

**JOINT NEUROSCIENCE MEETING OF THE
HUNGARIAN NEUROSCIENCE SOCIETY (MITT) & THE
AUSTRIAN NEUROSCIENCE ASSOCIATION (ANA)**

2023

**DETAILED PROGRAM
AND
POSTER ABSTRACT
BOOK**

1-3 FEBRUARY, 2023, BUDAPEST

Septal-preoptic connectivity involved in maternal adaptation

Gina Puska, Vivien Szendi, Szilvia Oláh, Máté Egyed, Diána Dimén, Árpád Dobolyi

Gina Puska (Hungarian Academy of Sciences and Eötvös Loránd University, MTA-ELTE Laboratory of Molecular and Systems Neurobiology, Budapest, Hungary), (University of Veterinary Medicine Budapest, Department of Ecology, Budapest, Hungary) Vivien Szendi (Hungarian Academy of Sciences and Eötvös Loránd University, MTA-ELTE Laboratory of Molecular and Systems Neurobiology, Budapest, Hungary) Szilvia Oláh (Hungarian Academy of Sciences and Eötvös Loránd University, MTA-ELTE Laboratory of Molecular and Systems Neurobiology, Budapest, Hungary) Máté Egyed (Hungarian Academy of Sciences and Eötvös Loránd University, MTA-ELTE Laboratory of Molecular and Systems Neurobiology, Budapest, Hungary) Diána Dimén (Hungarian Academy of Sciences and Eötvös Loránd University, MTA-ELTE Laboratory of Molecular and Systems Neurobiology, Budapest, Hungary), (Indiana University, Graduate School of the Department of Psychological and Brain Sciences, Bloomington, United States) Árpád Dobolyi (Hungarian Academy of Sciences and Eötvös Loránd University, MTA-ELTE Laboratory of Molecular and Systems Neurobiology, Budapest, Hungary)

The lateral septum (LS) is a forebrain area involved in the regulation of social behaviors including maternal care. However, the mechanisms how LS neurons control maternal behaviors are not well understood. Therefore, we addressed to characterize maternally activated LS neurons neurochemically and map their distribution pattern in mice. We established that LS neurons activated after pup exposure are GABAergic suggesting the importance of limbic inhibitory system in maternal care. As GABAergic calbindin (Cb) and calretinin cell groups localize in the LS, we determined their relation to pup induction. We showed that many c-Fos-activated neurons are positive for the marker Cb in the ventral part of LS (LSv). The ratio of Cb neurons in c-Fos activated neuron population was significantly higher in the presence of the pups compared with control mothers. We previously showed that LS contains a maternally induced neuropeptide, parathyroid hormone 2 (PTH2) positive fibers in high density. PTH2+ fibers closely apposed activated neurons suggesting synapses that was confirmed by electron microscopy in GABAergic neurons. Moreover, Cb neurons in the LS are also closely surrounded by PTH2+ terminals. As PTH2+ fibers arise from the posterior intralaminar nucleus of the thalamus (PIL), we examined the activation level of this region in the presence and absence of pups. We found that c-Fos expression was induced exclusively in PTH2+ neurons and all these PTH2+ cells were activated in response to pup exposure. PIL neurons are known to send PTH2+ projection to the medial preoptic area (MPOA), too. This phenomenon might be important in the aspect of maternal behavior as MPOA is the central regulatory area of parenting. We showed that the same neurons of PIL project to both LS and MPOA neurons which raises the possibility of simultaneous regulation of neurons in these 2 brain regions by PTH2+ PIL neurons. Based on our results of retrogradely transported tracer technique, we showed that a high number of MPOA-projecting LS neurons are Cb+ suggesting that these neurons may have an impact on maternal adaptation. We confirmed Cb+ projection by performing anterograde tract tracing in Cb-Cre mice too. Moreover, some LS-projecting neurons in the MPOA show synaptic-like vicinity to PTH2 terminals on dendritic process. In conclusion, the data suggest that PIL neurons convey stimulatory signal of pups to both LS and MPOA and the neurons of these areas may interact with each other.

Support: New National Excellence Program for VSz, NKFIH OTKA K134221 and MTA NAP2022-I-4/2022 (NAP 3) for AD.

