

HYDROXYTYROSOL A COMPONENT OF OLIVE OIL, MITIGATES ANXIETY-LIKE BEHAVIORS AFTER A TRAUMATIC EXPERIENCE IN OLD MICE BY PROMOTING ADULT NEUROGENESIS AND BY MAINTAINING BIODIVERSITY OF GUT MICROBIOTA

Giorgio D'Andrea¹, Laura Bertini², Roberta Bernini³, Andrea Fochetti³, Silvia Proietti², Agnese Bonato¹, Giada Raparelli¹, Carla Caruso², Maurizia Caruso¹, Marco Costanzi⁴, Felice Tirone¹, and Laura Micheli¹

¹*Institute of Biochemistry and Cell Biology, National Research Council (IBBC-CNR), Monterotondo, Rome, Italy*

²*Department of Ecological and Biological Sciences, University of Tuscia, Viterbo, Italy*

³*Department of Agriculture and Forest Sciences (DAFNE), University of Tuscia, Viterbo, Italy*

⁴*Department of Human Sciences, LUMSA University, Rome, Italy*

Background: Our research is focused on the effects of components of external exposome, such as diet and physical exercise, on age-associated neurogenesis defects^{1,2,3}, muscle dysfunctions and gut dysbiosis. We previously observed that Hydroxytyrosol (HTyr), a phenolic compound present in olive oil⁴, stimulates neurogenesis in the hippocampal dentate gyrus of aged mice⁵.

Methods and Results: Our current studies indicate that oral administration of HTyr, synthesised in our laboratories, to aged mice: 1) promotes neurogenesis of the dentate gyrus with a prevalent effect in the ventral region, and reduces anxiety symptoms and microglia inflammation in a model of post-traumatic stress disorder; 2) preserves the gut microbiota biodiversity, which is reduced after a traumatic event, and particularly prevents the decrease in the *Ruminococcaceae* family, which participates in the promotion of neurogenesis and neuron survival; 3) mitigates age-associated skeletal muscle atrophy and increases expression of genes involved in mitochondrial biogenesis, response to oxidative stress, autophagy and lysosome biogenesis.

Conclusions and Significance: Our data show that a diet supplemented with HTyr promotes stress resilience in aged mice by increasing ventral hippocampal neurogenesis, decreasing neuroinflammation, and modulating the microbiota-gut-brain axis. Moreover, HTyr appears to counteract the age-associated deterioration of skeletal muscle function.

Keywords: *Hydroxytyrosol, neurogenesis, post-traumatic stress disorder, microbiota-gut-brain axis, muscle atrophy*

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