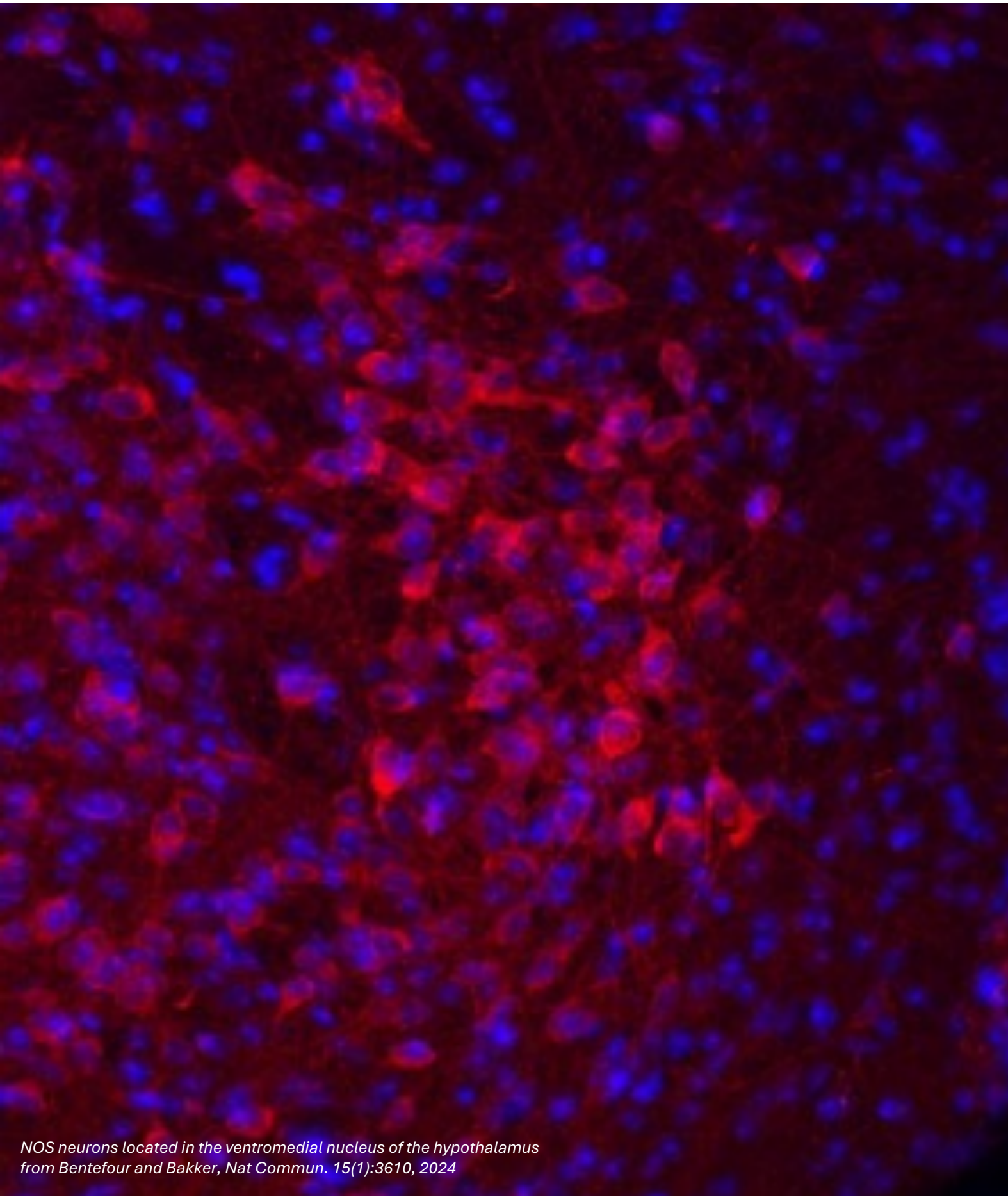
Société de Neuroendocrinologie Bulletin 2025



NOS neurons located in the ventromedial nucleus of the hypothalamus from Bentefour and Bakker, Nat Commun. 15(1):3610, 2024

Sommaire/Content

Save the Dates!

Colloque de Lausanne du 7 au 10 octobre 2025 (https://wp.unil.ch/sne2025lausanne/)

ICN2026 Nagoya (Japon) du 16 au 29 juillet 2026 (https://www.congre.co.jp/icn2026/)

Le mot du Président

Sébastien Bouret

Chers collègues et amis,

Alors que nous entamons une nouvelle année, c'est avec une immense joie et une profonde gratitude que je m'adresse pour la première fois à vous en tant que président de la Société de Neuroendocrinologie. C'est un réel honneur de prendre ces fonctions dans cette belle société que j'ai eu la chance de rejoindre dès le début de ma thèse.

L'année écoulée a été riche en accomplissements remarquables. En 2024, notre société comptait 167 membres actifs dont 80 jeunes chercheurs, un niveau d'engagement au plus haut depuis de nombreuses années. Le dynamisme de notre société s'est également témoigné lors de notre colloque annuel qui s'est tenu à Nice en septembre dernier. Ce colloque, Franco-Canadien, a réuni 152 congressistes venus de neuf pays (France, Canada, Belgique, Suisse, États-Unis, Angleterre, Allemagne, Espagne, et Norvège). Je tiens à ce sujet à vivement remercier Carole Rovère et Alexandre Caron d'avoir organisé un congrès qui restera gravé dans nos mémoires tant la qualité scientifique des présentations (que ce soit lors des symposia mais également les présentations orales de nos jeunes chercheurs) que le lieu et les activités sociales étaient exceptionnelles.

L'année 2024 a également été une excellente année pour nos laboratoires comme en témoigne le SNE Impacts qui regroupe les publications marquantes. Nous pouvons être fiers de nos étudiants, postdocs et chercheurs qui ont, de nouveau, publié de nombreux articles à la pointe non seulement de la neuroendocrinologie à l'échelle européenne et mondiale mais plus largement des neurosciences et de l'endocrinologie, deux disciplines avec lesquelles nous sommes très proches.

L'année 2025 débute sous le signe du changement pour notre conseil scientifique avec un nouveau bureau composé de Sakina Mhaouty-Kodja qui devient vice-présidente, Carole Rovère secrétaire, Virginie Tolle vice-secrétaire, Laurent Givalois trésorier, et Alexandre Caron vice-trésorier. Je souhaite remercier Youssef Anouar, Hervé Tostivint, et Ariane Sharif qui quittent leur fonction de président, secrétaire et trésorière après 3 ans de travail intense qui a permis à la SNE de poursuivre sa croissance.

Je tiens également à remercier notre bureau des jeunes chercheurs composé de Clara Sanchez et Cristina Miralpeix pour leur dynamisme qui a permis l'organisation de cinq webinaires destinés aux jeunes chercheurs. Notre société est caractérisée par un fort noyau de jeunes chercheurs qui non seulement insuffle un nouveau dynamisme mais également garantit la pérennité de notre société pour les années et décennies à venir. C'est pour ces raisons que notre société conduit de nombreuses actions destinées aux jeunes chercheurs dont des bourses de voyages pour participer à des colloques nationaux et internationaux (48 bourses de voyages ont été attribuées en 2024), des bourses d'échanges inter-labo, des prix de thèse et un prix SNE destiné à un.e postdoc. Je tiens notamment à adresser mes remerciements les plus sincères à la fondation Obélisque qui nous permet de soutenir depuis de nombreuses années nos actions envers nos jeunes chercheurs.

Pour 2025, je souhaite à chacune et chacun d'entre vous une année pleine de succès personnels et professionnels, d'épanouissement et de découvertes enrichissantes. Par souci de

simplification, nous aurons désormais deux dates clés pour la plupart de nos actions : une en juin et une en septembre. Le calendrier de l'ensemble de nos actions est disponible dans ce bulletin. Cette année, nous aurons le plaisir de nous réunir à Lausanne dans le cadre de notre colloque annuel qui aura lieu du 7 au 10 octobre 2025. Je compte sur vous pour venir nombreux à ce grand moment d'échange et de retrouvailles. Inscrivez également dès à présent dans vos agenda les dates du 26-29 juillet 2026 auxquelles se tiendra le congrès de l'ICN à Nagoya au Japon. Quatre de nos membres travaillent activement à l'élaboration du programme avec nos collègues neuroendocrinologistes du monde entier.

Au plaisir de vous revoir bientôt,

Sebastien

President's Words

Sébastien Bouret

Dear colleagues and friends,

As we embark on a new year, it is with immense joy and deep gratitude that I address you for the first time as the president of the French Society of Neuroendocrinology. It is a true honor to take on these responsibilities within this wonderful society that I have had the fortune to join since the beginning of my thesis.

The past year has been rich in remarkable accomplishments. In 2024, our society counted 167 active members, including 80 young researchers, a level of engagement at its highest in many years. The dynamism of our society was also evident during our annual conference held in Nice last September. This Franco-Canadian conference brought together 152 attendees from nine countries (France, Canada, Belgium, Switzerland, United States, England, Germany, Spain, and Norway). I would like to sincerely thank Carole Rovère and Alexandre Caron for organizing a conference that will remain etched in our memories, both for the scientific quality of the presentations (whether in symposia or oral presentations by our young researchers) and the exceptional venue and social activities.

