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Thalamic input of the medial preoptic area promotes maternal care in rats

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Mothers receive a set of different sensory cues from the pups, which are then processed by a complex integrative neural circuit. The medial preoptic area (MPOA) as the regulatory center of maternal behavior is a key component of this network by receiving diverse inputs from brain regions involved in sensory processing. Although, preoptic neuronal cell types promoting maternal care have been extensively studied, the specific afferent neural pathways participating in the integration of pup-related cues remain unknown. MPOA receives input from a thalamic region, the posterior intralaminar thalamic nucleus (PIL) which came into focus in recent years. PIL neurons expressing the maternally induced neuropeptide, parathyroid hormone 2 (PTH2), are supposed to transmit suckling stimuli to higher-order brain areas. In light of these data, our objective was to ascertain whether pup-related cues are transmitted from PIL neurons to the MPOA in mother rats. First, we examined the involvement of PIL neurons in the regulation of pup-directed behaviors. Therefore, chemogenetic stimulation of PIL neurons was performed by injecting a virus expressing an excitatory designer receptor into the PIL. Following ligand administration, the time spent with nest building and pup-related behaviors such as licking and grooming of the pups was increased. Furthermore, the latency of pup-retrieval was reduced upon stimulation. In order to examine the pup-induced activation of the PIL-MPOA pathway, we applied retrograde tracer injection into the MPOA and performed c-Fos immunolabelling. It was found that almost all MPOA-projecting PIL neurons are activated following pup exposure. Furthermore, a considerable proportion of these neurons are part of the PTH2-expressing neuronal cluster and were also labelled with calbindin (Cb). We also investigated whether Cb+ PTH2-expressing neurons of the PIL are activated specifically due to the exposure of touch-related pup stimuli. We established that these cells were prominently activated in mothers suckling their pups compared to mothers being separated from their pups. The MPOA is composed of various cell clusters involved in stimuli integration, and our findings demonstrate that one of these receives somatosensory inputs from the pups via Cb+ PTH2-expressing PIL neurons. In conclusion, our data indicate the role of the PIL-MPOA pathway in the formation of the maternal phenotype based on the processing of pup-associated direct contact-related cues.

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THALAMIC INPUT OF THE MEDIAL PREOPTIC AREA PROMOTES MATERNAL CARE IN RATS



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INTRODUCTION

Mothers receive a set of different sensory cues from the pups, which are then processed by a complex integrative neural circuit to promote maternal behavior. The **medial preoptic area (MPOA)** as the regulatory center of maternal behavior is a key component of this network. Although, preoptic neuronal cell types promoting maternal care have been extensively studied, the specific afferent neural pathways participating in the integration of pup-related cues remain unknown. MPOA receives input from a thalamic region, the **posterior intralaminar thalamic nucleus (PIL)** which came into focus in recent years (Yang, Mingyu et al., 2025). PIL neurons expressing the maternally induced neuropeptide, **parathyroid hormone 2 (PTH2)**, are supposed to transmit suckling stimuli to higher-order brain areas. In light of these data, our objective was to ascertain whether pup-related cues are transmitted from PIL neurons to the MPOA in mother rats.

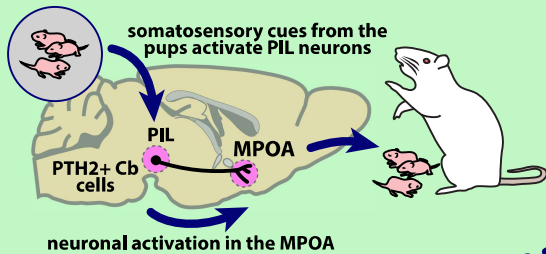
Reference: Mingyu Yang, Dávid Keller, Árpád Dobolyi*, Silvana Valtcheva*. 2025, The lateral thalamus: a bridge between multisensory processing and naturalistic behaviors, *Trends in Neurosciences*, 48; 1; 33-46.

SUMMARY OF THE RESULTS

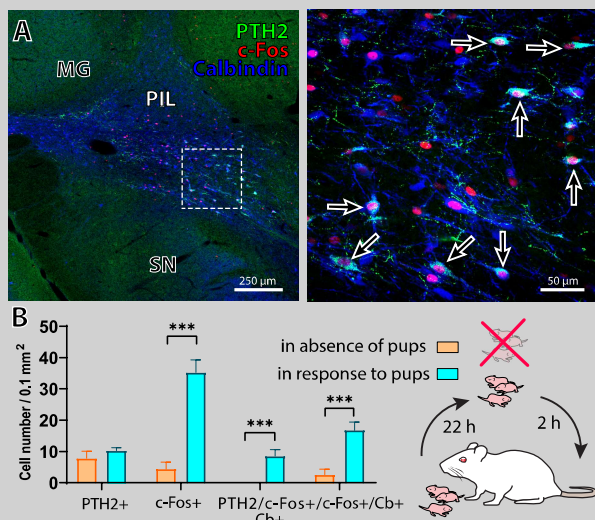
- PTH2-expressing calbindin neurons were activated after exposure to the pups, when the mothers were allowed to engage with their offspring.
- The stimulation of PIL neurons enhanced pup-directed behavior, nest building, pup preference, and pup retrieval
- PTH2-expressing calbindin neurons project to the MPOA and are activated following pup exposure.

