associated with BP in the non-African descent subjects. N-formylmethionine was the most consistent predictor for systolic BP across all subgroups. Future studies could focus on translating these findings in vitro in order to decipher the role of N-formylmethionine in BP regulation.



Explained variances of machine learning



Linear regression models