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OC.15- CHRONIC OVERWEIGHT SEVERELY IMPAIRS ADULT HIPPOCAMPAL NEUROGENESIS AND PLASTICITY

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Adult neurogenesis is a structural form of neural plasticity that contributes to the maintenance of normal brain function. Adult neural progenitors are present in the sub-ventricular zone of the forebrain, in the hippocampal dentate gyrus and in the hypothalamus. Within the dentate gyrus, newborn neurons are known to integrate into the pre-existing circuitry and to play a substantial role in the synaptic plasticity which underlies certain types of learning and memory. Several environmental and physiological factors, including high fat diet critically modulate almost every stage of neurogenesis. In previous studies we demonstrated that leptin signal deficiency in the brain of obese mice is coupled to high levels of orexin-A (OX-A) and endocannabinoid 2-Arachidonoylglycerol (2-AG). OX-A enhances neurogenesis, by promoting neuronal proliferation and differentiation, whereas chronic administration of leptin in adult mice increases cell proliferation in the dentate gyrus. However, the functional cross-talk between these molecular interplayers in the regulation of adult neurogenesis in not well understood. At this purpose, in the present study, we exploited leptin knockout ob/ob mice, which represent a model of obesity by mimicking the leptin inefficacy in the brain of mice made obese by a high fat diet, to investigate the effects of chronic overweight on the learning and memory by a functional evaluation of the long term potentiation (LTP) in adult dentate gyrus. By combining biochemical, morphological and functional studies with electrophysiology, in vitro and in vivo, we found an activation of orexinergic/endocannabinoid pathway which regulate the neuronal progenitor fate.