CONCLUSION

Posterior thalamic PTH2/calbindin neurons transmit pup contact information to the MPOA, thereby promoting maternal motivation and behavior

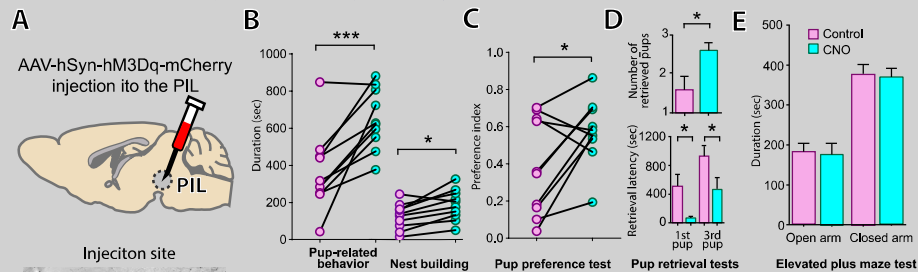


Activation of PIL neurons in mothers



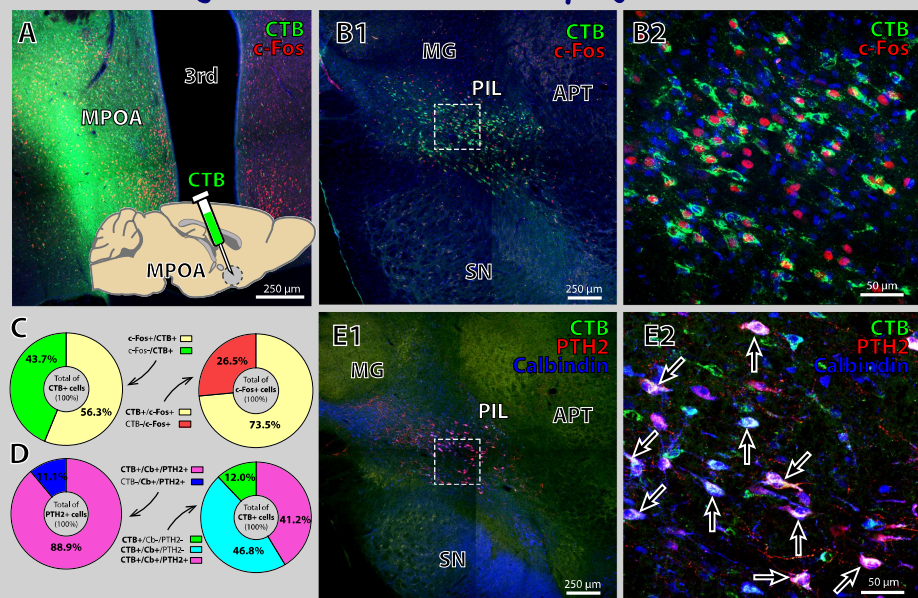
A) Confocal images of a brain section after PTH2/c-Fos/Calbindin triple immunolabelling of a mother rat after pup exposure. A high number of activated PTH2+/Cb+ neurons can be seen indicated by arrows. B) The density of PTH2+ neurons, c-Fos+ neurons, and Cb+ neurons in the PIL (N = 3 animal per group).

Stimulation of PIL neurons affects maternal behavior



A) Experimental design of the chemogenetic manipulation of PIL neurons. The microscopic image demonstrates the injection site of the adeno-associated virus (AAV) expressing excitatory designer receptor. B) The duration of pup-related behavior and nest building was increased after ligand (CNO, clozapine N oxide) administration. C) Pup preference was enhanced due to the activation of PIL neurons. D) Moreover, the latency of pup retrieving was reduced. E) The anxiety-level of the mother rats was not changed based on elevated plus maze test.

Maternally involved PIL neurons project to the MPOA



A) Experimental design of the retrogradely transporting neuronal tract tracer, cholera toxin B subunit (CTB) injection into the MPOA. The confocal image demonstrates the injection site of CTB after pup-induced c-Fos activation. B) MPOA-projecting PIL neurons show activation after pup exposure. C) Percentage of activated CTB+ neurons. D) Percentage of c-Fos+, PTH2+, and Calbindin+ (Cb+) neurons of the MPOA-projecting PIL neurons of one rat. E) The high resolution confocal image demonstrates that a high number of MPOA-projecting PIL neurons are calbindin and PTH2 positive (arrows).

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SZÉCHENYI

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