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## Decreased hippocampal efficiency in obese rats is expressed by impaired cognition, neurogenesis and proteomic changes

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### Abstract

Obesity associates with plethora of dysfunctions including changes in the brain structures, like hippocampus which is particularly susceptible to metabolic or inflammatory alterations. The is a need to expand knowledge about the obesity related brain changes in order to enable development of new therapeutic interventions, that would support not only weight loss but also could help to restore the after-effects of obesity in the brain. In the present report we evaluated the hippocampal efficiency of obese rats. In order to induce obesity 4 weeks old male rats were fed with a chow that mimics human western diet for 12 weeks (model of diet induced obesity). Then the cognitive functions (water maze), neurogenesis (BrdU detection) and global proteomic changes (MS/MS analysis) were analyzed in separate cohorts of animals. Obese rats had worsen cognitive flexibility than normal rats, but the spatial learning and long term memory were unaffected. The number of BrdU/NeuN positive cells was lowered in obese animals suggesting decreased hippocampal neurogenesis. The analysis of proteins revealed that about 120 proteins significantly differed between hippocampi of obese and normal rats. Neuronal calcium sensor 1 (NCS-1) which participates in mechanisms involving synaptic plasticity and acquisition of spatial memory was decreased in obese rats. Neuromodulin and vinculin, required for synaptic plasticity also decreased in these animals. Impaired neurogenesis was associated with decreased level of: receptor-type tyrosine-protein phosphatase zeta and cytoplasmic dynein 1 light intermediate chain 2, which play crucial roles in controlling axonal growth and neuronal migration. Altogether the data show that proteomic changes related to obesity associate with impaired hippocampal functioning. The same set of experiments was performed on the additional cohort of obese animals subsequent to weight loss to examine if the observed brain changes persist if obesity is reversed. This research is supported by Nutricia Foundation, grant no. RG 1/2017.

### Conflict of Interest

There is no conflict of interest.