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Renseignements:  
<https://www.societe-neuroendocrinologie.fr/>

energy homeostasis. In the hypothalamus, it has been described that AMPK mediates ghrelin, glucose-like peptide 1 and thyroid hormone induced changes in metabolism related neuropeptides secretion. However, in order to reach their hypothalamic targets, peripheral hormones must first cross the blood-brain barrier (BBB); transcellular transport via tanycytes, specialized glial cells of the hypothalamus, appears to be one of the routes used by these signals to enter the brain. Tanycytes line the floor of the 3rd ventricle (3V) and send processes towards the external zone of the median eminence where reside fenestrated capillaries; they have been shown to act as a physical barrier preventing the free diffusion of circulating molecules into the cerebrospinal fluid (CSF). AMPK being a key energy sensor and tanycytes putative channels for the transport of peripheral metabolic signals into the brain, here we sought to study the role of AMPK expression in tanycytes at the blood-CSF barrier interface in the median eminence (ME) of the hypothalamus.

Tanycyte specific AMPK ablation in mice induced changes in food intake, body weight and energy expenditure. Those metabolic modifications are accompanied with an increased hormonal sensitivity which could like be related to the changes in blood-brain barrier permeability we observe in these mice.

#### **P44 - See-through the brain: 3Dimensional Imaging of the Neuroendocrine Circuits Controlling Reproduction in Mice**

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The proper functioning of the reproductive axis guarantees the survival of a species, and fertility in mammals is controlled by a population of gonadotropin-releasing hormone (GnRH) neurons located in the hypothalamus. These neurons integrate several signals from their interactors and release GnRH in the hypothalamo-pituitary portal circulation to stimulate gonadotropin secretion in the pituitary. In mice, GnRH neurons are born in the olfactory placodes around embryonic day 10.5 (E10.5), then migrate during the embryonic life from the nasal region towards the brain, using olfactory/vomeroneasal nerve projections as guides. In the brain, the majority of the GnRH neurons migrate ventrally and settle in the hypothalamus, where they show little activity until puberty onset.

Most studies on GnRH neurons migration and their interactions in the brain were conducted on sections. Thus, there was a significant loss of information when trying to study the entire network involved in the control of fertility. Clearing and 3D-imaging techniques developed these last ten years are useful tools to allow easier visualisation and analysis of both physiological and pathological conditions at the network and organ scale.

Here, using whole-mount immunolabelling combined with tissue clearing and light-sheet microscopy, we analysed the ontogenesis, migration, and axonal targeting of GnRH neurons in mice from embryonic development to adulthood. Moreover, using transgenic mouse lines, we identified unexpected extrahypothalamic populations expressing GnRH, GnRH receptor, and kisspeptin in the postnatal mouse brain. These data raise the intriguing hypothesis that GnRH could be implicated in the modulation of multiple brain functions.

#### **P45 - Effect of the prebiotic lactulose on neurogenesis in a sheep model of early-life stress**

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The olfactory bulb and the hippocampus represent the main regions in the mammalian brain where new neurons continue to be added throughout life. Early-life stress affects the neurogenesis process in these areas. Gut microbiota modulates hippocampal neurogenesis and both probiotics and prebiotics supplementation can prevent the stress-induced reduction in hippocampal

neurogenesis. The impact of gut microbiota and its modifications on olfactory neurogenesis has not been explored yet. Here, we investigate the effect of the prebiotic lactulose – an artificial disaccharide – on bulbar neurogenesis in maternally deprived lambs, a sheep model of early-life stress.

Twenty-four female lambs were separated from their mothers 24 hours after parturition and randomly assigned to the Prebiotic group (P, N=12) or the Control group (C, N=12), housed separately. P lambs were fed with lactulose-supplemented (1%) artificial milk, while C lambs with non-supplemented artificial milk. At eleven weeks of age, olfactory neurogenesis was investigated by quantifying the number of neuroblasts (visualized with doublecortin (DCX) immunostaining) in the granular layer of the main olfactory bulb (MOB). DCX-positive cells were counted manually in frontal sections of the left MOB (four per animal) using Mercator software.

The number of DCX-positive cells observed in the granular layer of the left MOB did not significantly differ (unpaired t-test:  $t(71)=1.54$ ,  $P=0.128$ , two-tailed) between P lambs (mean  $\pm$  SEM =  $35.18 \pm 2.17$  cells/mm<sup>2</sup>) and C lambs ( $31.31 \pm 1.45$  cells/mm<sup>2</sup>).

We found no evidence that lactulose supplementation affects olfactory neurogenesis in maternally deprived lambs. However, we are currently investigating whether lactulose modulates hippocampal neurogenesis.