The year 2024 was also an excellent year for our laboratories, as evidenced by the SNE Impacts, which compiles examples of remarkable publications in our discipline. We can be proud of our students, postdocs, and researchers who have, once again, published numerous cutting-edge articles not only in neuroendocrinology at the European worldwide global scale but also more broadly in neuroscience and endocrinology, two disciplines to which we are very close.

The year 2025 begins with changes for our scientific council, with a new executive board composed of Sakina Mhaouty-Kodja as vice-president, Carole Rovère as secretary, Virginie Tolle as vice-secretary, Laurent Givalois as treasurer, and Alexandre Caron as vice-treasurer. I would like to thank Youssef Anouar, Hervé Tostivint, and Ariane Sharif, who are leaving their roles as president, secretary, and treasurer after three years of intense work that has allowed the SNE to continue its growth.

I would also like to thank our young researchers' office, composed of Clara Sanchez and Cristina Miralpeix, for their dynamism, which has enabled the organization of five webinars for early career researchers. Our society is characterized by a strong core of early career researchers who not only bring new dynamism but also ensure the sustainability of our society for the years and decades to come. For these reasons, our society conducts numerous actions aimed at early career researchers, including travel grants to attend national and international conferences (48 travel grants were awarded in 2024), inter-lab exchange grants, thesis prizes, and a SNE prize for a postdoc. I would like to express my sincere thanks to the Obélisque Foundation, which has supported our actions for early career researchers for many years.

For 2025, I wish each and every one of you a year full of personal and professional success, fulfillment, and enriching discoveries. For the sake of simplification, we will now have two key dates for most of our actions: one in June and one in September. The calendar for all our activities is available in this bulletin. This year, we will have the pleasure of gathering in Lausanne for our annual conference, which will take place from October 7 to 10, 2025. I count on you to attend this great moment of exchange and reunion. Also, mark your calendars for July 26-29, 2026, when the

ICN conference will be held in Nagoya, Japan. Four of our members are actively working on the program with our neuroendocrinologist colleagues from around the world.

Looking forward to seeing you soon,

Sebastien

Conseil Scientifique/Scientific Council

Bureau/Officers

Sebastien Bouret (Lille)
Président

Carole Rovère (Nice)
Secrétaire/Secretary

Laurent Givalois (Montpellier)
Trésorier/Treasurer

Sakina Mhaouty-Kodja (Paris)
Vice-Présidente/President-Elect

Virginie Tolle (Paris)
Vice-Secrétaire/Vice-Secretary

Alexandre Caron (Québec)
ViceTrésorier/Vice-Treasurer

Conseil Scientifique/Board members

Camille Allard (Bordeaux), Sandrine Chometton (Dijon), Marie-Stéphanie Clerget-Froidevaux (Paris), Sophie Croizier (Lausanne), Daniela Cota (Bordeaux), Elodie Desroziers (Paris), Giuseppe Gangarossa (Paris), David Jarriault (Bordeaux), Freddy Jeanneteau (Montpellier), David L'hôte (Paris), Cristina Miralpeix (Bordeaux)*, Marie Picot (Rouen), Carmelo Quarta (Bordeaux), Clara Sanchez (Stockholm)*

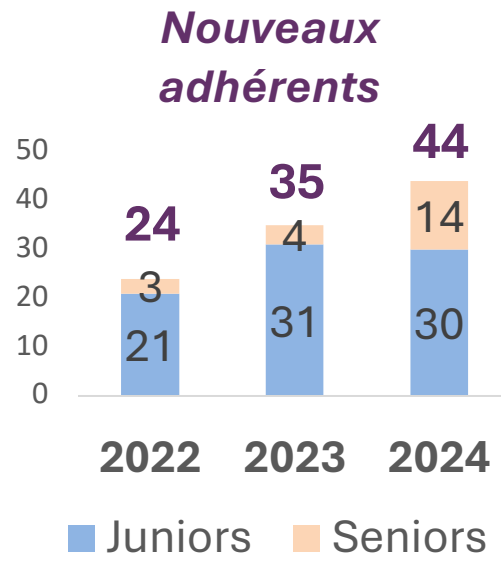
**représentants jeunes chercheurs/early career researcher representatives*

Cellule communication/Communication team

Alexandre Benani & Nathalie Bancod (website), Sebastien Bouret (LinkedIn), Elodie Desroziers (X), Giuseppe Gangarossa (Bluesky), Clara Sanchez (Facebook/Instagram)

Bienvenue à nos nouveaux membres!
Welcome to our new members!

NOM	Prénom	Ville
14 statutaires:		
BARRES	Romain	Nice
CABEZA	Lidia	Besançon
CALON	Frédéric	Québec, Canada*
DE VADDER	Filipe	Lyon
FULTON	Stéphanie	Montréal, Canada*
HADDAD TOVOLLI	Roberta	Barcelone, Espagne*
LE FOLL	Christelle	Zurich, Suisse
MAYEUF-LOUCHART	Alicia	Lille
MICHAEL	Nathalie	Québec, Canada
MURPHY-ROYAL	Ciaran	Montréal, Canada
SOUMIER	Amélie	Lyon
FILLINGER	Clémentine	Strasbourg
RAJAS	Fabienne	Lyon
WRAY	Susan	Bethesda, USA
30 juniors:		
AMAOUCHE-ACCARY	Mouna	Lille
AMMARI	Rachida	Londres, UK*
BARBIER	Marie	Lausanne, Suisse
CUTUGNO	Giulia	Bordeaux
DEHEDIN	Julie	Rouen
DELIT	Maxime	Lille
DUMARGNE	Marie-Charlotte	Nice
EYGRET	Louise	Bordeaux
FREDOC-LOUISON	Justine	Paris
GRELOT	Valentin	Strasbourg
HABIB	Marina	Lyon
JANTZEN	Lucas	Besançon
JOLY	Amélie	Lyon
KACIMI	Loïc	Lille
KYRIAKIDOU	Evangelia	Bordeaux
MAILLAUT	Maud	Nice
MENAGER	Lola	Rouen
NASRI	Nabil	Lille
NIED	Elisa	Strasbourg
PERROT	Gwendoline	Lyon
PIGNOL	Marie	Nice
RENARD	Margot	Lausanne, Suisse
RIVAGORDA	Manon	Lübeck, Allemagne
ROUX	Marine	Nice
ROUX	Mathilde	Lille
RUFFINO	Lou	Nice
SEVRIN	Elena	Liège, Belgique
TURMEL	Audrey	Québec, Canada
WALLART	Lisa	Rouen
WU	Shijia	Lyon
*Adhésion offerte (speaker invitée SNE 2024)		



Why Joining the SNE?

A group of 160+ dynamic and friendly scientists with half early career researchers (ECRs)

Travel awards to attend national and international conferences

Inter-lab exchange grants

Webinars given by ECRs

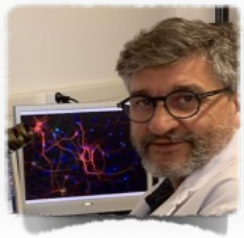
Société de Neuroendocrinologie SNE

An annual conference with ~150 participants

Discounted rates at ICN meetings

Two annual prizes: a thesis award and a prize for a postdoc

Annual membership: 35 euros for ECRs, 50 euros otherwise



How to Apply?

Just contact our treasurer Laurent Givalois (laurent.givalois@igf.cnrs.fr)

Mark your calendar

Deadlines for SNE actions

June 1, 2025

- Application for travel awards to attend the SNE conference in Lausanne
- Application for travel awards to attend non-SNE national and international conferences
- Application for the SNE Prize (for postdocs)
- Application for the Thesis Prize (for theses defended in 2024)
- Application to become a member of our Scientific Council

December 1, 2025

- Application for travel awards to attend non-SNE national and international conferences
- SNE Impacts article submission (articles published in 2025)
- Proposal of talks for the SNE Thematic Day to be held in 2026 (no annual congress due to the ICN 2026 meeting in Japan)
- Proposal to be candidate city for the 2027 SNE congress

All year long

- Application for inter-laboratory exchange grants
- Application to present an SNE early career webinar
- Application to return assistance program

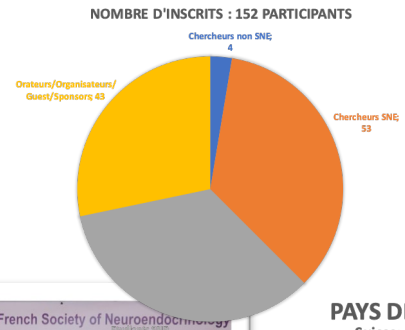
SNE2025 Lausanne

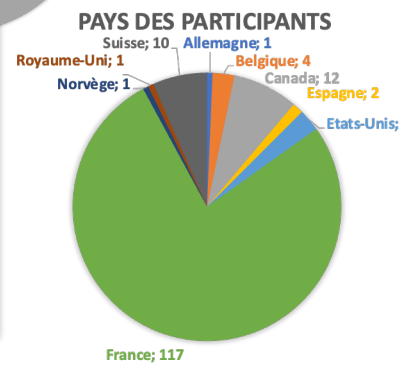
- Early bird registration opens on April 1, 2025
- Early bird registration ends on June 30, 2025
- Conference dates: October 7-10, 2025

Bilan du 46ème Colloque de SNE à Nice

Report of the 46th SNE congress in Nice

Colloque joint France-Canada





Fifteen years after the last SNE conference was held in Nice, we were delighted to welcome over 150 scientists of many nationalities to the Hôtel Saint-Paul on the Côte d'Azur.

