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Mitochondrial DNA methylation is associated with Mediterranean diet adherence in a population of older adults with overweight and obesity.

Sarah Corsi[1], Simona Iodice[2], Oliver Shannon[1], Mario Siervo[3], John Mathers[1], Valentina Bollati[2] and Hyang-Min Byun[1]

[1]*Newcastle University, Newcastle upon Tyne, United Kingdom,*
[2]*Universitá degli Studi di Milano, Milano, Italy and*
[3]*The University of Nottingham, Nottingham, United Kingdom*

Abstract

Introduction

Adherence to the Mediterranean dietary pattern (MeDiet) and adiposity, respectively, decreases and increases the risk of multiple common age-related diseases through several mechanisms including inflammation, reactive oxygen species (ROS) production in the mitochondria, and DNA methylation. For example, adverse changes in platelets from obese and overweight adults include hyper-aggregability and increased ROS. Since platelets are anuclear, their prothrombotic function is fully orchestrated by the mitochondria and the only DNA present is the mitochondrial DNA (mtDNA). In this study, we tested the hypothesis that MeDiet influences patterns of mtDNA methylation in platelets from older adults with greater adiposity.

Material and methods

We selected 134 participants with overweight or obesity (mean BMI = 35.5 ± 5.1 and age = 62 ± 10 years) from the "Susceptibility to particle health effects, miRNA and exosomes"(SPEHRE) Study. Dietary intake was assessed using a food frequency questionnaire and MeDiet adherence was calculated using the MeDiet Score described by Martínez-González et al.(2012). MtDNA was extracted from platelets, linearized, bisulfite converted and DNA methylation was quantified by pyrosequencing at 13 CpG in seven genes that encode for tRNAs (*MT-TF* and *MT-TL1*), regulatory regions (D-Loop and *MT-OLR*), and subunits of the electron-transport-chain (*MT-CO1*, *MT-CO2*, and *MT-CO3*).

Results

In these participants, MeDiet score ranged from 3 to 12 (mean = 6.5), with higher scores reflecting greater MeDiet adherence. Regression analysis showed that higher MeDiet score was associated with lower D-loop ($\beta = -0.031$, $P = 0.019$) and higher *MT-CO2* CpG1 ($\beta = 0.040$, $P = 0.023$) methylation. No associations were found between MeDiet Score and methylation level at *MT-CO1*(2 CpGs), *MT-CO2*(CpG2), *MT-CO3*(2 CpGs), *MT-TL1*(2 CpGs), *MT-TF*(CpG1), *MT-OLR*(3 CpGs).In addition, there was no association between mtDNA methylation and BMI.

Discussion

The D-loop is critical for mitochondrial function since it initiates mtDNA replication and transcription. Increased D-loop methylation has been associated with reduced mitochondrial functionality, and insulin resistance. Our results suggest that higher adherence to MeDiet lowers D-loop methylation which may protect against obesity-related comorbidities (e.g. insulin resistance).

Higher MeDiet scores are associated with *MT-CO2* CpG1 hypermethylation. *MT-CO2* encodes for a subunit of the Cytochrome-C-oxidase, a highly regulated enzyme involved in the oxidative metabolism. *MT-CO2* demethylation, induced by Valproic-Acid administration, has been reported to be associated with increased ROS production. Our results suggest a possible role of MeDiet in mitochondrial ROS regulation via methylation of *MT-CO2*.

For the first time, we observed associations between MeDiet adherence and mtDNA methylation. Validation of these findings in independent cohorts is required.

Conflict of Interest

There is no conflict of interest