EXPLORING THE IMPACT OF OBSTRUCTIVE SLEEP APNEA AND ITS TREATMENT ON DNA METHYLATION AND EPIGENETIC AGING

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Background: Obstructive sleep apnea (OSA) has been associated with multiple molecular and cellular alterations that underlie the aging process. Yet, whether OSA aggravates/accelerate aging is still not clear. DNA methylation has emerged as one of the most robust indicators of biological aging. In this study, we proposed to evaluate the impact of OSA and OSA treatment with continuous positive airway pressure (CPAP) on DNA methylation and epigenetic aging.

Methods: This study was approved by the ethical committees of the Faculty of Medicine of the University of Coimbra and of Coimbra Hospital and University Center. It includes six patients with severe OSA (56 ± 3 years), before and after 4 months (short-term) and 2 years (long-term) treatment with CPAP, seven healthy subjects of the same age group (middle-age, 49 ± 3 years), and seven young adults (24 ± 1 years). Blood samples were collected from all participants at 11 a.m., and genomic DNA was extracted from peripheral blood mononuclear cells (PBMCs). DNA methylation was profiled using the Illumina ® Infinium Methylation EPIC Bead Chip array (Illumina, San Diego, CA, USA) and iScan. We evaluated differentially methylated positions (DMPs) between groups and performed functional enrichment analyses. Epigenetic age was estimated using published chronological and phenotypic clock models.

Results: Patients with OSA showed 206 significant DMPs, associated with 139 genes, in PBMCs, relative to middle-aged controls (mostly hypomethylated in OSA: 86 %, adj.p < 0.05). Among these DMPs, 56 were also significantly hypomethylated at baseline (before treatment) vs after long-term CPAP (adj.p < 0.05). We did not find significant DMPs between treated patients and control subjects. Yet, the PhenoAge epigenetic clock model evidenced an increased epigenetic age acceleration in long-term treated patients compared to baseline (adj.p < 0.05).

Conclusions: OSA promotes changes in DNA methylation that seem to be reversed by CPAP treatment. However, the increased epigenetic age acceleration observed in long-term treated patients relative to baseline suggests an accelerated/aggravated biological aging in patients with OSA even after CPAP treatment. This study opens new avenues for OSA research and clinical management.