REDUCED CCL11/EOTAXIN MEDIATES THE BENEFICIAL EFFECTS OF SENSORIMOTOR STIMULATION ON THE AGED HIPPOCAMPUS

Gaia Scabia¹,², Giovanna Testa³, Manuela Scali⁴, Serena Del Turco¹, Genni Desiato⁵,⁶, Nicoletta Berardi⁴,⁷, Alessandro Sale⁴, Michela Matteoli⁵,⁶, Lamberto Maffei⁴, Margherita Maffei¹,²*, Marco Mainardi³,⁴* on behalf of “the Train the Brain” Consortium

1. Institute of Clinical Physiology, National Research Council (IFC-CNR), Pisa, Italy
2. Obesity and Lipodystrophies Center at Pisa University Hospital, Pisa, Italy
3. Laboratory of Biology “Bio@SNS”, Scuola Normale Superiore, Pisa, Italy
4. Institute of Neuroscience, National Research Council (IN-CNR), Pisa, Italy
5. Institute of Neuroscience - National Research Council (IN-CNR), Milan, Italy
6. Humanitas Clinical and Research Center - IRCCS, Rozzano, Milan, Italy
7. Department of Neuroscience, Psychology, Drug Research and Child Health, NEUROFARBA University of Florence, Florence, Italy

*correspondence to: Marco Mainardi (marco.mainardi@in.cnr.it), and Margherita Maffei (m.maffei@ifc.cnr.it)

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ABSTRACT

A deterioration in cognitive performance accompanies brain aging, even in the absence of neurodegenerative pathologies. However, the rate of cognitive decline can
be slowed down by enhanced cognitive and sensorimotor stimulation protocols, such as environmental enrichment (EE). Understanding how EE exerts its beneficial effects on the aged brain pathophysiology can help in identifying new therapeutic targets. In this regard, the inflammatory chemokine ccl11/eotaxin-1 is a marker of aging with a strong relevance for neurodegenerative processes. Here, we demonstrate that EE in both elderly humans and aged male mice decreases circulating levels of ccl11. Interfering, in mice, with the ccl11 decrease induced by EE ablated the beneficial effects on long-term memory retention, hippocampal neurogenesis, activation of local microglia and of ribosomal protein S6. On the other hand, treatment with an anti-ccl11 monoclonal antibody was sufficient to mimic the effects of EE on memory and hippocampal neurogenesis. Our findings point to a decrease in circulating ccl11 concentration as a necessary and sufficient mediator of the benefits of sensorimotor stimulation on the aged hippocampus, thus suggesting promising therapeutic avenues for counteracting age-related cognitive- decline.