A nutrigenomics approach for the study of anti-aging interventions: olive oil phenols and the modulation of microRNA profiles in mouse brain

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Many epidemiological studies and clinical trials have been undertaken to evaluate the effect of dietary intake or supplementation with vitamins, dietary antioxidants or specific fatty acids in the elderly, focusing mainly on cognitive decline, often with limited results. The phenolic compounds present in high concentration in extra-virgin olive oil (oleuropein, oleocanthal, hydroxytyrosol and tyrosol) have been shown to improve a number of inflammation- and oxidation-related parameters associated with cardiovascular risk in human intervention studies (Cicerale et al., 2012; Covas, 2008; Raederstorff, 2009). At the molecular level, they are able to modulate targets and pathways which have been implicated in the aging process and in age-related diseases (Giovannelli, 2013).
The aim of this study was to evaluate whether changes in brain genes and microRNAs expression were associated with the cognitive and motor improvement observed in mice treated with olive oil phenols. C57Bl/6J mice were fed from middle age to senescence with extra-virgin olive oil (10% wt/wt) rich in phenols (H-EVOO, phenol dose/day: 6 mg/kg) or with the same oil deprived of phenolic compounds (L-EVOO).
Transcriptomics analysis identified 53 genes and 6 gene sets significantly modulated in the mice cortex after 6 months of feeding with the H-EVOO diet, such as Notch1, a synaptic plasticity-related gene and the pathway of agrin, a glycoprotein involved in cholinergic synaptic differentiation and maintenance. Moreover, 63 miRNAs were also differentially expressed in the cortex of H-EVOO mice compared to the L-EVOO group. Interestingly, mice fed with the extra virgin olive oil rich in phenols showed miRNA expression profiles similar to those observed in young mice, while the L-EVOO mice exhibited profiles very different and, on the contrary, similar to those observed in TgCRND8 mice, a mouse model of Alzheimer's disease. Analyzing the changes in microRNA and target gene expression, we found 5 miRNAs down-regulated in the H-EVOO group and up-regulated in aging: miR-30a-5p and -126-3p, previously associated with aging, miR-434-5p and -369-5p, related to cell differentiation and reprogramming control, and miR-451. This study may contribute to clarify the mechanisms underlying the health benefits associated with the intake of dietary polyphenols contained in olive oil and support our previous data demonstrating that they were able to counteract age-related dysfunctions.

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