Septal-preoptic connectivity involved in maternal adaptation

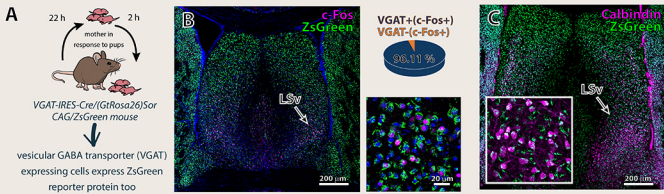
Gina Puska^{1,2}, Vivien Szendi¹, Szilvia Oláh¹,
Máté Egyed¹, Diána Dimén^{1,3}, Árpád Dobolyi¹

1 MTA-ELTE Laboratory of Molecular and Systems Neurobiology Hungarian Academy of Sciences and Eötvös Loránd University Budapest Hungary
2 Department of Ecology University of Veterinary Medicine Budapest Hungary
3 Graduate School of the Department of Psychological and Brain Sciences Indiana University Bloomington

Introduction

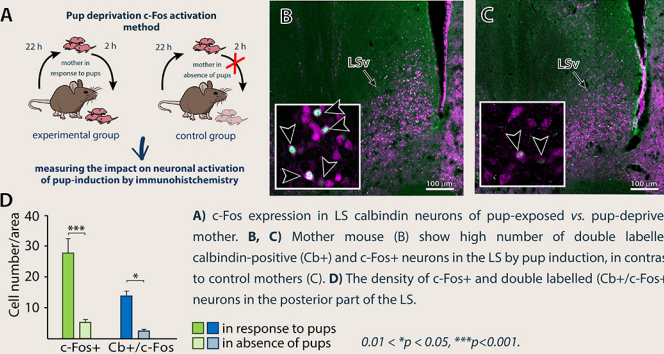
The **lateral septum (LS)** is a forebrain area suggested to be involved in the regulation of maternal care based on showed by previous c-Fos activation methods in lactating rodents. However, it is not known: 1) which LS neurons are activated by pups, and 2) how they control maternal behavior. Our research group has previously described that fibres containing a maternally induced neuropeptide, **parathyroid hormone 2 (PTH2)** localize in the LS. PTH2 expressing neurons are mainly located in the **posterior intralaminar nucleus of the thalamus (PIL)** in the maternal brain. Therefore, we addressed if PIL PTH2+ neurons activate subgroups of LS neurons in mothers. Neurons in the **medial preoptic area (MPOA)**, which is a central regulator of maternal care, receive prominent input from lateral septal neurons. In this study, our second aim was to reveal the interaction between lateral septal and medial preoptic neurons in the aspect of maternal care.

1) Maternally activated neurons are GABAergic in the LS

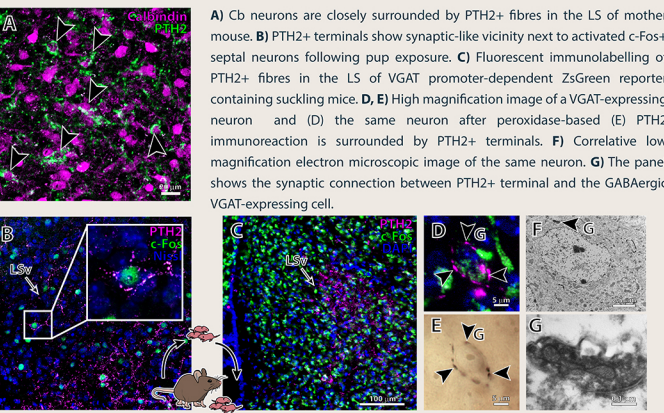


A, B ZsGreen fluorescent reporter expressing mouse brain section shows that a high number of maternally activated neurons localize in the lateral septum (LS) especially in the ventral subdivision (vLS) following pup exposure. Nearly all pup-induced c-Fos+ neurons are GABAergic (VGAT+/c-Fos+). **C** A high number of calbindin (Cb) neurons are present in the same area. They are all GABAergic, suggesting that maternally activated neurons are Cb+.

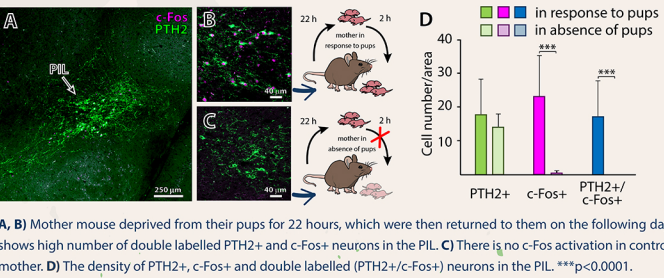
2) Calbindin neurons in the maternal brain following pup exposure