This 3-day symposium was a great success and received a lot of positive feedback. The scientific program included a total of 5 symposia, 8 oral communications, 12 Flash talks and 50 posters.

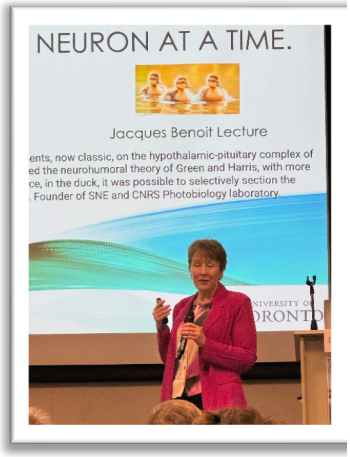
The Jacques Benoît lecture was given by Pr Denise Belsham (Toronto, Canada), the Claude Fortier lecture was given by Dr Serge Luquet (Paris, France), and a lay public lecture was given in French by Dr. Sakina Mhaouty-Kodja (Paris, France).

Two prizes for best oral communication were awarded to Manon Duquenne (Montreal) and Judith Estrada-Meza (Lausanne); a flash talk prize to Amélie Joly (Lyon), a special poster prize as part of the Université Côte d'Azur-Université Laval partnership to Audrey Turmel (Quebec) and, finally, four prizes for best poster to Marie Barbier (Lausanne), Chloé Glachet (Liège), Margot Renard (Lausanne) and Benjamin Thomas (Rouen).

All prizes were funded by the Fondation Obélisque, the Université Côte d'Azur/IDEX,, the Journal of Neuroendocrinology and Karger Editions.

Claude Benoit Lecture 2024 – The amazing molecular diversity of hypothalamic neurons: Tackling mechanisms one neuron at a time

Denise D Belsham, PhD
Departments of Physiology and Medicine, University of Toronto

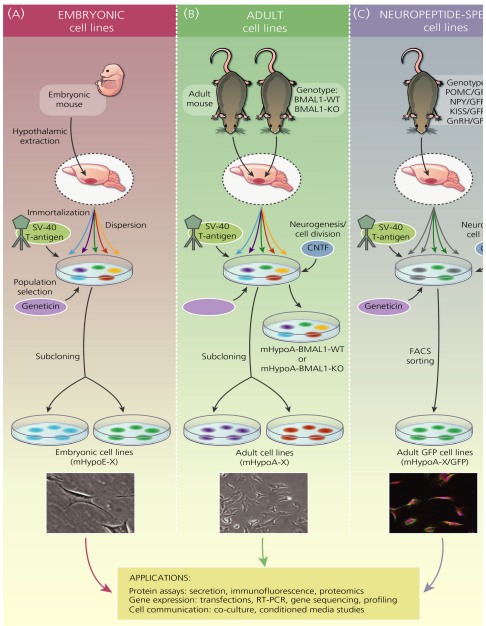


The hypothalamus maintains whole-body homeostasis by integrating information from circulating hormones, nutrients and signaling molecules. Distinct neuronal subpopulations that express and secrete unique neuropeptides execute the individual functions of the hypothalamus, including, but not limited to, the regulation of energy homeostasis, reproduction, and circadian rhythms. Alterations at the hypothalamic level can lead to a myriad of diseases, such as type 2 diabetes mellitus, obesity, and infertility. The excessive consumption of saturated fatty acids can induce neuroinflammation, endoplasmic reticulum stress, and resistance to peripheral signals, ultimately leading to hyperphagia, obesity, impaired reproductive function, and disturbed circadian rhythms. This lecture focuses on the how the changes in the underlying molecular mechanisms caused by palmitate exposure, the most commonly consumed saturated fatty acid, and the potential involvement of microRNAs, a class of non-coding RNA molecules that regulate gene expression post- transcriptionally, can result in detrimental alterations in protein expression and content. Studying the involvement of microRNAs in hypothalamic function holds immense potential, as these molecular markers are quickly proving to be valuable tools in the diagnosis and treatment of metabolic disease.

The hypothalamus is home to distinct neuronal populations. Each population has unique neuropeptide and receptor expression patterns rendering them uniquely sensitive to certain signals. The regulation of these responses is governed by a combination of population-specific signal transduction components and transcription factors. In addition, there is heterogeneity within neuronal populations. Single-cell RNA sequencing studies have revealed functionally distinct subpopulations of AgRP and POMC neurons, demonstrating the heterogeneous nature of neurons in the hypothalamus (1).

It is difficult to study responses of individual cell populations *in vivo* (2). Furthermore, *in vitro* mechanistic studies are essential to study biochemical and signaling pathways of compounds, such as estrogen, palmitate or insulin. Primary culture of hypothalamic neurons prove ineffective due to the difficulty of culturing, their limited lifespan, and their heterogeneous composition. The Belsham lab has generated over 250 neuronal cell models to date, both clonal and non-clonal in composition (2). Clonal cell lines consist of both embryonic and adult models (Figure 1). These were generated by immortalization with SV40 large T-antigen (2). Currently, we have a number of models expressing key reproduction- and feeding-related neuropeptides from both the male and female mouse and rat, both from embryonic- and adult-derived primary hypothalamic cultures.

From Belsham JNE 2020(19)



Non-clonal or mixed population cell lines are all adult-derived. These were created by extracting the hypothalamii of mice expressing eGFP under the control of a neuron-specific promoter, such as the POMC, NPY or GnRH promoter. Upon immortalization with SV40 T-antigen and selection, cells were sorted with fluorescence activated cell sorting to obtain the entire immortalized

population of POMC, NPY, KISS or GnRH-expressing cells in the hypothalamus (3-6). Further, we have recently derived cell models from the BMAL knockout mouse, from both male and female littermates, with wildtype controls (7). These cell lines have neuronal characteristics, including the expression of neuronal markers, neuronal morphology and secretory properties. They express specific neuropeptides and receptors and respond to hormonal stimulation, making them functional models to study mechanisms underlying feeding, reproduction, circadian rhythms and metabolic disorders.

Kisspeptin is a highly conserved reproductive peptide that was first discovered in the 1990s. Kisspeptin is largely expressed in two regions of the hypothalamus that are responsible for coordinating distinct aspects of reproductive signaling. In the ARC, the kisspeptin neurons coordinate pulsatile secretion of GnRH, which is required for the functioning of the HPG axis, while in the AVPV they mediate the female pre-ovulatory GnRH surge. Accordingly, estrogen feedback inhibits the ARC kisspeptin population and stimulates the AVPV population. Cell lines derived from each region have thus been generated to study the mechanism underlying this divergent regulation; mHypoA-Kiss/GFP-3 and mHypoA-Kiss/GFP-4 were immortalized from microdissections of the arcuate and AVPV nuclei, respectively, from female Kiss-GFP mice (6). The estradiol-induced downregulation of kisspeptin in the ARC mHypoA-55 cell line was dependent on nuclear ERs and CREB activation, which likely occurs through estradiol acting at the membrane-bound estrogen receptor, GPR30(6). Meanwhile, in the AVPV mHypoA-50 cell line, the estradiol-induced downregulation of kisspeptin was mediated by the nuclear estrogen receptor ERα (6).

With the development of bioinformatics, several novel reproductive peptides have been identified that coordinate GnRH signaling; therefore, they have potential to be used as therapeutics. One such peptide, phoenixin (PNX), was identified using a bioinformatics algorithm and is expressed throughout the hypothalamus(8). A crucial role for PNX in the HPG axis was identified using hypothalamic neuronal cell lines: phoenixin upregulated GnRH mRNA and secretion in the mHypoA-GnRH/GFP cell line and upregulated kisspeptin mRNA in the mHypoA-Kiss/GFP cell line(6). Hypothalamic cell lines also allowed for the discovery and de-orphanization of the PNX receptor, GPR173. siRNA knockdown of GPR173 in hypothalamic neurons then confirmed the dependence of PNX-responses on GPR173 (6,9). However, to our surprise, a whole-body knockout of PNX did not result in reproductive dysfunction or any major phenotypic difference from the wildtype mouse(10). Extensive analysis of this knockout revealed a modest change in anxiety with behavioural testing. We suggest that a temporal and tissue-specific knockout may be more effective to tease out the role of PNX in the brain and in neuroendocrine function.

Understanding how hypothalamic neurons contribute to the control of whole-body metabolism is another interest in our laboratory. We have studied many of the contributing factors to metabolic disease, including the saturated fatty acid palmitate, leptin, and insulin, and whether there are potential anti-inflammatory or beneficial dietary fats that can resolve the detrimental effects of excessive exposure of these compounds to neurons (11-17). Some of the issues that result in over-exposure of palmitate and insulin includes insulin resistance, endoplasmic reticulum stress, and inflammation. Omega-3 fatty acids and the monounsaturated fatty acid oleate are protective.

