Epigenetic modifications linked to memory impairments induced by a high-fat diet during adolescence

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Abstract

We have previously reported that an unrestricted high fat diet consumed during the adolescence period has been causally linked with hippocampal memory impairments in adulthood. Causal mechanisms reported include, prolonged stress induced inflammatory response, neuronal hyperexcitability and cerebral plasticity disruption in hippocampus. In this study we have looked at hippocampal gene expression and protein levels in mice fed normal chow (NC) or high fat (HF) diet for 12 weeks since weaning and sacrificed 30 min after the training phase of contextual fear conditioning (CFC), a classical hippocampus-dependent memory test, and compared them to home cage controls. We found that many immediate early genes were induced by CFC in both NC and HF groups compared to controls. Interestingly, 2-way ANOVA diet by CFC interaction was found for genes encoding for epigenetic modifiers such as histone deacetylase (Hdac3) and DNA methylase (Dnmt3a) or histone methylase (Suv39h2). Finally, phosphorylated glucocorticoid receptor was up-regulated and BDNF downregulated in CFC mice on HF diet. These data are interesting in view of similar modifications observed in hippocampus in age-related memory impairments.