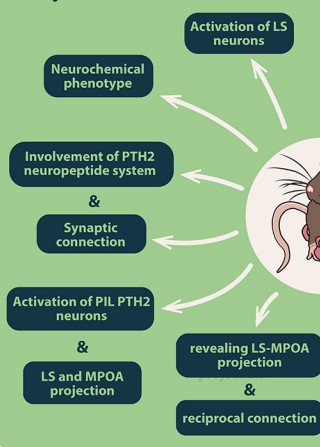
3) PTH2+ terminals in the LS of mothers



4) PTH2-expressing neurons are maternally activated in the PIL



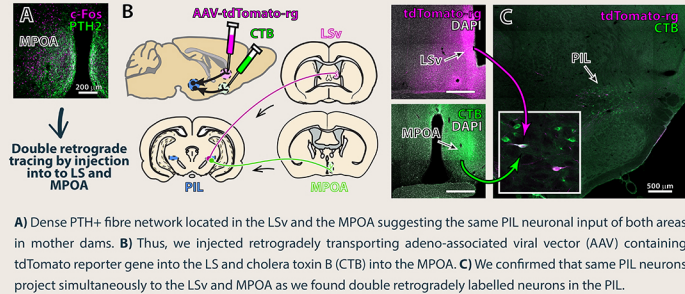
Objectives



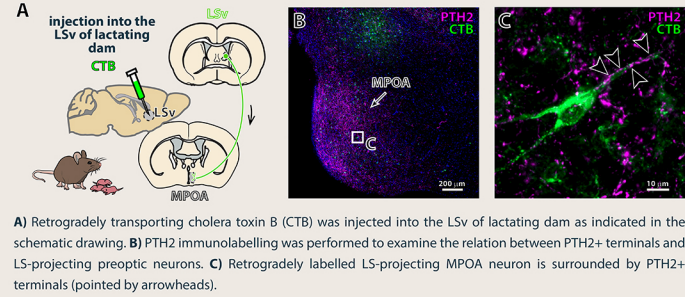
Summary of results

- 1) LS neurons activated in response to pup exposure are all GABAergic.
- 2) The ratio of calbindin neurons in c-Fos activated neuron population was significantly higher in the presence of the pups compared to control mothers.
- 3) PTH2+ fibers innervate GABAergic LSv and probably calbindin neurons.
- 4) In the PIL, c-Fos expression is induced exclusively in PTH2+ neurons. In turn, essentially all PTH2+ neurons were activated by exposure in the PIL.
- 5) Same neurons of PIL project to both LS and MPOA neurons.
- 6) Presumed LS-projecting MPOA neurons are innervated by PTH2+ terminals.
- 7) Calbindin neurons of the LSv project to the MPOA.

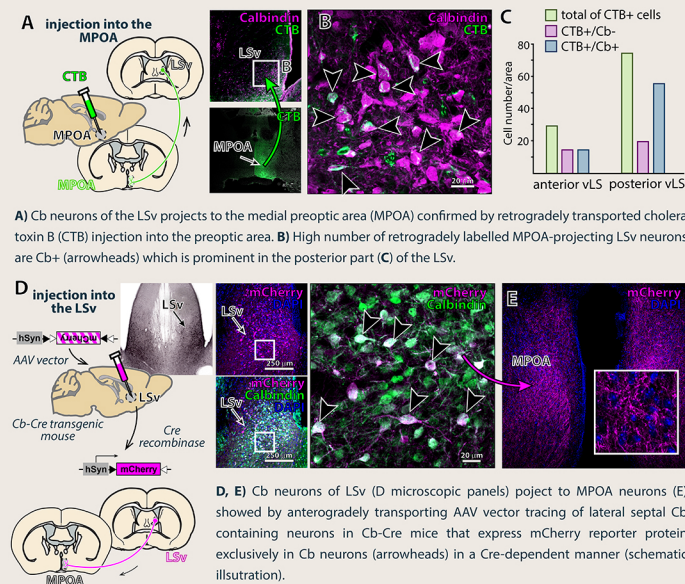
5) PTH2+ terminals in the LS of mothers



6) LS-projecting MPOA neurons and PTH2+ network

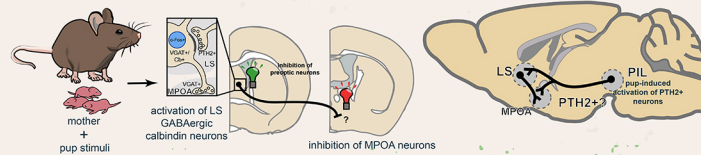


7) Calbindin LS neurons project to the medial preoptic area



Conclusions

Pup exposure activates GABAergic calbindin neurons in the LSv by PTH2+ projections ascending from the PIL, which are collaterals of the PIL neurons projecting to the major brain region controlling maternal behaviours, the medial preoptic area. In turn, the GABAergic calbindin neurons in the LSv also project to the medial preoptic area.



Acknowledgements: We would like to thank **Nikolett Hanák** and **Ágnes Konrád** for their technical assistance.
Supported: NKFIH OTKA K134221 and MTA NAP2022-1-4/2022 (NAP3)