Normal insulin actions in the hypothalamus are essential in the regulation of energy balance; however, research indicates that excessive insulin exposure is harmful as it may lead to obesity. We have studied the role of microRNAs (miRNAs) in the control of insulin resistance. miRNAs expressed in the hypothalamus are capable of regulating energy balance and peripheral metabolism by inhibiting transcription and translation of target mRNAs. An unanswered question is whether central insulin resistance creates a specific hypothalamic miRNA signature that can be identified and targeted. We demonstrated that miR-1983 is upregulated *in vitro* in multiple insulin-resistant immortalized hypothalamic neuronal NPY-expressing models, and *in vivo* in hyperinsulinemic mice, with a concomitant decrease of insulin receptor beta (IRb) protein, a target of miR-1983 (18). Importantly, we demonstrate that miR-1983 is detectable in human serum or plasma and that levels correlate with plasma insulin, BMI and HOMA insulin resistance ($p<0.0001$). Levels of miRNA are normalized with metformin exposure, both in mouse hypothalamic neuronal cell culture and in human plasma (18). Our findings provide evidence for miR-1983 as a unique biomarker of early insulin resistance, and a potential therapeutic target for human metabolic disease (19)

The importance of the hypothalamus in maintaining homeostatic functions, including reproduction, energy balance, circadian rhythms and stress cannot be overstated. Several hypothalamic nuclei and regions regulate these critical physiological functions. Each of these hypothalamic regions comprises a complex network of heterogeneous neurons; however, cellular mechanisms underlying the function of these individual neurons remain largely understudied. The aspiration of our research program has been to provide key tools to delineate the complex mechanisms involved in neuroendocrine physiology with a goal of translational relevance.

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Claude Fortier Lecture 2024
Susceptibility to modern food environment: a role for brain lipid sensing?

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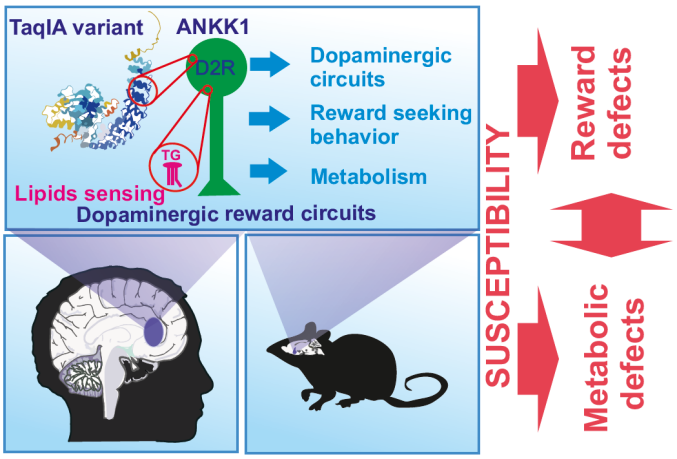
Feeding behavior results from a complex and dynamic interplay of signals reflecting not only metabolic needs but also cognitive, appetitive, and emotional drives, all contributing to adaptive mechanisms for sustaining caloric intake and body weight. The mesocorticolimbic dopamine (MCL-DA) system encodes the motivational and reinforcing properties of food (Di Chiara and Imperato, 1988; Dallman et al., 2005; Volkow et al., 2012). Dopamine (DA) neurons in the ventral tegmental area (VTA) and substantia nigra pars compacta are the primary sources of DA in both the dorsal and ventral striatum, where it binds to receptors on striatal medium spiny neurons (MSNs). These DA receptors are G-protein-coupled, with the D1 family (DRD1) linked to Gsα/olf proteins, and the D2 family (DR2) associated with Gi proteins, forming two distinct neuronal populations: DRD1- and DR2-MSNs (Gerfen et al., 1990; Jackson and Westlinddanielsson, 1994; Baik, 2013). These neurons also integrate inputs from the prefrontal cortex, thalamus, and limbic regions. DA signaling within the MCL system is crucial for processing reward prediction errors (Schultz, 2016), associative learning (Frank and Fossella, 2011), motor planning, decision-making, and attributing incentive salience to reward-related stimuli (Berridge, 2009).

Substantial evidence now indicates that both excessive consumption of palatable foods and metabolic disorders like obesity induce maladaptive changes within the MCL system. These alterations contribute to impulsivity (Babbs et al., 2013; Guo et al., 2014; Adams et al., 2015), disrupted hedonic and motivational states, uncontrolled cravings, and ultimately compulsive or addictive-like feeding behaviors (Wang et al., 2001; Johnson and Kenny, 2010; Vucetic and Reyes, 2010; Michaelides et al., 2012). For example, in rodents, a high-fat diet increases impulsivity, correlating with decreased DR2 but not DRD1 signaling (Adams et al., 2015). Moreover, genetic downregulation of striatal DR2 results in a reward-deficit state, leading to compulsive eating when exposed to high-fat foods (Johnson and Kenny, 2010). In humans, body mass index (BMI) is linked to alterations in striatal DR2 distribution and tendencies toward habitual or opportunistic eating (Guo et al., 2014). Additional findings suggest dietary fat may directly impact DA signaling independent of adiposity and BMI. High-fat diets have been shown to reduce DR2 expression and DA turnover, diminishing reward-seeking behavior (Davis et al., 2008; South and Huang, 2008; Hryhorczuk et al., 2015), impairing cognitive function (Farr et al., 2008),

and increasing impulsivity {Adams, 2015 #10}. Triglycerides (TG), a major lipid source, naturally rise after meals but remain chronically elevated in obesity (Ruge et al., 2009). In rodents, postprandial TG levels predict weight gain and uncontrolled feeding (Karatayev et al., 2009), while in obese mice, they contribute to cognitive impairments (Farr et al., 2008). Human brain imaging studies have linked circulating TG with neural responses to food rewards (Sun et al., 2014). Experiments using radiolabeled free fatty acids (FFA) or TG confirm that these lipids cross the blood-brain barrier, where they are metabolized within the brain (Banks et al., 2018). Collectively, these studies suggest that plasma TG can influence DA signaling, thereby modulating reward processing.



Genetic polymorphism affect Dopamine transmission can influence brain lipid sensing. Circulating TG can act onto DR2 neurons to control metabolism and reward-driven behavior. In condition of high circulating TG such as in obesity, and/or and in the context of genetic variant that account for susceptibility for addictive behavior (TaqIA/Ankk1), the function of DR2 might be compromised leading to heighten susceptibility for metabolic and psychiatric diseases.

Plasma TG are typically a postprandial signal, indeed after a meal, the gut packages and releases Triglyceride (TG)-rich particles that will be hydrolysed by tissues through the action of the lipoprotein lipase (LPL), an enzyme which catabolizes TG into free fatty acids, a necessary step for cell lipid oxidation. The enzyme lipoprotein lipase (LPL), which regulates TG metabolism, is expressed in the human and rodent brain (Goldberg et al., 1989; Ben-Zeev et al., 1990; Bessesen et al., 1993; Paradis et al., 2004; Wang et al., 2011; Wang and Eckel, 2014). Central LPL activity has been linked to both body weight regulation and reward-driven behaviors (Wang et al., 2011; Picard et al., 2014). In the brain reward circuit, the neurons that release or respond to dopamine (DA) in the midbrain and striatal structures express the LPL. Therefore, the presence of LPL onto DA neurons of the "reward circuit" suggests a possible role for circulating TG as regulatory signals to modulate neuronal activity and the subsequent cognitive and reinforcing aspects of food.

In order to test this hypothesis in mice, we have developed a model of central TG delivery through the carotid artery in the direction of the brain to mimics the entry of TG particle in the brain after a meal in condition that only target central structures (Cansell et al., 2014; Berland et al., 2020). This protocol allowed us to demonstrate that circulating TG, once reaching the central DA circuit, modulate reward-driven food consumption, act as reinforcing signals as assessed in the conditioned place preference test, and control cellular and behavioral responses to psychotropic drugs such as amphetamine. In a following study, we present evidence highlighting the significant role of dietary TG-induced adaptations in DR2-expressing neurons. First, we show that Lpl mRNA is present in mesocorticolimbic regions of both human and mouse brains, including VTA DA neurons and striatal MSNs. Second, through in vivo brain-specific TG delivery and ex vivo whole-cell patch-clamp recordings, we demonstrate that circulating TG influence the excitability and cellular responses of DR2-expressing neurons within the reward system. Third, we reveal that central TG function as direct reinforcers, modulating reward-seeking and other DA-dependent behaviors. Using animal model allowing for conditional knock-down of LPL, we further confirmed that central TG sensing is mediated - at least in part - by LPL activity in the VTA and STR. Taking advantage of *ex vivo* patch-clamp electrophysiology and *in vivo* calcium imaging of DR2-expressing neurons, we also highlighted a direct action of TG onto the activity of DR2-neurons (Berland et al., 2020).

