



ABSTRACT BOOK

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RESEARCH ORGANIZATION



P8.16 Calbindin neurons of the lateral septum control maternal behaviour

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The lateral septum (LS) is a forebrain area that has a role in forming prosocial behavioural elements such as maternal care. LS is supposed to have a role in maternal behaviour based on lesion studies, however, the responsible cellular networks are not known yet. Therefore, we aimed to characterize maternally activated septal neurons and their function in maternal regulation. First, we established that all of the pup-induced c-Fos+ septal neurons are inhibitory GABAergic neurons. A population of these GABAergic neurons in the ventral subdivision of the LS (LSv) contain calbindin (Cb+). The number of c-Fos-activated Cb+ neurons was markedly higher in mothers following pup exposure than pup deprivation. We demonstrated by viral based, cell type-specific anterograde tracing that Cb+ LSv neurons send massive projection to the medial preoptic area (MPOA) a centre for regulating maternal behaviour and confirmed this projection by retrograde tracing. To establish how maternal input arrives at the Cb+ LSv neurons, we first established that these neurons contain receptors of the maternally induced neuropeptide, parathyroid hormone 2 (PTH2) using Cb immunolabelling in reporter mice expressing ZsGreen in PTH2 receptor-expressing neurons. These receptors are likely activated by PTH2 released from the PTH2 terminals we also identified around Cb+ neurons in the LSv. Moreover, a synaptic connection was established between PTH2+ fibres and maternally activated inhibitory neurons in the LSv using electron microscopy. These PTH2+ terminals might arrive from the PTH2+ neurons located in the posterior intralaminar thalamic nucleus (PIL), which all show c-Fos-activation in mothers following pup exposure compared to pup-deprived controls. Functional investigation of LS Cb+ neurons in Cb-Cre mice demonstrated that the inhibition of these neurons reduced the time spent with the licking of the pups, but caused no other behavioural effects. Therefore, we conclude that the activation of the inhibitory Cb+ neurons is required for the pup licking behaviour, which may be executed by their projection to the MPOA neurons. Finally, this activation of Cb+ LSv neurons is executed via the excitatory PTH2+ input from maternally activated PIL neurons.

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Introduction

Maternal care is regulated by a complex neural network, which includes the **lateral septum (LS)**. LS has prominent connection with different brain regions involved maternal regulation including the **medial preoptic area (MPOA)**, a well established brain site driving maternal motivation. LS contains an elevated number of activated neurons in lactating rodents following pup exposure. However, the cell types of LS participating in the control of maternal behaviours, and the inputs, which activate LS neurons by pup exposure are unknown. 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. Dense PTH2+ fibre network can be found in the LS, as well.

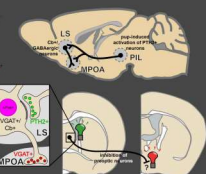
We hypothesize that the LS contains specific cell types taking part in maternal adaptation via their projection to the MPOA driven by the PTH2+ pathway originated from the PIL.

Summary of results

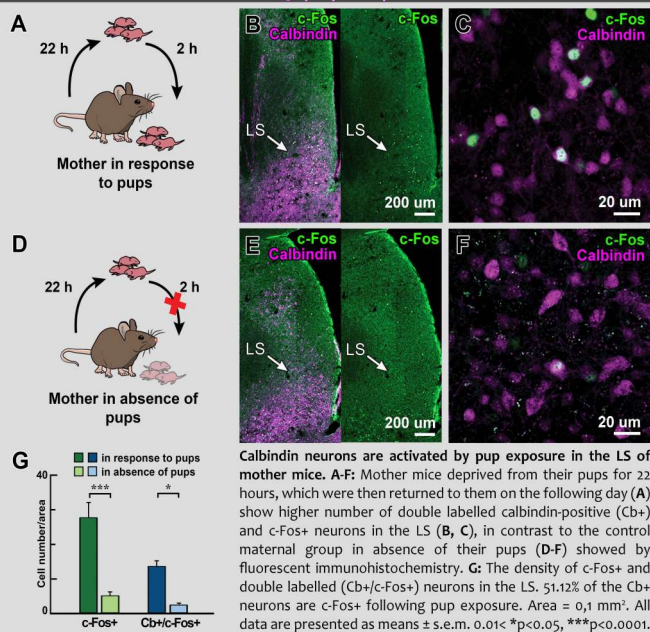
- Inhibitory calbindin neurons of the LS are activated following pup-exposure.
- Calbindin+ LS neurons send prominent projection to the MPOA.
- PTH2R and PTH2+ fibres are located in the same area as pup-induced c-Fos+ septal neurons.
- PTH2+ terminals innervate the inhibitory neurons of LS.
- PTH2+ fibres probably arrive from the pup-induced c-Fos+ neurons of the PIL.
- Inhibition of calbindin+ LS neurons reduced the time spent with licking of the pups in sensitized female mice.

Conclusion

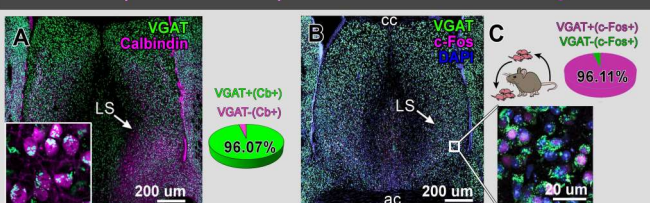
Pup exposure mediated by PTH2+ input activates GABAergic calbindin neurons of lateral septum (LS), which regulate the pup licking behaviour of female mice. This modulation may happen through their projection to the medial preoptic area (MPOA), the major brain region controlling maternal behaviour.



