

Title: Identification of metabolic pathways activated by different learning strategies in mice

Abstract

Alexandre Carrea¹, Filippo La Greca¹, Gabriele Imperato¹, Elena Marcello¹, Nico Mitro^{1,2} & Diego Scheggia¹.

¹Department of Pharmacological and Biomolecular Sciences “Rodolfo Paoletti”, University of Milan, Milan, Italy

²Department of Experimental Oncology, IEO, European Institute of Oncology IRCCS, Milan, Italy.

Metabolic cost for the nervous system is very high due to the complexity of neuronal morphology and the processes to sustain neuronal transmission and synaptic plasticity. Cognitive functions underlying complex behaviors further increase brain energy demands. Over the past decade, there has been increasing interest in understanding how changes in metabolic function may affect neural functions, thereby increasing vulnerability for brain disorders. Despite the interest given to brain metabolism during the last years, how modification of metabolism might contribute to cognitive dysfunctions in brain disorders is not clear. Thus, we aim to identify the key metabolic pathways activated during complex cognitive functions.

In this study, we will focus on metabolic pathways activated by different learning strategies in mice, such as self-experience and observational learning, and by different contextual cues (social and non-social). On the other hand, using liquid chromatography coupled with tandem mass spectrometry we will analyze the distribution of metabolic substrates following the behavioral experiments. As a result, we are expecting to identify specific metabolic pathways associated with different cognitive functions related to different learning strategies. Furthermore, we will analyze how the identified pathways are changed during aging and in health and disease, using aged mice and an animal model of Alzheimer disease.

This approach could provide better understanding of the metabolic pathways associated with cognitive processes and might offer insights into the physiological basis of learning formation and maintenance and its implications in brain disorders such as neurogenerative and neuropsychiatric disorders.

The outcome of this project might change current paradigms in neuroscience research and open new avenues for the development of innovative therapeutic strategies for cognitive dysfunctions associated with neurogenerative and neuropsychiatric disorders.