# POSTERIOR INTRALAMINAR COMPLEX OF THE THALAMUS AFFECTS SOCIAL INTERACTIONS

**PhD thesis**


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Budapest, 2023

## 1. Introduction

Social behavior can be defined as behavior affected by other members of the same species. It can be classified into different categories, including aggressive, mutualistic, cooperative, altruistic and parental. Different social behavior elements have different neuronal and endocrine background. Recent results indicate that two neural circuits are essential in forming the social behavior: the social behavior network and the mesolimbic reward system.

The social behavior network (SBN) includes all the neural components that regulate social behavior. The core nodes of the SBN take part in the regulation of several social behavior elements, they are connected to each other, and they often contain steroid hormone receptors. The SBN includes the following nodes: lateral septum, preoptic area, ventromedial hypothalamus, anterior hypothalamus, the periaqueductal gray, the medial amygdala, and the bed nucleus of the stria terminalis. All of these brain regions have been determined in mammals to participate in regulating reproductive and aggressive behaviors. The mesolimbic reward system is involved in the assessment of the relative importance and implications of an environmental stimulus, which evaluation is essential in forming a suitable behavioral response. A key element of this network is the dopaminergic innervation of the nucleus accumbens originating from the ventral tegmental area.

Rodents are the most used research subjects in many scientific fields. Due to the numerous social behavior studies, it is now also apparent how complex their social life is. It has also been demonstrated that rodents can acquire information on their environment through social transmission. They also use different modalities for social interactions, among them, the social touch is a major component. Although social touch is important in both sexual and nonsexual contexts in humans, too, in rodents, where modes of communication between conspecifics are more limited (note the lack of speech and limited mimicry) the role of social touch is relatively more important as part of the stereotypic behavioral repertoire for social interactions between individuals.

The hypothalamus is a major regulatory center of rodent social behavior. It is also likely to be involved in the control of instinctive behaviors in humans. Social sensory inputs are known to reach the cerebral cortex via the thalamus, however, it is not known how information needed for social behavior arrives at the hypothalamus. Although, it is

possible that information on social context reaches the hypothalamus via the cerebral cortex, it is also conceivable that ascending sensory pathways carrying information on social touch might project directly to the hypothalamus. Within the responsible neuronal circuits, neuropeptides have been implicated in the control of a variety of social behaviors.

Oxytocin, as a reproductive hormone, is secreted from the neurohypophysis to evoke uterus contraction and milk ejection in females during parturition and lactation, respectively. Oxytocin release within the central nervous system has recently gained major attention as a neuromodulator involved in promoting maternal behaviors as well as social behaviors during non-lactating periods. In the rat brain, oxytocin-expressing neurons are located in the paraventricular (PVN) and the supraoptic (SON) nuclei. Magnocellular oxytocin neurons project to the pituitary and secrete oxytocin into the circulation. Although, initially, only parvocellular oxytocin neurons were thought to project into brain and spinal cord regions, axon collaterals of magnocellular oxytocin neurons have recently been shown to also reach a number of brain areas. The targets of oxytocin neurons are often limbic areas involved in the social brain network. Despite growing knowledge on the effects of oxytocin on social interactions, and the potential use of the oxytocin system as a drug target, e.g. in autism, eating and addictive disorders, surprisingly little information is available on the neuronal inputs leading to the activation of oxytocin neurons. Studies using electrophysiological and lesion techniques identified the mesencephalic lateral tegmentum, and more rostrally, the ventroposterior thalamic - peripeduncular area as parts of the milk ejection reflex arch. However, the relay neurons in the milk ejection reflex pathway remained to be elucidated. Furthermore, it has not been established how information on social interactions reaches the oxytocin neurons.

