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Differential Trajectories in Altered Insulin Sensitivity Following Weight Loss and Their Impact on Circulatory Amino Acids: Results from the PREVIEW: New Zealand Sub-study (OR27-07-19)

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Objectives: Metabolite profiling studies have consistently identified altered circulatory concentrations of amino acids (AAs) in individuals with heightened risk of type 2 diabetes and cardiovascular diseases. Of the changes reported to date, the branched-chain amino acids (BCAA) may be a reliable biomarker of disease risk and have been reported to be elevated many years prior to the onset of diabetes. We hypothesised that energy restriction-associated weight loss in pre-diabetes individuals would result in altered profile of circulatory AAs, including BCAA, with the changes correlating with the improvement in insulin sensitivity.

Methods: Pre-diabetic individuals (confirmed using the American Diabetes Association criteria) aged 25–70 years with BMI $>$ 25 kg/m^2 recruited into the New Zealand arm of the PREVIEW diabetes prevention trial, participated in an 8-week weight reduction program, with a requirement to lose $\geq$ 8% initial body weight using a commercial low-calorie diet (LCD, Cambridge Diet, UK^{TM}). Among those who succeeded, current analysis based on available samples ($n = 168$) from baseline (week-0) and end of weight loss (week-8). Serum free AA concentrations measured by ultra-high pressure liquid chromatography (UPLC) and all other metabolites measured using standard assays.

Results: Significant weight loss (11.1 $\pm$ 0.2% from baseline) accompanied improved insulin sensitivity and lipid profile. BCAA concentration positively correlated with insulin resistance measured at week 0 and 8, correspondingly ($P < 0.05$). Although the concentration of some AAs reduced significantly from week 0 to 8 ($P < 0.05$), reduction in fasting BCAA concentration was not significant ($P > 0.05$). However, regression analysis demonstrated that independent of weight loss, every 1.0 standard deviation (SD) reduction in BCAA concentration was associated with improvement in insulin sensitivity by 1.9 SD ($P < 0.05$).

Conclusions: As expected, dietary energy restriction-associated weight loss in individuals with pre-diabetes contributes towards normalisation of insulin sensitivity. Further, the responsiveness of AA and BCAA profiles to weight loss may be beneficial for monitoring and overseeing disease risk and improvement.

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