In addition, using functional magnetic resonance imaging (fMRI) in human we complemented this study by showing that, in humans, the activity of the prefrontal cortex - a brain region involved in integrating food-related cues - is correlated with postprandial increase in TG and responds to food-related cues in a opposite manner according to the presence or absence of a genetic polymorphism TaqIA A1 which is associated with a ~30-40% reduction in striatal DR2 levels, predisposes individuals to uncontrolled eating and obesity (Ritchie and Noble, 2003; Stice et al., 2008, 2015). Altogether, these results suggest that circulating nutritional lipids could, in both humans and rodents, directly act onto

brain structures regulating food-associated rewards and as such be instrumental in the physiological regulation of feeding behavior but also in contributing to compulsive behaviors associated with diets rich in lipids. While these results establish D2R-neurons as an integrative platform for circulating lipids, it does not explain why -despite the ubiquitous presence of palatable fat food- not everyone develops metabolic or eating disorders. This raises the possibility that genetic variants that influence DA transmission confer risk for overeating, behavioral/cognitive alterations and metabolic diseases, indeed we found that the inheritable genetic polymorphism TaqIA A1/Ankk1 influence the way circulating TG affect brain response to foo cues in human (Berland et al., 2020). This result also suggests that genetic make-up such as TaqIA A1 might be an integral component of brain susceptibility to food cues, and specifically lipid sensing in the reward circuit. Indeed, a growing body of evidence highlights that obesity also results from cognitive perturbations such as altered reward processing, increased impulsivity or decreased behavioral flexibility, that could account for disadapted food-directed behaviors (Sun et al., 2017). Interestingly, such endophenotypes are main features of several psychiatric diseases making obesity increasingly viewed as a "metabo-psychiatric" disorder (Weiss et al., 2020). This suggests the existence of an overlap in the pathogenic mechanisms that underlie neuropsychiatric and metabolic symptoms. In this context, the addiction-susceptibility TaqIA/Ankk1 polymorphisms bear particular relevance. Taq1A/Ankk1 is a single nucleotide polymorphism located in the gene near the D2R that codes for the Ankyrin repeat and kinase domain containing 1 kinase (Ankk1) and corresponds to three variants, A1/A1, A1/A2 and A2/A2. The function of this kinase is not yet known, but A1 carriers are more likely to have increased waist circumference and risk for obesity (Comings et al., 1993; Nisoli et al., 2007; Stice et al., 2008). In addition, pharmacologically-induced weight loss has been reported to be easier in obese individuals bearing the A1 variant (Mullally et al., 2021). Altogether, this suggests that A1 might be a genetic node for the convergence of neuropsychiatric and metabolic symptoms.

At the neurobiological level, Taq1A/Ankk1 polymorphism is characterized by defective D2R-signaling and dopamine transmission (Sun et al., 2017), a shared neurobiological feature found across several psychiatric diseases as well as obesity. Using several gain and loss of approaches of the Ankk1 gene in the reward circuit, we found that *Ankk1* transcript is preferentially enriched in striatal D2R-expressing neurons and that Ankk1 loss-of-function in dorsal and ventral striatum leads to alteration in learning, impulsivity and flexibility resembling endophenotypes described in A1 carriers. We also observed an unsuspected role of Ankk1 in striatal D2R-expressing neurons of the ventral striatum in the regulation of energy homeostasis and documented differential nutrient partitioning in humans with or without the A1 allele. These data demonstrate that the Ankk1 gene is necessary for the integrity of striatal functions and reveal a new role for Ankk1 in the regulation of body metabolism.

This result also suggests that genetic make-up such as TaqIA A1 Ankk1 variant might be an integral molecular component that influence brain susceptibility to nutrient signals, and specifically lipid sensing in the reward circuit.

We are now pursuing this endeavor using animal model in which the 2 variants of Ankk1 SNP have been reproduced in order to mimics human condition. Preliminary result confirms that, although discrete, the SNP in the Ank1 gene has influence on bot metabolic and behavioral aspect associated with food-reward driven behaviors. In conclusion, our working hypothesis is that fluctuation of circulating lipid might influence brain response to food cues, reward -driven behavior and metabolism in a manner that is modulated by genetic variant TaqIA A1 Ankk1 variant, providing therefore new potential avenue for personalized approaches to oppose food-induced reward deficit and metabolic diseases.

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SNE Prize

Hypothalamic POMC neurons control competing behaviours

Cristina Miralpeix

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Survival in natural habitats forces animals to constantly adapt their behavior according to their intrinsic needs and environmental conditions. This situation can put basic physiological responses in competition, forcing the animal to make a choice. For instance, a hungry animal in a threatening situation will favor fear responses over their motivation to eat to ensure survival. However, in this context, how the brain senses the inner state and a threatening situation to orchestrate an optimal survival response has been poorly studied. Within the hypothalamus, pro-opiomelanocortin (POMC)-expressing neurons classically promote satiety during energy surfeit and have a role in the physiological adaptations that occur during stressful and fearful events. Recent findings from our lab have demonstrated that POMC neurons activity is regulated by cannabinoid type 1 (CB1) receptors, key physiological determinants of synaptic and behavioral functions. Here, we hypothesized that CB1 receptor-dependent signaling in POMC neurons is at the intersection of fear and feeding responses. Mice lacking CB1 in POMC neurons POMC-CB1-KO, did not show any relevant change in food intake in basal condition compared to their control littermates. However, when POMC-CB1-KO mice were fasted and in a fearful situation (using fear-conditioning protocol), they displayed higher motivation for eating and decreased fear response than their control littermates. Immunofluorescence and chemogenetic studies showed that POMC activation is necessary for suppressing the motivation to eat in a threatening situation. However, POMC neurons without CB1 are hyperactive, possibly impairing proper decision-making. In addition, POMC neurons are a heterogeneous population that can express both inhibitory and excitatory neurotransmitters. We have observed that mice with impaired release of GABA in POMC neurons, also favor eating behavior over fear responses. Thus, these results suggest that CB1 receptors and GABA release in POMC neurons are key to balancing fear and feeding behaviours. Finally, since a threatening situation can activate the stress response and POMC neurons modulate stress hormones release through CRH neurons, we evaluated corticosterone plasma levels observing that corticosterone levels of POMC-CB1-WT and KO correlate with their eating behaviour and fear response. Therefore, we are now deciphering a POMC-to-CRH neurons circuit as a possible key to control competing behaviors.

Thesis Prize

Dietary fatty acid composition drives neuroinflammation and impaired behavior in obesity.

Clara Sanchez

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Nutrient composition in obesogenic diets may influence the severity of disorders associated with obesity such as insulin-resistance and chronic inflammation. Here we hypothesized that obesogenic diets rich in fat and varying in fatty acid composition, particularly in omega 6 (ω6) to omega 3 (ω3) ratio, have various effects on energy metabolism, neuroinflammation and behavior. Mice were fed either a control diet or a high fat diet (HFD) containing either low (LO), medium (ME) or high (HI) ω6/ω3 ratio. Mice from the HFD-LO group consumed less calories and exhibited less body weight gain compared to other HFD groups. Both HFD-ME and HFD-HI impaired glucose metabolism while HFD-LO partly prevented insulin intolerance and was associated with normal leptin levels despite higher subcutaneous and perigonadal adiposity. Only HFD-HI increased anxiety and impaired spatial memory, together with increased inflammation in the hypothalamus and hippocampus. Our results show that impaired glucose metabolism and neuroinflammation are uncoupled, and support that diets with a high ω6/ω3 ratio are associated with neuroinflammation and the behavioral deterioration coupled with the consumption of diets rich in fat.

Actions en faveur des jeunes chercheurs en 2024

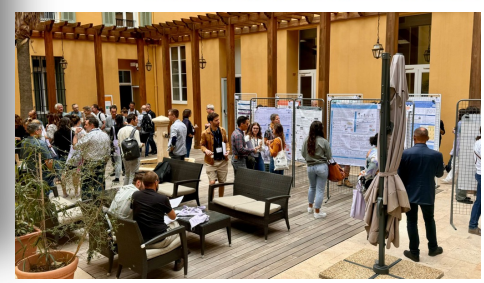
Actions in support of early career researchers in 2024

Notre société compte plus de 80 jeunes chercheurs. Le soutien continu de la Fondation Obelisque nous a permis de mener de nombreuses actions à leur égard en 2024 qui sont résumées ici

Our society has more than 80 early carreer researchers. The continuous support of the Obelisque Foundation has enabled us to carry out numerous actions for them in 2024 that are listed here

48 bourses de voyage attribuées pour participer au congrès de la SNE à Nice et à d'autres congrès nationaux et internationaux

48 travel awards to attend the SNE congress in Nice and other national and international conferences



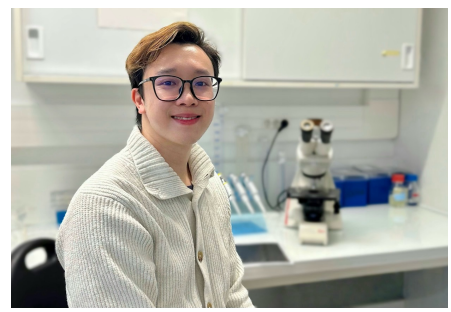
5 webinaires organisés par le bureau Jeunes Chercheurs composé de Clara Sanchez & Cristina Miralpeix

5 webinars organized by the ECR bureau Jeunes Chercheurs composed of Clara Sanchez & Cristina Miralpeix

1 bourse d'échange inter-labo

1 inter-lab exchange grant

Thomas Lee, Doctorant
Inserm Bordeaux



Hommage à Jean-Didier Vincent (1935-2024)
ancien Président et Président d'honneur de la SNE

Bernard Bioulac
Professeur Emérite Université Bordeaux
Membre de l'Académie Nationale de Médecine

Jean-Didier Vincent est mort le 4 décembre 2024. Né sous le Front Populaire, il aimait à rappeler qu'il avait accompli sa scolarité au Collège protestant de Sainte Foy la Grande comme le fit, un siècle plus tôt, Elisée Reclus. Il admirait l'œuvre de ce savant géographe anarchiste. Son influence forgea peut-être son côté provocateur. Mais la cité foyenne était aussi le berceau de Paul Broca un des fondateurs du localisationnisme, conception qui ne laissa pas indifférent JD. Vincent. Il va parcourir d'un trait le cursus de médecine à la Faculté de Bordeaux jusqu'à l'agrégation de Physiologie et devenir Professeur des Universités-Praticien Hospitalier et Chef de service en explorations fonctionnelles du système nerveux au CHU. Il sera même Doyen de la Faculté dénommée alors Paul Broca. Il crée un des premiers Laboratoires d'études du sommeil et dirige l'Unité INSERM « Neurobiologie des comportements » de 1978 à 1991. En 1992, il quitte Bordeaux pour prendre la direction de l'Institut « Alfred Fessard » du CNRS à Gif sur Yvette et devient Professeur des Universités à la Faculté de Paris-Sud.