The posterior intralaminar complex of the thalamus (PIL) is a triangular shape area in the thalamus, located ventromedial to the medical geniculate body and dorsal to the substantia nigra. The area can be easily distinguished from surrounding brain regions with the examination of the distribution of calcium binding proteins in and around the PIL. Parvalbumin (PV) immunolabeling was used to partially define the region. The ventral and the dorsomedial borders of the PIL can be identified by PV-immunoreactive (PV-ir) cell bodies in the substantia nigra and the anterior pretectal area, respectively. In contrast, the lateral and dorsal borders of the PIL made up of the peripeduncular area and the triangular subdivision of the posterior thalamic nucleus, cannot be differenciated

using PV immunohistochemistry as they contain a low density of PV-ir cell bodies and fibers, as does the PIL. PTH2-immunoreactive (PTH2-ir) neurons, which are evenly distributed within the PIL, differentiate it from the peripeduncular area and the triangular subdivision of the posterior thalamic nucleus that do not contain PTH2-ir cell bodies.

The distribution of calbindin (CB) immunoreactivity is in sharp contrast to that of PV immunoreactivity in and around the PIL. The PIL contains a high density of calbindin-immunoreactive (CB-ir) cell bodies. Other brain regions adjacent to the PIL contain only very low density of CB-ir cell bodies.

The parathyroid hormone 2 receptor (PTH2R) was discovered on the basis of its sequence similarity to other class B G-protein coupled receptors and was named PTH2R because of its significant sequence similarity to the known parathyroid hormone receptor, which is now referred to as PTH1R; and because the human PTH2R is activated by parathyroid hormone (PTH). Subsequently, an endogenous ligand of the receptor was identified following its purification from bovine hypothalamus. The new peptide was termed tuberoinfundibular peptide of 39 residues (TIP39) that time. The peptide is now categorized as parathyroid hormone 2 (PTH2). Despite its name, however, it is likely not a hormone as its presence in the blood has not been demonstrated. Rather, it is expressed mainly in the brain and has neuromodulatory functions.

PTH2 was recently demonstrated to sense the presence of conspecifics in zebrafish via mechanoreceptors in the lateral line organ. The level of PTH2 increased after the social exposure in previously isolated fish and decreased after isolation is socially reared fish. They also demonstrated that the sensory modality that controls the expression of PTH2 was not visual in origin but was mechanical, induced by the movements of neighboring fish. Based on these data, ***we hypothesize that the PIL gives neuronal input to the oxytocin secreting cells and has a potential role in the control of social behavior.***

## 2. Objectives

### A, Investigation of the connection of the PIL with the social brain network

1. Description of the efferent projections of the PIL using adeno-associated viral tract tracing.

2. Injection of cholera toxin b subunit (CTB) retrograde tracer into the PIL to reveal the sources of information that activate these neurons. CTB-immunoreactive cells are examined in the spinal cord, as well as in lower and higher brain regions.

### B, Functional evidence of the role of the PIL in the control of social behavior

1. Assessment the c-Fos activation in the PIL following social interaction of females, in comparison with isolated control animals. Neurochemical identification of the c-Fos activated neurons is also addressed.

2. Demonstration of the functional evidence of the role of the PIL in social interactions by means of stimulation and inhibition of its neurons using viral gene transfer and chemogenetics. Freely moving social behavior test, as well as social interaction test without direct contact. Test of locomotion is also performed as behavioral control.

3. Examination of the effect of chemogenetic-based manipulation of PIL neurons tagged by previous social contact experience. A Tet-Om system is used to express stimulatory and inhibitory receptors into c-Fos activated neurons.

### C, Role of the PTH2-expressing neurons of the PIL during social interactions

1. To establish the activation of PTH2 in the control of social behavior, the expression level of PTH2 mRNA in the PIL neurons is compared between animals kept in social environment or chronically isolated using quantitative real-time PCR.

2. The role of PTH2 in social interactions is addressed in experiments investigating the effect of antagonizing PTH2 receptor on the social behavior of female rats. For that purpose, a PTH2 receptor antagonist is injected into the lateral ventricle using osmotic minipumps.

3. To address where PTH2 may exert its actions on social behavior, we describe the distribution of PTH2 fibers in relation to the social neuropeptide oxytocin.

4. The origin of PTH2 fibers in the PVN is determined by injection of the retrograde tracer CTB into the PVN. The type of retrogradely labeled PIL neurons is also evaluated.

## 3. Methods

The Workplace Animal Welfare Committee of the National Scientific Ethical Committee on Animal Experimentation at Semmelweis and Eötvös Loránd Universities specifically approved this study (PE/EA/926-7/2021 and PE/EA/568-7/2020, respectively).

