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THALAMO-SEPTAL-HYPOTHALAMIC CIRCUIT INVOLVED IN MATERNAL BEHAVIOURAL CONTROL IN RODENTS

POSTER SESSION 03 - SECTION: MIDBRAIN AND FOREBRAIN FUNCTION IN STRESS AND EMOTION

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Maternal care is a special form of social behaviour regulated by both hormones and neuronal inputs. Our research group previously described a thalamo-hypothalamic pathway containing the maternally induced neuropeptide, parathyroid hormone-2 (PTH2) expressed by neurons of the posterior intralaminar thalamic nucleus (PIL). Additional to the hypothalamic medial preoptic area (MPOA), the central regulator of maternal behaviour, PIL neurons also project to the lateral septum (LS). The LS is known to show pup-induced activation in rodent mothers and to have reciprocal connection with the MPOA. Therefore, we hypothesize that LS participates in the PIL-MPOA circuit controlling maternal care. Here, we demonstrate that LS receives input from maternally-activated PIL neurons and fibres arising from the PIL are PTH2+. Furthermore, we found elevated number of pup-induced activated calbindin LS neurons closely apposed by PTH2-terminals. We also revealed, all calbindin and maternally-activated LS neurons are GABAergic. Synaptic connection of GABAergic LS neurons with PTH2-terminals was confirmed by electron microscopy. We showed that LS GABAergic and calbindin neurons send prominent input to the MPOA. Since MPOA also receives dense PTH2+ projection from PIL neurons, we provided evidence that LS-projecting PIL neurons send axon collaterals to the MPOA by identifying double labelled PIL neurons following injection of different retrograde neuronal tracers into the LS and MPOA simultaneously. We conclude that pup directed information is conveyed to the LS and the MPOA via the PTH2+ input from the PIL. PTH2-innervated calbindin LS neurons may regulate maternal-related neurons of the MPOA via inhibitory signal. Support: NKFIH-4300-1/2017-NKP_17-0002, OTKA K134221, TKP2020-IKA-05

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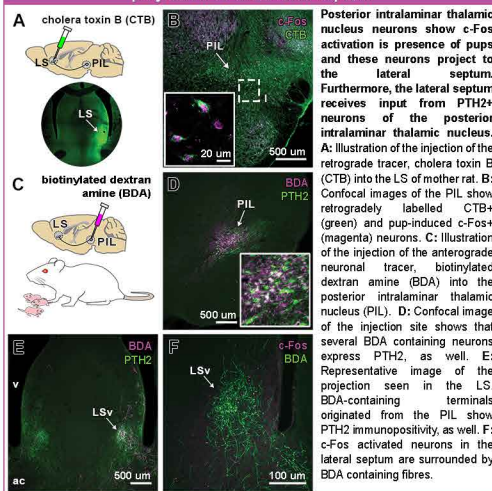
Introduction

Parental care is a special form of social behaviour, which requires the survival of the offspring. The neural network behind maternal behaviour is complex and includes different brain areas. Our research group previously described that neurons in the posterior intralaminar thalamic nucleus (PIL) express an excitatory neuropeptide, parathyroid hormone 2 (PTH2), whose expression is induced in mothers. We also showed that the medial preoptic area (MPOA), a well established, major site to control maternal behaviour, receives pup induced sucking information from the PIL via PTH2+ fibres. MPOA also receives prominent input from the neurons of the lateral septum (LS), which a forebrain area involved in the regulation of social behaviours including maternal care. LS show elevated number of activated neurons in lactating rodents following pup exposure and contains PTH2+ fibres, as well. However, the mechanisms how LS neurons control maternal behaviour are not well understood. Therefore, we hypothesize that the LS takes part in maternal adaptation via its MPOA-projection driven by the PTH2+ pathway originated from the PIL.

To support our hypothesis, we addressed the following specific objectives:

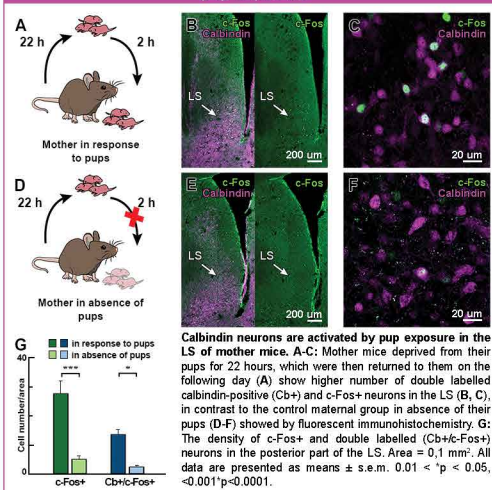
- Identification of the origin of PTH2+ fibres in the LS by anterograde and retrograde tract tracing
- Neurochemical characterization of LS neurons activated by pup-exposure
- Investigation whether PTH2 fibres in the LS represent synaptic input to neurochemically identified LS neurons
- Determination of preoptic projections of neurochemically identified LS neurons
- Comparison of neuronal populations in the PIL projecting to the LS and the MPOA using double retrograde tracing

2. PIL neurons activated following pup-exposure send PTH2+ projection to the lateral septum

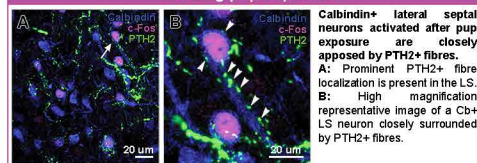


Posterior intralaminar thalamic nucleus neurons show c-Fos activation is presence of pups and these neurons project to the lateral septum. Furthermore, the lateral septum receives input from PTH2+ neurons of the posterior intralaminar thalamic nucleus. **A:** Illustration of the injection of the retrograde tracer, cholera toxin B (CTB) into the LS of mother rat. **B:** Confocal images of the PIL show retrogradely labelled CTB+ (green) and pup-induced c-Fos+ (magenta) neurons. **C:** Illustration of the injection of the anterograde neuronal tracer, biotinylated dextran amine (BDA) into the posterior intralaminar thalamic nucleus (PIL). **D:** Confocal image of the injection site shows that several BDA-containing neurons express PTH2, as well. **E:** Representative image of the projection seen in the LS. BDA-containing terminals originated from the PIL show PTH2 immunopositivity, as well. **F:** c-Fos activated neurons in the lateral septum are surrounded by BDA containing fibres.

