Understanding Determinants of Carbohydrate Metabolism and Their Contribution to Metabolic Health; The Impact of AMY1 CNV (P21-015-19)

Nathan O'Callaghan,[1] Armand Valsesia,[2] Sameer Kulkarni,[3] Julien Marquis,[3] Patricia Leone,[3] Polina Mironova,[3] Ondine Walter,[3] Wim Saris,[4] Patrick Descombes,[3] Jorg Hager,[3] Wim Saris,[4] Arne Astrup,[4] and Chrsitian Darimont[3]

[1]CSIRO; [2]Nestle Research; [3]Nestle Research Centre; and [4]University of Copenhagen

Objectives: Salivary α- amylase (AMY1) is responsible for the breakdown of starch into oligosaccharides, tri and di-saccharides giving a start to the starch digestion in the oral cavity on food consumption. Several studies recently reported contradicting results regarding the link between AMY1 copy numbers (CNs) and obesity and type 2 diabetes.

Objective: We investigated whether CN in the *AMY1* gene was associated with differential anthropometrics and glycaemic outcomes in obese individuals who underwent a dietary plan varying in macronutrient intake, as a part of weight loss and weight maintenance program. We also investigated whether there existed an interaction between nutrient intakes and *AMY1* CNs and if *AMY1* CNs have influence on body weight, body composition and glycemic trajectories during dietary interventions.

Methods: Using the Paralogue Ratio Test, we accurately measured the *AMY1* CNs in 761 obese individuals from the Diogenes study. Subjects underwent first an 8-week low-caloric diet (LCD, at 800 kcal/d) and those achieving >8% weight loss were then randomized to a 6-month weight maintenance dietary (WMD) intervention. The association between AMY1 CNs and weight- and glycemic- parameters was tested at baseline and following each intervention phase (LCD, WMD) with the use of linear mixed effect models adjusting for gender, age, center and total energy intake.

Results: At baseline, a modest association between *AMY1* CN and BMI ($P = 0.04$) was observed. *AMY1* CN was not associated with baseline glycemic variables. Additionally, *AMY1* CN was not associated with anthropometric or glycemic-outcomes following either LCD or WMD. Interaction analyses between *AMY1* CN and nutrient intake did not reveal significant association with any clinical parameters (at baseline and following LCD or WMD) or when testing gene x WMD interactions during the WMD phase

Conclusions: In the absence of association with weight trajectories or glycemic improvements, the *AMY1* CN cannot be considered as an important biomarker for response to a clinical weight loss and weight maintenance programs in overweight/obese subjects.

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