The retrograde tracer CTB was targeted to the PVN, and to the PIL in lactating mother rats. The relation of the injection site to the position of PTH2 immunoreactivity was verified by double labeling. Some of the misplaced injections were used as controls.

Female rat littermates kept together were used in the social c-Fos study. The two rats were isolated for 22 h to reduce basal c-Fos activation. Then, the rats were reunited again in a cage. Control females continued to be kept isolated. All animals were sacrificed 24 h after the beginning of isolation, i.e. 2 h after reunion of the socially interacting group.

rAAV-$\mathbf{P}_{hSYN}$-hM3D(Gq)-mCherry; rAAV-$\mathbf{P}_{hSYN}$-hM4D(Gi)-mCherry or rAAV-$\mathbf{P}_{hSYN}$-mCherry was injected to the PIL. For injections of the vGATE viral cocktail into the PIL, the following viruses were used: 1. rAAV-$(tetO)_7$-$\mathbf{P}_{fos}$-rtTA; 2. rAAV-$\mathbf{P}_{tet}$bi-Cre/YC3.60; 3. rAAV-$\mathbf{P}_{hSYN}$-DIO-hM3D(Gq)-mCherry or rAAV-$\mathbf{P}_{hSYN}$-DIO-hM4D(Gi)-mCherry or rAAV-$\mathbf{P}_{hSYN}$-DIO-mCherry. After two weeks of recovery, the animals were treated with i.p. doxycycline hyclate injection, then, the following day, they were reunited with one of their cagemates for 2 hours for expression of DREADD in neurons that are c-Fos-positive in the PIL in response to social interaction.

In case of the viral vector-based chemogenetics, 1.5 h before the behavioral experiments, the intraperitoneal administration of CNO or vehicle. On the first day of the experimental session, we used control vehicle. One day later, CNO was administered i.p. This was followed by another control injection three days later.

For the direct and sustained infusion of PTH2R antagonist, HYWH-TIP39 into the lateral ventricle, we used Alzet® Osmotic Minipump, Durect™ combined with Alzet® Brain Infusion Kit 2, Durect™ with two spacers attached.

On the experimental day, the animals were placed in the open field arena where the subject and the stimulus rat could freely interact with each other and 10 minutes of footage was recorded. The duration of the different types of performed behaviors were measured by using Solomon Coder software.

For qRT-PCR of PTH2 in the PIL, brains were dissected from female adult rats kept in social environment and 10 female adults isolated for two weeks prior to dissection.

## 4. Results

### Efferent projections of the PIL

To determine neuronal connections of PIL neurons, rAAV-**P**$_{hSYN}$-hM3D(Gq)-mCherry virus was injected into the PIL of female rats. The infected cells withdrew the virus and it was transported anterogradely. Labeled axons were found in a number of socially-relevant brain regions, such as the infralimbic cortex (ILC), lateral septum (LS), medial preoptic area (MPOA; including the medial preoptic nucleus (MPN) and the medial preoptic area (MPA)), ventral bed nucleus of stria terminalis (vBNST), paraventricular hypothalamic nucleus (PVN), amygdala (A), dorsomedial hypothalamic nucleus (DMH) and periaqueductal central grey (PAG). Following control injections of the virus into the adjacent substantia nigra the labeled fibers were present only in the caudate-putamen, and not in the target areas of the PIL.

### Afferent projections of the PIL

We also investigated the afferent connections of the PIL. We injected the retrograde tracer cholera toxin b subunit (CTB) into the PIL to identify the neurons that project to it and used injections into adjacent regions for comparison. Injections that did not overlap the PIL resulted in labeling patterns markedly different from those following PIL injections and generally lacked labeling in areas that were labeled by PIL injections. The majority of cells projecting to the PIL were ipsilateral to the injection side except for the gracile and cuneate nuclei and the spinal cord, where there was contralateral dominance.

