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Higher-centre regulation of feeding behaviour

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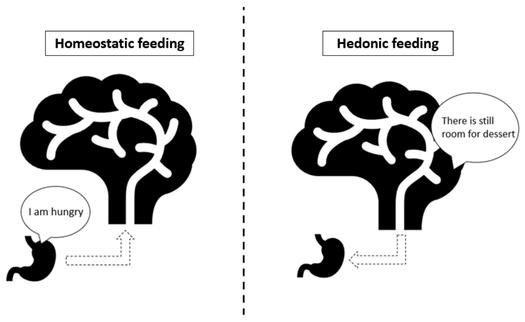
I. Introduction

Feeding is a complex behaviour that involves both metabolic and neuronal processes. The neural circuits that control **homeostatic** and **hedonic** feeding are extensively **overlapping**.



When individuals are faced with the challenge of choosing what to eat, their choice is deeply influenced by both circuits. However, animals display an innate bias towards **high-fat food**.

The detrimental effects of a high-fat diet (HFD) are not limited to body weight gain, but include effects on the neural circuits that regulate feeding. In particular, HFD consumption has been reported to **dampen neuronal activity** in response to a normo-caloric diet.

II. Research question

? Can HFD consumption leave a **memory trace** in the brain that facilitates the development of **HFD preference** upon repeated consumption?

III. Aims and Objectives

a. To **identify** a neuronal population that encodes HFD consumption.

b. To elucidate the **mechanisms** through which these neurons may mediate the development of food preference and the associated maladaptive outcomes.

c. To **manipulate** the neuronal population of interest in order to **attenuate** voracious HFD consumption and **rescue** normo-caloric diet consumption.

IV. Methods - the 3Rs principles

Replacement: animal models are still **essential** to the study of the neuronal control of feeding and cannot be **replaced.**

Reduction: the number of animals used can be only partly **reduced** by sample size calculation and sample pooling.

Let's Refine!

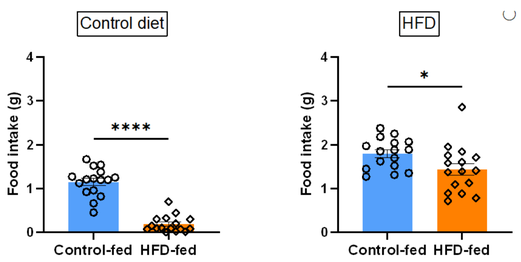
a. Automated food intake monitoring system to **minimise** contact time and therefore distress.

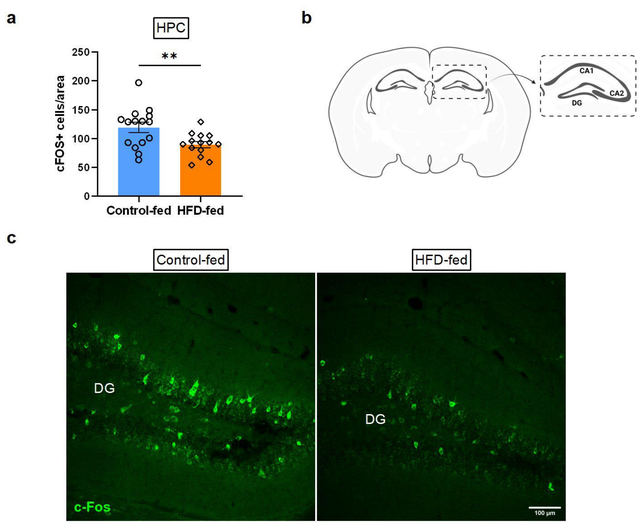
b. Pilot studies to optimise experimental timing and **minimise** exposure to HFD to produce significant responses while limiting unnecessary exposure to an obesogenic diet.

c. Periods of fasting no longer than 16 hours.

V. Results

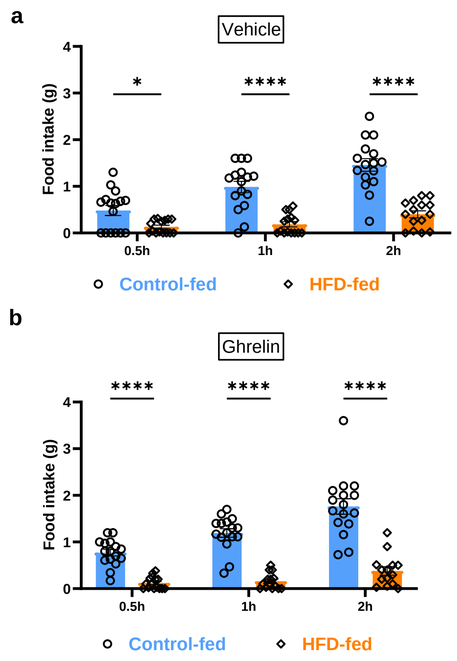
Normo-caloric diet intake is **decreased** by previous HFD consumption and this attenuated response is associated with a **decrease** in neuronal activity in the **hippocampus (HPC).**



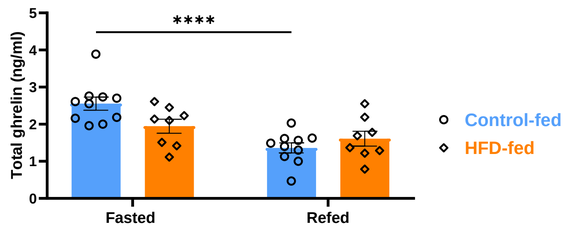


VI. Results

Normo-caloric diet consumption is **not** rescued by administration of the **appetite-stimulating** hormone **ghrelin.**

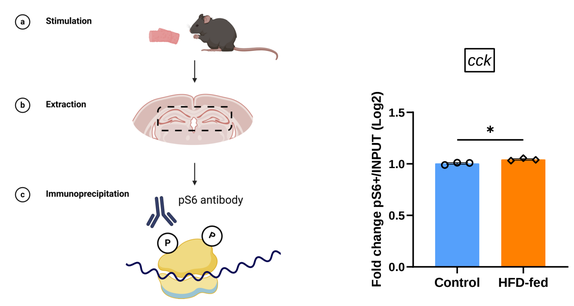


Accordingly**, endogenous** ghrelin plasma levels do not follow physiological fluctuations in HFD-fed mice.



VII. Results

Molecular profiling of highly activated neurons in the hippocampus reveals activation of **CCK-expressing neurons**.



VIII. Conclusions

CCK plays a **dichotomous** role in the regulation of food intake: it **suppresses** food consumption, while driving food selection towards **HFD**.

a. The hippocampus may represent the neural substrate for the development of HFD-related memories.

b. CCK signalling in the hippocampus could facilitate the development of HFD preference while suppressing normo-caloric diet consumption.