

Sexual dimorphism of hypothalamic cilia

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Abstract:

The maintenance of healthy body weight is ensured by the balance between energy intake (e.g. food intake) and energy expenditure (e.g. exercise). Understanding how the brain controls this equilibrium is not only of fundamental physiological importance but also of medical relevance due to the dramatic effects of overweight on health.

According to the literature, the hypothalamus is a key player of energy balance control and notably the arcuate (ARH) and the paraventricular (PVH) nuclei where neurons expressing specific neuropeptides are found. Neurons are not the only actors known to mediate energy balance, other specialized cells and organelles such as primary cilia also play a crucial role in maintaining this balance. Cilia are non-motile air-like organelles present at the surface of specific hypothalamic neurons. It has been shown that defects affecting cilia integrity cause various metabolic disorders including obesity in males. However information on female is still missing. Interestingly, Croizier lab showed a sexual dimorphism in the differential expression of key cilia genes in the ARH. As the brain development is under control of sexual hormones, notably a neonatal surge of testosterone in males, we wonder whether sexual hormones can participate to the sexual dimorphic ciliogenesis in the hypothalamus, and somehow participate to the sexually dimorphic prevalence of obesity.

To address these questions, we will:

- 1) Characterize the sexual dimorphism of cilia in several hypothalamic nuclei
- 2) Assess the role of sexual hormones in hypothalamic ciliogenesis
- 3) Study functional aspects

For this, we will use a combination of histological techniques (immunohistochemistry), molecular biology and in vivo assays in different mouse models.

This project will provide insight into the sexual dimorphism of key hypothalamic actors of the control of energy balance and pave the way for a better understanding of the gender-specific prevalence of obesity.