*Inputs from lower brain regions and the spinal cord*

The spinal cord contained CTB labeled neurons contralateral to the injection site. These neurons were distributed in Rexed laminae IV-VII throughout the thoracic and lumbar segments that were sectioned. The cells were typically located in laminae IV-V in thoracic segments and laminae VI-VII in lumbar segments. We rarely found more than one labeled cell in a coronal section; on average, every 4th coronal spinal cord section contained a labeled cell. The labeled cells usually had oval perikarya with multiple dendrites.

In the medulla oblongata, the gracile and cuneate nuclei had the highest density of CTB-containing cells. The spinal trigeminal nucleus, particularly the deep layers of its ventral portion, also contained a significant number of labeled cells. In these nuclei, the CTB-labeled neurons were located contralateral to the injection site. Only a few regions

in the upper brainstem contained any CTB-positive neurons. The highest number of labeled cells was in the external cortex of the inferior colliculus while the lateral parabrachial nucleus, the periaqueductal gray and the deep layers of the superior colliculus contained a low number.

*Inputs from higher brain regions*

Within the cerebral cortex, the auditory areas contained a considerable number of retrogradely labeled neurons. The insular cortex and the medial prefrontal cortex contained a few CTB-positive neurons, with the highest density of labeled cells in the infralimbic cortex. Other cortical areas were devoid of CTB signal. Retrograde labeling was also absent from most other forebrain structures. Within the diencephalon, the largest number of labeled cells was within the ventromedial hypothalamic nucleus, particularly in its ventrolateral subdivision. A considerable number of CTB neurons were also located in the lateral preoptic area, and the zona incerta.

**Activation of the PIL neurons in response to social interaction between female rats**

As the next step, we examined the c-Fos activation of PIL neurons following social interactions. Female littermates grown up together were separated for 22 h to reduce basal c-Fos activity. When females were reunited for 2 h, they engaged in social interactions. These behaviors were associated with a significantly elevated number of c-Fos immunoreactive (c-Fos-ir) neurons in the PIL as compared to rats that were kept isolated. C-Fos-ir neurons appeared evenly distributed within the PIL. Their distribution corresponded with that of the calbindin-ir neurons. In fact, the majority (86%) of the c-Fos-ir neurons contained calbindin. The number of Fos-ir neurons in the PIL section with the largest number of labeled cells was 169 ± 14 after social interaction with a familiar female while there were only 41 ± 8 in the isolated group, which represents a highly significant increase. The activation of cells in the PIL was specific as adjacent structures, did not show an increase in the number of c-Fos-ir neurons.

**Behavioral effects of chemogenetically manipulated PIL neurons**

To investigate whether PIL manipulation affects social behaviors, we injected excitatory (recombinant adeno-associated virus (rAAV)-**P**$_{hSYN}$-hM3D(Gq)-mCherry), inhibitory (pAAV-**P**$_{hSYN}$-hM4D(Gi)-mCherry) designer receptor exclusively activated by designer

drug (DREADD) expressing or control viruses (rAAV-$\mathbf{P}_{hSYN}$-mCherry) into the PIL of female rats. The rats, in which over 80% of the virally infected cells were only included in the behavioral analysis. The animals were subsequently housed individually for two weeks, and then reunited for 1 week prior to injection of clozapine-N-oxide (CNO), the agonist of the DREADD. Almost all (90.4 ± 3.4%) activated cells contained mCherry and almost all (88.9 ± 3.0%) mCherry-positive neurons in the PIL showed c-Fos-positivity 1.5 hours after CNO administration, which validates the effectiveness of our chemogenetic stimulation.

Next, we investigated several distinct social behavioral elements during a 10 min test period. Duration of social grooming significantly increased upon the chemogenetic stimulation as compared to previous day but also as compared to vehicle injection on the following day. In turn, inhibition of the PIL neurons reduced grooming as compared to the control days. In the absence of a DREADD, the viral infection and the CNO administration did not affect social grooming. Note that the stimulation and the inhibition of PIL neurons has the opposite effect of social grooming while other behavioral elements were not affected by the manipulation or changed the same direction by the different treatments (non-anogenital sniffing).

We also performed an experiment in which direct contact between the animals was prevented by separating them by a bar wall which still allowed them to smell, hear and see each other. Chemogenetic activation of the PIL had no effect on the duration of social interaction under these conditions, highlighting the importance of direct contact as the effect of induced activation of the PIL.