Dès son internat il fréquente le Laboratoire de Médecine Expérimentale associé à l'Institut National d'Hygiène (ancêtre de l'INSERM) créé par le Pr Jacques Faure dont il sera l'élève. Il perçoit d'emblée l'importance, dans l'étude des comportements, des modèles animaux en situation chronique pour analyser le couplage entre activité électrique cérébrale et libération et/ou modulation hormonales. Une de ses premières publications avec J. Faure concerne la relation entre l'ovulation et une séquence comportementale particulière qui sera interprétée, plus tard par Michel Jouvet, comme étant du sommeil paradoxal.

L'étude qu'il conduit sur le rôle de l'hypothalamus antérieur, dans le comportement de boisson, est un bon exemple de sa démarche scientifique. Il montre comment l'activité électrique des osmorécepteurs du noyau supraoptique (NSO) code non seulement le besoin en eau et le déclenchement du comportement dipsique mais aussi la neurosécrétion pulsatile de l'ADH. De plus, il détecte, autour du NSO et proches des voies dopaminergiques, des neurones qui anticipent la satisfaction du besoin en eau et contribuent à arrêter le comportement de boisson bien avant le rétablissement de l'osmolalité plasmatique. Il attribuera à ces neurones une valeur motivationnelle correctrice.

Jean-Didier Vincent (au centre) entouré de William Rostène et Claude Kordon (à gauche) et Andrée Tixier-Vidal et André Calas (à droite) – Lille 1998

Il défendra cette approche qui relie activité neuronale, libération hormonale pulsatile et séquence comportementale tant pour le système hypothalamique magnocellulaire : boisson et ADH *et* lactation et ocytocine, que pour le système parvocellulaire : ovulation et LH-RH. En cela JD Vincent a contribué à fonder la neuroendocrinologie.

Il va, ainsi, définir une physiologie de « l'inconstance » qui s'oppose à celle de la fixité du milieu intérieur de Claude Bernard ou de l'homéostasie de Walter Cannon. Il s'agit d' « un état central fluctuant » soumis sans cesse à des variations physiologiques ou psychologiques. Ces écarts suscitent des « drives » ou pulsions motivationnelles (soif, faim, désir sexuel…) qui s'extériorisent par des séquences motrices correctrices.

Il n'aura de cesse de décrypter les bases neuronales des grands comportements : boisson reproduction, sommeil ou de grandes fonctions : olfaction, mémoire mais en les liant à la motivation et aux émotions. A cette fin il usera d'un constant « va et vient » entre le normal et le pathologique en s'appuyant sur des approches très intégratives mais aussi sur des modèles simplifiés. Cette vision contribuera au développement des neurosciences à Bordeaux. Il y a créé une véritable école où cohabitent scientifiques et médecins. Plusieurs de ses élèves ont dirigé ou dirigent des formations INSERM ou CNRS. Cette capacité à bâtir, il l'instillera au Laboratoire de Gif sur Yvette et aussi comme Président du Conseil de Département des sciences de la vie du CNRS.

Autre aspect de sa singularité celle d'écrire pour expliquer le fonctionnement de notre cerveau, celui de nos émotions, de nos sentiments. En 1986, sa « *Biologie des passions* » rencontre un énorme succès. A une vision sèche et désincarnée d'un cerveau-ordinateur, il oppose un cerveau humidifié par les humeurs que sont les hormones. C'est de ce « cerveau de chair » qu'émergeront désir, plaisir et douleur ou sexe, amour et pouvoir… De nombreux autre essais ou livres suivront : *La chair et le diable, Voyage au centre du cerveau, La vie est une fable, Eve épouse Adam, Casanova, la contagion du plaisir, Biologie du couple, Le sexe expliqué à ma fille, Biologie du pouvoir…*

Tous ces ouvrages recèlent la même volonté de disséquer, souvent de façon métaphorique et en mêlant physiologie, littérature et philosophie, les états de notre psychisme. Cette force se retrouvera dans les émissions de diffusion des sciences qu'il animait sur France Culture. Ces qualités pédagogiques l'amèneront à siéger au Conseil National des Programmes qu'il présidera plusieurs années.

Jean-Didier Vincent, personnalité créative et provocatrice, aimant la bonne chair et profondément humaniste était membre de l'Académie Nationale de Médecine, de l'Académie des Sciences et de nombreuses sociétés savantes internationales. Il était Officier dans l'Ordre de la Légion d'Honneur et Commandeur dans l'Ordre des Palmes Académiques.

47th Congress of the French Society of Neuroendocrinology

LAUSANNE, October 7-10, 2025

UNIL | Université de Lausanne

Organizing committee

Sophie CROIZIER
Sarah GELLER
Fanny LANGLET
Virginie MANSUY-AUBER
Andrea MESSINA

https://wp.unil.ch/sne2025lausanne/

Detailed program

Tuesday, October 7, 2025

4:00-6:00 pm. Participant Registration and Welcome – *Amphimax, UNIL Sorge*

7:00-8:00 pm. **Public Lecture** – *Amphimax, UNIL Sorge* **OPEN to all.**

Prof. Bernard THORENS – *Le diabète de type 2, une histoire de cerveau et de sucre*

8:00-9:30 pm. "Welcome to Switzerland" Cocktail Dinner – *Amphimax, UNIL Sorge*

8:30 pm-late "Meet & Greet" Cocktail reserved for Early Career Researchers – *location tbd*

Wednesday, October 8, 2025

8:00-8:45 am. Participant Registration and Welcome – *Agora-Atrium, UNIL/CHUV Bugnon*

8:45-9:00 am. Opening Ceremony – *Agora-Auditorium, UNIL/CHUV Bugnon*

9:00-11:00 am. **Symposium 1. Body-Brain Interoceptive Mechanisms Regulating Feeding and Energy Homeostasis** – *Agora-Auditorium, UNIL/CHUV Bugnon*

Amandine Gautier-Stein – *Deciphering the gut-brain pathway induced by intestinal gluconeogenesis*
Virginie Mansuy-Aubert – *The Role of SCFAs and Neural Pathways in Energy Balance and Metabolic Health*
Jean-Philippe Krieger – *The vagal gut-brain axis links food intake with anxiety states: insights from rodents and humans*
Giuseppe Gangarossa – *The gut-brain vagal axis governs natural and recreational rewards by gating dopamine dynamics*

11:00-11:30 am. Coffee Break – *Agora-Atrium, UNIL/CHUV Bugnon*

11:30 am -12:30 pm. Flash Talks – *Agora-Auditorium, UNIL/CHUV Bugnon*

12:30-1:15 pm. Lunch – *Agora-Atrium, UNIL/CHUV Bugnon*

13:15-2:45 pm. Poster Session 1 (Even Numbers) – *Agora-Atrium, UNIL/CHUV Bugnon*

2:45-3:00 pm. Tribute to JD Vincent – *Agora-Auditorium, UNIL/CHUV Bugnon*

3:00-4:00 pm. **Oral Communications Session 1** – *Agora-Auditorium, UNIL/CHUV Bugnon*

4:00-8:00 pm. Activities – *Lausanne and Surroundings*

Thursday, October 9, 2025

8:30-9:00 am. Welcome – *Agora-Atrium, UNIL/CHUV Bugnon*

9:00-11:00 am. **Symposium 2. Molecular mechanisms of neuroendocrine secretion** – *Agora-Auditorium, UNIL/CHUV Bugnon*

Sponsored by the Exocytosis-Endocytosis Club

Aurélien Roux – M*echanisms of membrane remodelling by ESCRT-III*
Emeline Tanguy – *Deciphering the multiple functions of membrane phospholipid species in neurosecretion*
Maité Montero – *Chromogranin A, a central multifaceted protein controlling neuroendocrine secretion*
Fanny Langlet – *Tanycyte-derived extracellular vesicles: from molecular mechanisms to the control of energy balance*

11:00-11:30 am. Coffee Break – *Agora-Atrium, UNIL/CHUV Bugnon*

11:30 am-12:30 pm. **Jacques Benoit Lecture** – *Agora-Auditorium, UNIL/CHUV Bugnon*

Yves Tillet – *Contrôle neuroendocrinien de la reproduction : ce qu'un mouton nous dit*

12:30 am-1:30 pm. Lunch – *Agora-Atrium, UNIL/CHUV Bugnon*

1:30-3:00 pm. **Poster Session 2** (Odd Number) – *Agora-Atrium, UNIL/CHUV Bugnon*

3:00-4:00 pm. SNE General Assembly – *Agora-Auditorium, UNIL/CHUV Bugnon*

4:00-5:30 pm. **Early-Career Researcher Symposium. Non neuronal cells and Neuroendocrine regulation** – *Agora-Auditorium, UNIL/CHUV Bugnon*

Sreekala Nampouthiri (France, Lille) - *Sexually dimorphic immune-competence of tanycytes*