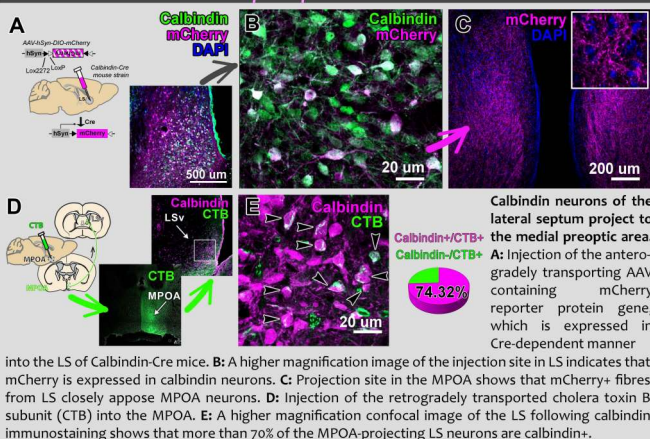
1. Lateral septal calbindin neurons in the maternal brain following pup-exposure



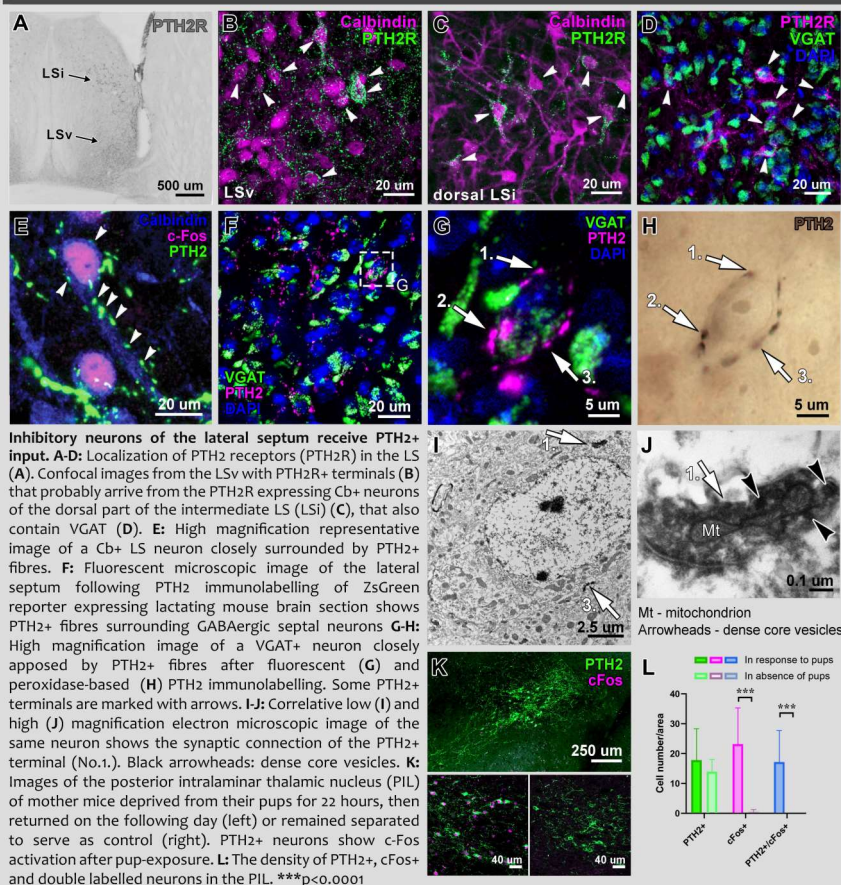
2. Pup activated septal neurons are GABAergic



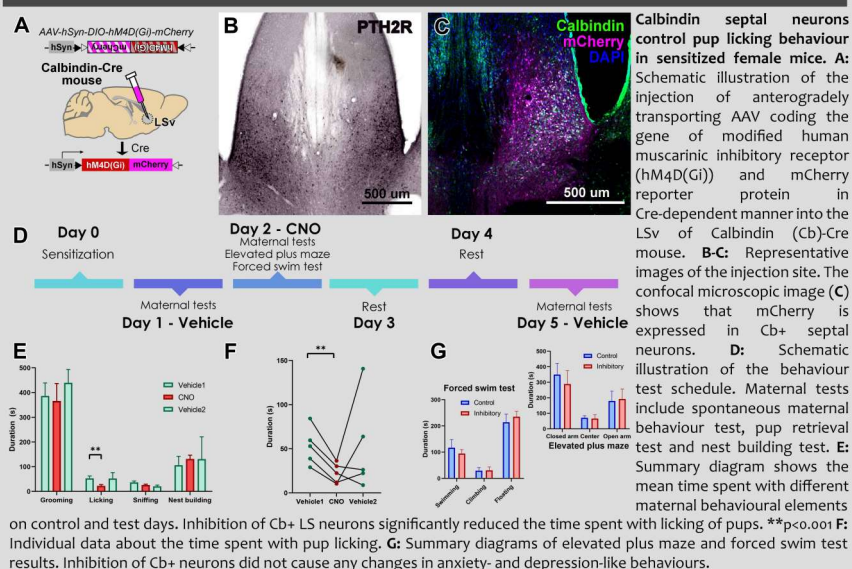
3. Lateral septal calbindin neurons project to the medial preoptic area



4. The localization of PTH2R and PTH2+ fibres in the lateral septum



5. Inhibition of calbindin neurons reduces maternal licking behaviour



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