**Chemogenetic investigation of socially tagged PIL neurons**

To selectively manipulate PIL neurons activated by previous social exposure, we used the **v**irus-delivered **G**enetic **A**ctivity-induced **T**agging of cell **E**nsembles (vGATE) method. Excitatory, inhibitory and control viral cocktails (rAAV-$(tetO)_7$-$\mathbf{P}_{fos}$-rtTA; rAAV-$\mathbf{P}_{tet}$bi-Cre/YC3.60; rAAV-$\mathbf{P}_{hSYN}$-DIO-hM3D(Gq)-mCherry/ rAAV-$\mathbf{P}_{hSYN}$-DIO-hM4D(Gi)-mCherry/pAAV-$\mathbf{P}_{hSYN}$-DIO-mCherry) were injected into the PIL of female rats. In the vGATE system, a c-fos promoter ($\mathbf{P}_{fos}$) fragment drives the expression of the reverse tetracycline sensitive (tet) transactivator (rtTA). Following the recovery of the animals, a single intraperitoneal doxycycline administration launched the autoregulatory

expression loop of $(tetO)_7$-rtTA, thus opening the labeling period. The following day, the subjects were reunited with a cagemate in their home cage for 2 hours, which resulted in the expression of the DREADD in social contact experienced vGATE-tagged neurons only (encoded in the third virus: rAAV-$\mathbf{P}_{hSYN}$-DIO-hM3D(Gq)-mCherry, rAAV-$\mathbf{P}_{hSYN}$-DIO-hM4D(Gi)-mCherry or rAAV-$\mathbf{P}_{hSYN}$-DIO-mCherry). Social behavior experiments were conducted 10 days later and then the brains were processed for histological analysis.

Labeling of calcium-binding proteins revealed that the PIL region infected with the vGATE viruses was surrounded by parvalbumin-positive cells, and that the vast majority of the calbindin-positive cells were vGATE labeled (90.6%; n =3). To validate the applied vGATE method, we performed c-Fos immunolabeling after direct social exposure or isolation. 2.4-times more cells were labeled for c-Fos after social exposure ($32.2 \pm 4.0$; $n = 3$) than after isolation ($13.4 \pm 4.3$; $n = 2$), which is a significant difference. $54.0\% \pm 5.5\%$ of the mCherry cells were double labeled with c-Fos after social interaction compared with $21.5\% \pm 6.7\%$ after isolation.

During the direct contact social behavior test, where the animals could freely interact with each other, the duration of social grooming significantly increased following the stimulation of PIL vGATE-tagged neurons, and in turn, the duration of social grooming significantly decreased following the inhibition of PIL vGATE-tagged neurons. Furthermore, no behavioral changes were found in the group injected with the control virus. Notably, only direct physical contact elicited an increase in social interactions time after chemogenetic manipulation of vGATE-tagged PIL neurons.

We also performed an open-field test with the CNO injected animals to measure their locomotor activity. The total distance covered by the animals was not affected by driving the activity of PIL neurons suggesting that the altered social behaviors were not a consequence of altered locomotor drive.

Social behaviors initiated by the experimental and opponent animals were separately examined. Manipulation of socially tagged PIL neurons by the injection of CNO changed the behavior initiated by experimental animals. In contrast, the social interactions initiated by the other animal were not affected.

**Role of PTH2-expressing PIL neurons in the control of social behavior**

Our further aim was to investigate the role of PTH2 in the control of social behavior.

Following the microdissection of PIL, we compared the expression of PTH2 mRNA using quantitative real-time PCR. We found that the expression of PIL PTH2 mRNA was 2.4-times higher in animals kept in a social environment (together with conspecifics in their home cage) compared to control animals socially isolated for two weeks.

We also performed an experiment infusing PTH2R antagonist into the lateral ventricle of female rats via osmotic minipumps. The results demonstrate an important role of PTH2 in the control of social grooming because this behavioral element was specifically reduced in the experimental group of the animals, which received the PTH2R antagonist, compared with the artificial cerebrospinal fluid infused control group.