Evagelia Kyriakidou (France, Bordeaux) - *Microglial mTORC1 regulates metabolic adaptation to calorie surfeit in a sex-dependent manner*

Elena Garcia Calve (Allemagne, Munich) - *Astrocytes & Insulin: A new player in liver metabolic control*

5:30-6:00 pm. **Early-Career Researcher Workshop**

Neuroholics - Panagiota Nti Konstantzo & Eleftheria Varmazi *(Greece) – Engaging storytelling for effective neuroscience communication*

Friday, October 10, 2025

8:30-9:00 am. Welcome – *Agora-Atrium, UNIL/CHUV Bugnon*

9:00-11:00 am. **Symposium 4. Oxytocin as regulator of physiological functions – an integrative vision** – *Agora-Auditorium, UNIL/CHUV Bugnon*

Alexandre Charlet – *Oxytocin shapes astrocytes to control the stress response*
Julie Buron – *The oxytocin-modulated neuronal circuit that amplifies cardiorespiratory coupling: implication for recovery from stress*
Stephanie Schimmer – *Oxytocin facilitates social behavior of female rats via selective modulation of interneurons in the medial prefrontal cortex.*
Ron Stoop – *Oxytocin recruits « buffer » neurons in the central amygdala to induce a social buffering of fear memory.*

11:00-11:30 am. Coffee Break – *Agora-Atrium, UNIL/CHUV Bugnon*

11:30 am-12:30 pm. **SNE Awards Lectures** – *Agora-Auditorium, UNIL/CHUV Bugnon*

12:30 am-1:30 pm. Lunch – *Agora-Atrium, UNIL/CHUV Bugnon*

1:30-2:30 pm. **Oral Communications Session 2** – *Agora-Auditorium, UNIL/CHUV Bugnon*

2:30-3:30 pm. Coffee Break – *Agora-Atrium, UNIL/CHUV Bugnon*

3:00-5:00 pm. **Symposium 5. Genetics and Epigenetics in Neuroendocrinology** – *Agora-Auditorium, UNIL/CHUV Bugnon*

Katharina Gapp – *Epigenetic Inheritance of Stress Responses: Implications for Neuroendocrine Disorders*
Ali Seifinejad – *Epigenetic silencing of hypothalamic neuropeptides in narcolepsy*
Nelly Pitteloud – *Genetics of GnRH deficiency*
Giles Yeo – *Mapping the appetite circuitry in the human brain*

6:00 pm-2:00 am. Gala Dinner, Award Ceremony, and Closing – *Olympic Museum*

Registration will open in April 2025

SNE student	Non-SNE Student & Postdoc	SNE Researcher	Non-SNE researcher
CHF200	CHF250	CHF350	CHF430

Registration fees after July 1, 2025

SNE student	Non-SNE Student & Postdoc	SNE Researcher	Non-SNE researcher
CHF250	CHF300	CHF400	CHF480

Registration includes: access to all conference sessions and lectures, coffee breaks and lunches, and the gala dinner

ICN2026
NAGOYA, JAPAN

The 11th International Congress of Neuroendocrinology

in conjunction with The 52nd Annual Meeting of Japan Neuroendocrine Society

Fascinating Neuroendocrinology

Date July 26 – 29, 2026

Venue WINC AICHI
(Aichi Industry & Labor Center)
Nagoya, Japan

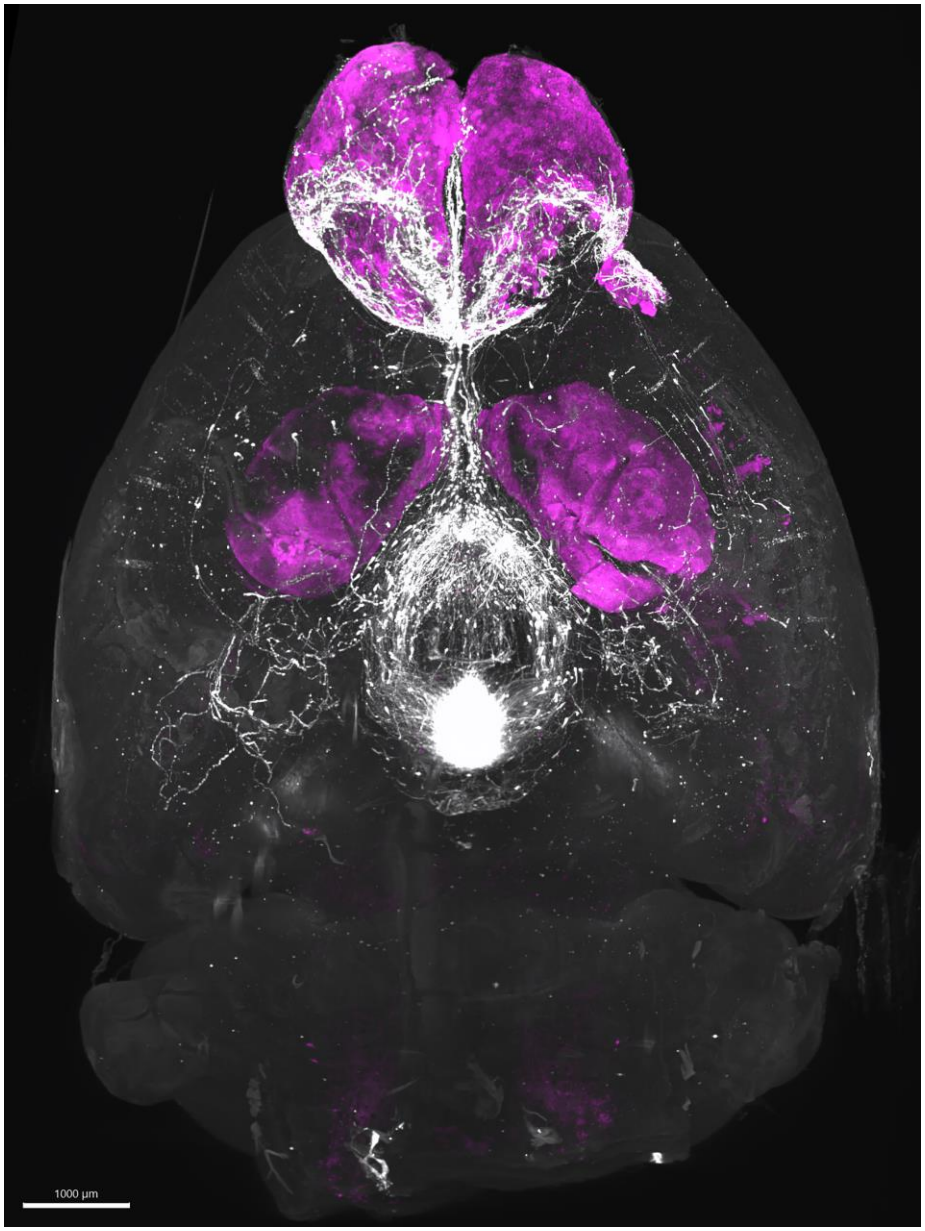
Chair Hiroshi Arima
Department of Endocrinology and Diabetes,
Graduate School of Medicine, Nagoya University

International Neuroendocrine Federation

Japan Neuroendocrine Society

https://www.congre.co.jp/icn2026

SNE Impacts 2024



Localization of the distribution of GnRH neurons (immunolabelled in white) and catecholaminergic neurons (labelled with tyrosine hydroxylase in magenta) in the transparent adult mouse brain.
©Gaëtan Ternier and P Giacobini, Inserm, Lille

A summary of breakthroughs in Neuroendocrinology in 2024
https://www.neuroendocrinologie.fr/

List of selected papers

Bentefour Y and Bakker J. Stress during pubertal development affects female sociosexual behavior in mice. ***Nat Commun.*** *2024 Apr 30;15(1):3610. doi: 10.1038/s41467-024-47300-w.*

Borie A, Dromard Y, Chakraborty P, Fontanaud P, Andre E, François A, Colson P, Muscatelli F, Guillon G, Desarménien M, Jeanneteau F. Neuropeptide therapeutics to repress lateral septum neurons that disable sociability in an autism mouse model. ***Cell Rep Med****. 2024 Nov 19;5(11):101781. doi: 10.1016/j.xcrm.2024.101781.*

Castel J, Li G, Onimus O, Leishman E, Cani PD, Bradshaw H, Mackie K, Everard A, Luquet S, Gangarossa G. NAPE-PLD in the ventral tegmental area regulates reward events, feeding and energy homeostasis. ***Mol Psychiatry.*** *2024 May;29(5):1478-1490. doi: 10.1038/s41380-024-02427-6. Epub 2024 Feb 15.PMID: 38361126*

Decoster L, Trova S, Zucca S, Bulk J, Gouveia A, Ternier G, Lhomme T, Legrand A, Gallet S, Boehm U, Wyatt A, Wahl V, Wartenberg P, Hrabovszky E, Rácz G, Luzzati F, Nato G, Fogli M, Peretto P, Schriever SC, Bernecker M, Pfluger PT, Steculorum SM, Bovetti S, Rasika S, Prevot V, Silva MSB and Giacobini P. A GnRH neuronal population in the olfactory bulb translates socially relevant odors into reproductive behavior in male mice. ***Nat Neurosci.*** *2024 Sep;27(9):1758-1773. doi:10.1038/s41593-024-01724-1.*

