

## **The effects of obesity on hippocampal function in the rat**

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**Introduction:** Obesity is a low-grade inflammatory state, which constitutes an inhospitable intrauterine environment. After birth, children of obese mothers are further at increased risk of neurodevelopmental abnormalities, eg reduced cognitive capacity, developmental delay, attention deficit hyperactivity disorder, and autism spectrum disorders. In adults, high BMI and metabolic syndrome are associated with lower cognitive performance, and poor executive function and memory. The hippocampus is a major centre for memory, learning and decision making, and is important in emotional regulation. The aim of the present study was to determine the effects of obesity *in utero* and beyond, on hippocampal function in rat.

**Methods:** Dams were placed on control chow or a high fat (HF) diet for 6 weeks and then mated with lean males. Offspring were retained on the diet of their dam. At 7 weeks of age, cognitive function was assessed using behavioural testing. Subsequently hippocampal brain slices were studied electrophysiologically using multielectrode arrays.

**Results:** The Barne's maze showed enhanced learning in males on HF diet but not in females, while memory was strikingly poor in HF fed females. With the Elevated Plus maze, HF males spent less time in the open arms suggesting anxiety-like behaviour. In hippocampal slices, HF diet had a greater effect on long-term potentiation (LTP) in HF males vs control fed. A significant observation was that in all our obese males, slices of hippocampus had a dramatically greater tendency to produce oscillatory network (epileptiform) activity compared with lean counterparts.

**Conclusions:** Obesity affects behaviour and hippocampal function in a sex-dependent manner. These effects include epileptiform/hyperactivity that occurs in obese males. Since hippocampal hyperactivity has been strongly implicated as underlying at least some of the age-related cognitive impairment, obesity may exacerbate age-related cognitive impairment, either in terms of earlier onset (premature aging) and/or degree of severity of impairment.