**Close apposition of oxytocin neurons by PTH2-containing axon terminals**

Within the anterior hypothalamus, the PVN, its anterior subdivision, the anterior commissural nucleus (ACN), and the SON receive a dense innervation by PTH2 containing fibers. In these nuclei, the distribution of PTH2 fibers overlapped with the distribution of oxytocin neurons. We also found that the majority of oxytocin neurons were closely apposed by PTH2-containing varicosities. The average number of close apposition on the soma and proxymal dendrites of oxytocin neurons was $2.28 \pm 0.38$ in the parvocellular paraventricular, $1.90 \pm 0.39$ in magnocellular paraventricular, and $0.42 \pm 0.20$ in supraoptic oxytocin neurons. We did not observe a clustering of the oxytocin neurons that were closely apposed by PTH2-containing varicosities.

**Retrograde labeling in the PIL following tracer injections into the PVN**

To identify the source of its PTH2 innervation we injected the retrograde tracer CTB into the PVN. The pattern of retrogradely labeled cells was similar for these injections including a particularly high number of CTB-immunoreactive (CTB-ir) neurons in the ipsilateral lateral septum, the bed nucleus of the stria terminalis, several hypothalamic regions, the supramamillary nucleus, some thalamic regions, and the parabrachial nuclei. In addition, all these injections resulted in a large number of labeled neurons in the PIL. There was a predominantly ipsilateral labeling of cells that were distributed uniformly throughout the PIL but there were no labeled cells in adjacent brain regions. Double-labeling showed that 45% of the CTB labeled neurons in the PIL contained PTH2 immunoreactivity. In turn, the PVN-projecting PIL neurons contained calbindin.

## 5. Conclusions

1. The PIL neurons project to different parts of the social brain network including the paraventricular nucleus of the hypothalamus.

2.. PIL neurons received ascending input from the spinal cord and inferior colliculus suggesting multimodal, e.g. somatosensory and auditory inputs.

3. PIL contained a high number of activated neurons in response to social encounter with an adult. The PIL neurons activated by social interaction contain calbindin.

4. Chemogenetic stimulation increased the activity of the PIL neurons expressing stimulatory receptors. Stimulation of PIL neurons evoked social grooming between conspecific animals.

5. Chemogenetic inhibition reduced social grooming behavior of female rats while control virus injected animals did not change their grooming behavior.

6. Stimulation and inhibition of PIL neurons, which were activated during previous social encounter, increased and decreased social grooming of the animals, respectively, without affecting their locomotor activity.

7. PTH2 is induced in the PIL region of thalamus in response to social interaction.

8. Antagonizing PTH2 receptor selectively inhibited social grooming.

9. Oxytocin neurons were closely apposed by an average of 2.0 and 0.4 PTH2 terminals in the PVN and the supraoptic nucleus, respectively.

10. Retrograde tracing identified PVN-projecting neurons in the PIL, many of which may be PTH2 neurons.

## 6. Summary

We discovered a novel neuronal pathway from the posterior intralaminar complex of the thalamus (PIL) to the paraventricular hypothalamic nucleus (PVN) and showed that the PIL neurons are involved in the control of social grooming. We provided evidence that the PIL contains relay neurons that convey stimuli from social partner via the spinal cord to oxytocin neurons of the PVN. We found that neurons in the PIL were activated by physical contact between female rats. In turn, chemogenetic stimulation and inhibition of PIL neurons increased and decreased social grooming behavior, respectively. Activity-dependent tagging of PIL neurons was performed in rats experiencing physical social contacts. Chemogenetic manipulation of these neurons also affected social grooming between familiar rats without altering locomotor activity. Neurons projecting from the PIL to the PVN express the neuropeptide parathyroid hormone 2 (PTH2) and central infusion of its receptor antagonist diminished social grooming. We propose that the discovered neuronal pathway facilitates physical contacts in mammals. Since the similarity of the PTH2-PTH2 receptor system between human and rodent has been demonstrated, the results may be relevant to human social interactions, too.