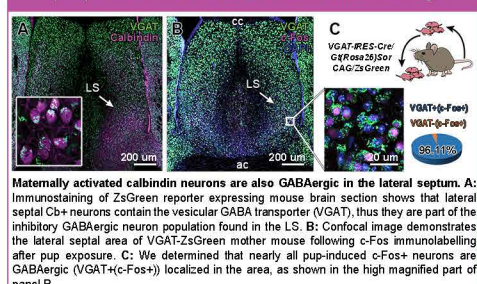
3a) Calbindin neurons in the maternal brain following pup-exposure



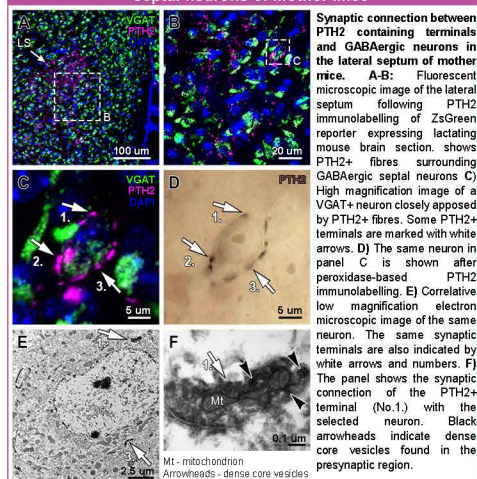
3b) PTH2+ fibres closely appose c-Fos activated LS neurons following pup-exposure



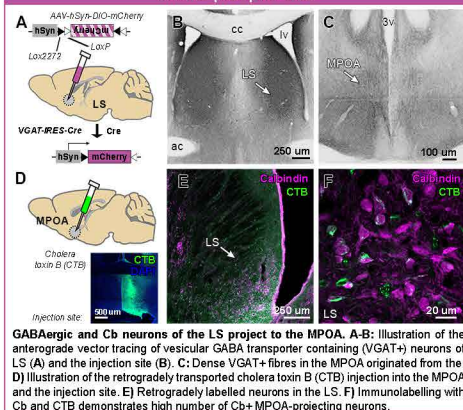
3c) Pup induced activated LS neurons are GABAergic



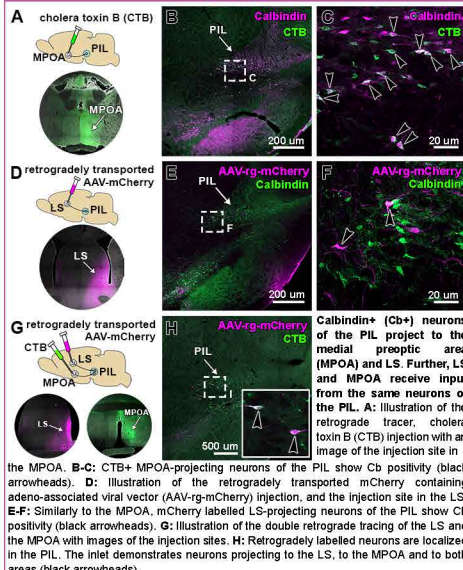
4. PTH2-expressing neurons innervate GABAergic lateral septal neurons of mother mice



5. GABAergic calbindin septal neurons project to the medial preoptic area



6. Calbindin+ neurons of PIL project to the MPOA and the LS of rats

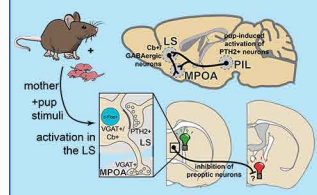


Results

- Significantly higher number of LS neurons are c-Fos+ in rat dams in response to pups, than in control mothers in absence of pups.
- LS shows a significantly increased number of activated calbindin GABAergic neurons in lactating female mice following pup-exposure, which are closely apposed by PTH2+ fibres
- The dense PTH2+ projection in the lateral septum originates from the pup induced c-Fos-activated and Cb+ neurons of the PIL
- We confirmed by correlative light and electron microscopy that VGAT-expressing GABAergic neurons are innervated by PTH2+ terminals in the lateral septum
- GABAergic calbindin lateral septal neurons send prominent projection to the MPOA. Furthermore, Cb+PIL neurons project to the MPOA neurons, as well.
- Same neuron population of PIL can send input to both the LS and MPOA simultaneously.

Conclusion

Activation of LS neurons during pup-exposure may be accomplished via the PTH2 mediated signalling pathway from the PIL. In turn, PIL neurons convey the stimulatory signal of pups to both the lateral septum and the MPOA thereby contributing to their roles in maternal behaviour. Furthermore, pup exposure activated LS cells are GABAergic Cb neurons, which may control maternal behaviour by transferring PTH2 input from the PIL towards the MPOA.



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1. c-Fos activation in the lateral septum of mother rats

