

## Alterations on the kynurenine pathway as potential mechanisms underpinning obesity-induced cognitive impairment

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In addition to be a primary risk factor for type 2 diabetes and cardiovascular disease, obesity is associated with learning disabilities. However, the mechanisms underlying the cognitive impairment induced by obesity are poorly understood. Here we examined whether a dysregulation of the brain kynurenine pathway (KP) might underlie the learning deficits exhibited by obese individuals. The KP pathway is the major route of tryptophan (Trp) metabolism. It is initiated by the enzymatic conversion of Trp into kynurenine (KYN) by indoleamine 2,3-dioxygenase (IDO). KYN is further converted to several signalling molecules including Kynurenic acid (KA) and Quinolinic acid (QA) which have a negative impact on learning. Wistar rats were exposed either to standard chow or to a free choice high-fat high-sugar (fCHFHs) diet from weaning to 120 days of age. Their learning capacities were then evaluated using a combination of the novel object recognition and the novel object location tasks and the concentrations of tryptophan and kynurenine-derived metabolites in several brain regions determined by ultra-performance liquid chromatography-tandem mass spectrometry. Obese rats exhibited reduced learning capacity characterized by impaired encoding and consolidation of memory along with increased concentrations of Trp, QA and Xanthurenic acid (XA) in the hippocampus, but not in the frontal cortex and brain stem. Conversely, obesity enhanced the expression of IDO in the former regions but not in the hippocampus. QA and XA stimulate the glutamatergic system and their increased production leads to cognitive impairment. These results therefore suggest, that altered kynurenine pathway metabolism contributes to obesity-associated learning disabilities.

### Biography

Carla Elena Mezo-González is a Mexican second-year-PhD student in the program of Biology and Health at the Université de Nantes, France. She holds a Bachelor of Science in Biology with a minor in Biotechnology (2012) and a Master of Science in Molecular Biomedicine (cum laude, 2016) from the Instituto Politécnico Nacional (IPN), in Mexico City. From 2016 to 2018 she worked at the Laboratory of Gastroenterology and Nutrition at the Hospital Infantil de México. She has been a research fellow at the Laboratory of Cell Biology and Natural Products (2014-2016) and the Laboratory of Zoology at the IPN (2010-2012).