## 7. Magyar nyelvű összefoglalás (Summary in Hungarian)

Sikerült felfedeznünk egy új, a talamusz posterior intralamináris komplexumából (PIL) a hipotalamusz paraventricularis magjába (PVN) vetülő neuronális útvonalat, és megmutattuk, hogy a PIL neuronjai részt vesznek a direkt kontaktussal járó társas érintkezés szabályozásában. Bemutattuk, hogy a PIL átkapcsoló neuronjai aktiválódnak társas interakciók hatására, mely információt továbbíthatják a PVN oxitocin neuronjai felé. Megállapítottuk a PIL neuronjainak projekciós célterületeit, és hogy a PIL neuronjai aktiválódnak nőstény patkányok közötti fizikai kontaktus hatására. A PIL neuronok kemogenetikai stimulálása serkentette, míg gátlása csökkentette az egymás tisztogatásával, fizikai kontaktussal töltött időt. A PIL neuronok aktivitástól függő jelölését olyan patkányokon végeztük, melyekben mesterséges receptor csak olyan sejtekben fejeztünk ki, melyek korábban szociális interakció során aktiválódtak. Ezen neuronok kemogenetikai manipulálása szintén hasonló hatással volt az ismerős patkányok közötti direkt kontaktussal járó társas érintkezés idejére. A PIL-ből a PVN-be vetülő neuronok a parathormon 2-es neuropeptidet (PTH2) fejezik ki, és ezen neuropeptid receptorának antagonistájának agykamrai infúziója csökkentette a társas tisztálkodást. Eredményeink alapján feltételezhetjük, hogy a felfedezett neuronális útvonal serkenti az emlősök fizikai érintkezését. Mivel korábban már leírásra került a humán és rágcsáló PTH2-PTH2 receptor rendszere közötti hasonlóság, az eredmények relevánsak lehetnek az emberi társas interakciók szempontjából is.

## 8. Bibliography of the candidate's publications

### Publications related to this dissertation


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**9. Acknowledgements**

I would like to express my special thanks of gratitude to my supervisor, Prof. Árpád Dobolyi, for the patient guidance, encouragement and advice he has provided throughout my time as his student. I have been extremely fortunate to have a supervisor who cared so much about my work and personal development, and who responded to my questions and queries so promptly. I am pleased that I could learn how to be a good researcher from him.

I would like to also extend my gratitude to all the members of the Laboratory of Neuromorphology, whose continuous support helped me through my doctoral years. I am grateful to Melinda Vitéz-Csevenák, with whom I started my first research project, to Éva Renner for her daily soul-stirring advice, Fanni Dóra to be my associate during the doctoral years and Tamás Láng and Luca Darai for their assistance with my projects. This thesis would have been not possible without the technical support of Viktória Dellaszéga-Lábas, Nikolett Hanák and Erzsébet Horváthné Oszwald. I am thankful for their thorough work and I am feeling lucky that I was able to learn the technical skills from them. I also appreciate the guidance of Magdolna Toronyay-Kasztner, especially in scientometrics. I cannot thank enough Szilvia Deák and Zoltán Gróti for their assistance with the animals. Altogether, I am delighted for working together with these people and for sharing so many memories.

I would also like to thank András Lékó, Gina Puska and János Barna for their advice and help during my doctoral years. I am also grateful for Vivien Csikós, Szilvia Oláh and Diána Dimén for their support and for our stimulating conversations which guided me through difficult times. I would like to also thank Prof. Miklós Palkovits for all his insights into my project and advice on my personal development. I also appreciate our collaborators from the University of Heidelberg, especially Prof. Valery Grienvich. I am obliged to Prof. Alán Alpár and all members of the Department of Anatomy, Histology and Embryology for their help.

I would also like to give special thanks to my family and my friends as a whole for their continuous support and understanding my devotion to my research and to writing my project.

**Funding**

Support was provided by Hungarian National Research, Development and Innovation Office OTKA K134221, NKFIH-4300-1/2017-NKP_17-00002 and Excellence Program of the Semmelweis University for AD; Gedeon Richter Plc. Centenary Foundation (Gyömrői út 19-21. Budapest, 1103), Excellence Program of the Semmelweis University, New National Excellence Program of the Ministry of Innovation and Technology and Doctoral Student Scholarship Program of the Co-operative Doctoral Program of the Ministry of Innovation and Technology financed from the National Research and EFOP-3.6.3-VEKOP-16-2017-00009 for DK.