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Leg length, a marker of early childhood conditions, associates with specific clusters of serum fatty acids

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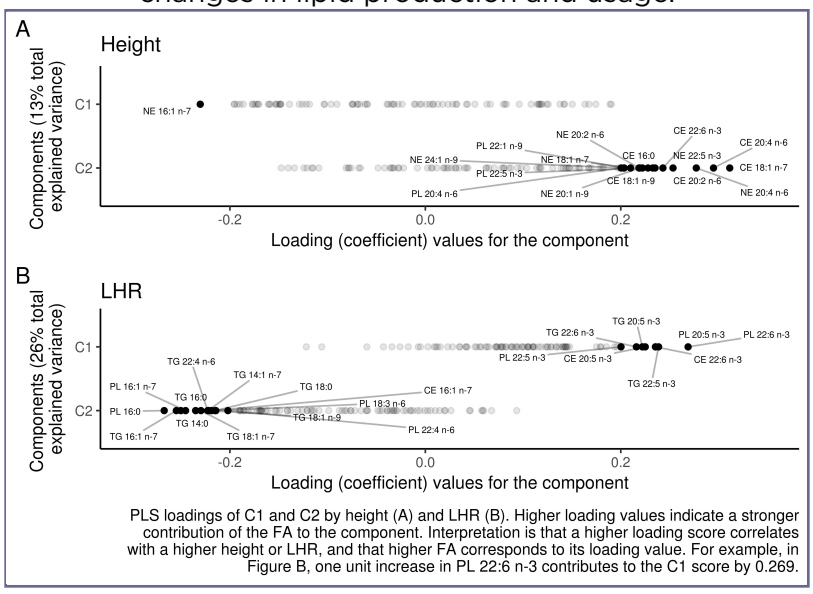
Abstract:
Background and aims: Adverse early childhood conditions have been associated with greater risk for adult chronic diseases such as type 2 diabetes (T2DM) and cardiovascular disease. However, the specific mechanism of action is not well elucidated. Adult leg length is an established biomarker of early childhood conditions. We aimed to explore distinct clusters of a broad spectrum of serum fatty acids (FA) by height and leg length.
Materials and methods: Canadian adults (n=453) at risk for T2DM from the Prospective Metabolism and Islet Cell Evaluation (PROMISE) cohort had detailed personal and metabolic data collected, including the measurement of FA and stature. The concentrations of 22 FA in the cholesteryl ester (CE), phospholipid (PL), triacylglycerol (TG), and non-esterified (NE) fractions were quantified. Height and sitting height were measured, which were used to compute leg to height ratio (LHR). To identify clusters in the FA profile, we used the supervised dimensionality reduction method partial least squares (PLS) with the stature components as the constraining variables and the FA as the predictor variables. Separate models were analyzed for height and LHR.

Results: The participants were mostly female (72%) and of European-ancestry (71.6%). Mean (SD) age was 50.4 (10.0) years, height was 166.1 (9.1) cm, and LHR was 0.47 (0.02). The four FA with the largest proportion in serum were CE 18:2 n-6 (20.6%), PL 16:0 (11.5%), PL 18:2 n-6 (8.2%), TG 18:1 n-9 (7.8%). For each PLS model, we extracted the first two components (C1 and C2; Figure). Higher LHR tended to load with a higher C1 cluster (i.e. more 20:5n-3 and 22:6n-3 in multiple lipid fractions) and loaded with a lower C2 cluster (i.e. less 14:1n-7, 14:0, 16:0, 16:1n-7, 18:0 in primarily the TG and PL fractions). There were no well defined specific cluster of FA in C1 for height, which may reflect that higher height correlates positively with total FA concentration. Height tended to load with a higher C2 cluster (e.g. 20 or more carbon long FA in multiple fractions).

Conclusion: We found that shorter adult leg length had a distinct lipid profile compared to shorter height, reflecting more omega-3 long chain FA and less of the 14 and 16 chain FA. Previous research has shown that these 14-16 chain FA associate with greater de novo lipogenesis and exert lipotoxic effects. Our results suggest that early childhood conditions, as reflected in adult leg length, may lead to changes in lipid production and usage.



PLS loadings of C1 and C2 by height (A) and LHR (B). Higher loading values indicate a stronger contribution of the FA to the component. Interpretation is that a higher loading score correlates with a higher height or LHR, and that higher FA corresponds to its loading value. For example, in Figure B, one unit increase in PL 22:6 n-3 contributes to the C1 score by 0.269.

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