Duquenne M, Deligia E, Folgueira C, Bourouh C, Caron E , Pfrieger F, Schwaninger M, Nogueiras R, Annicotte JS, Imbernon M, Prévot V. Tanycytic transcytosis inhibition disrupts energy balance, glucose homeostasis and cognitive function in male mice. ***Mol Metab.*** *2024 Sep:87:101996. doi: 10.1016/j.molmet.2024.101996. Epub 2024 Jul 22.*

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*Leon S, Simon V, Lee TH, Steuernagel L, Clark S, Biglari N, Lesté-Lasserre T, Dupuy N, Cannich A, Bellocchio L, Zizzari P, Allard C, Gonzales D, Le Feuvre Y, Lhuillier E, Brochard A, Nicolas JC, Teillon J, Nikolski M, Marsicano G, Fioramonti X, Brüning JC, Cota D and Quarta C. Single cell tracing of Pomc neurons reveals recruitment of "Ghost" subtypes with atypical identity in a mouse model of obesity****. Nat. Commun.*** *2024 Apr 24;15(1):3443. doi: 10.1038/s41467-024-47877-2.*

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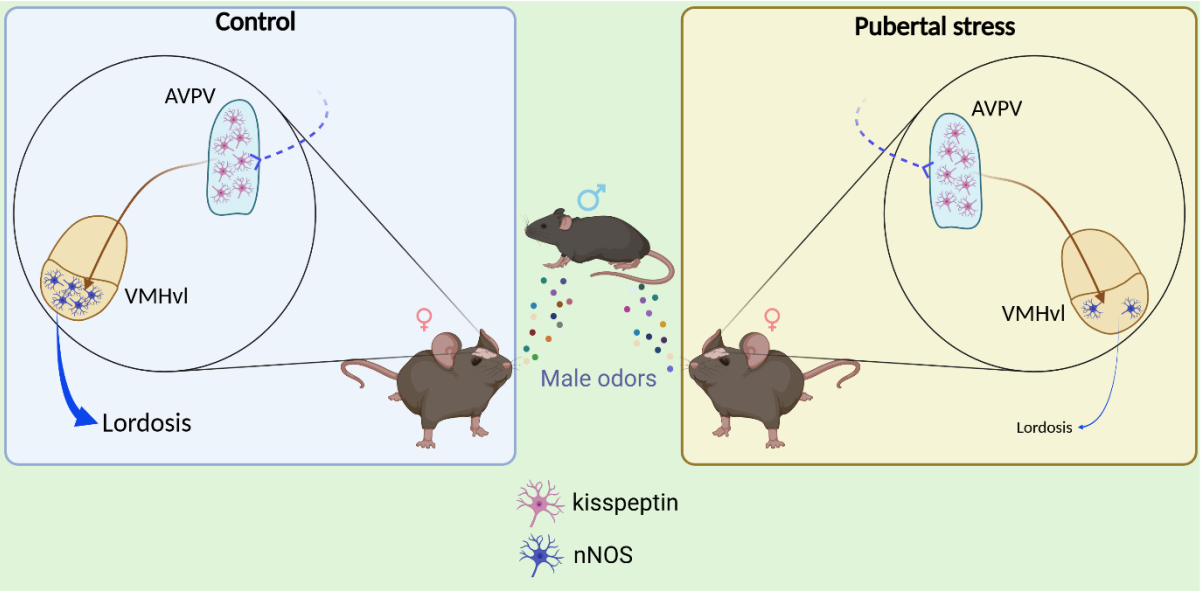
Stress during pubertal development affects female sociosexual behavior in mice

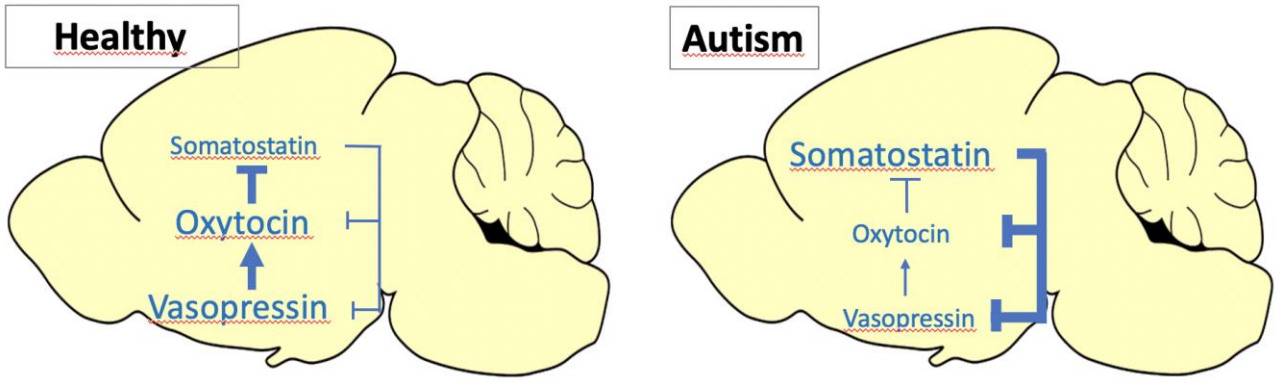
Low sexual desire is a deleterious condition that causes marked distress and interpersonal difficulties. It has a general negative impact on the quality of life. The prevalence of low sexual desire is high: up to 39.5% of women aged between 18 and 44 years old reported deficient or absent sexual fantasies, sexual arousal, and orgasm. Puberty is defined as the transition to a mature reproductive state and is a crucial phase in the development of female sexual functioning. There is growing evidence that exposure to stress during puberty might lead to sexual dysfunction. Therefore, in the present study, the effects of chronic stress over the pubertal period on the neural circuit regulating female sexual behavior was investigated. It was found that pubertal stress permanently disrupted sexual performance in female mice. This reduction in female sexual behavior was associated with a reduced expression and activation of a population of nitric oxide producing neurons in the ventromedial hypothalamus, a brain region critical for the expression of female sexual behavior. This reduced neural activation was particularly observed when females were exposed to male odors, suggesting that the integration of sexually important cues into the brain was affected by exposure to pubertal stress. In sum, adverse effects such as stress, during puberty might lead to long-lasting negative effects on sexual functioning in females.



Bentefour Y and Bakker J. Stress during pubertal development affects female sociosexual behavior in mice. ***Nat Commun.*** *2024 Apr 30;15(1):3610. doi: 10.1038/s41467-024-47300-w.*

Towards more effective therapies against autism

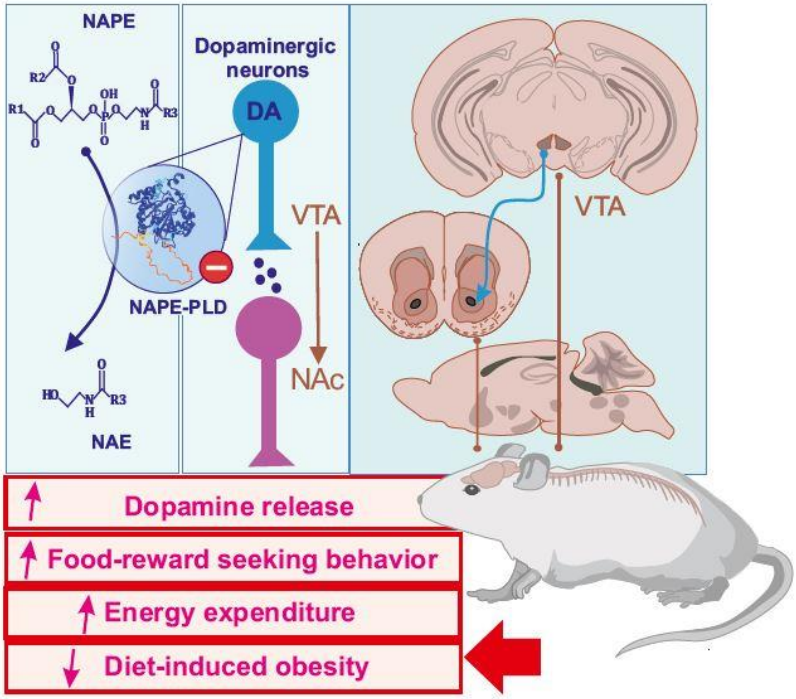
Treatment of autism spectrum disorders is insufficient. The results of recent clinical trials involving the use of oxytocin or vasopressin are mixed. Scientists hypothesized that mixed clinical effects might arise from interrelated actions on prosocial and antisocial responses.
Using mice as model, scientists identified somatostatin inhibitory neurons in the lateral septum that respond to oxytocin and vasopressin, depending on the degree of peer affiliation. Oxytocin receptors inhibit these neurons via the GABA-B receptor, while vasopressin acts via GABA-A neurotransmission on presynaptic connections. Together, these neuropeptides prolonged social contacts by inhibiting intraseptal somatostatinergic activity according to the degree of affiliation between individuals.
When somatostatin is injected into the lateral septum, social contacts are shortened, while a somatostatin antagonist prolongs their duration. However, in animals carrying a mutation in the autism gene MAGEL2, treatment resistance resulted in a hypersomatostatinergic state with premature termination of social contacts.
The results suggest that co-therapy with oxytocin and vasopressin could reduce the hypersomatostatinergic state observed in autism. Furthermore, the use of somatostatinergic antagonists appears to be an alternative to oxytocin and vasopressin notably in subjects featuring endocrine resistance.



Borie A, Dromard Y, Chakraborty P, Fontanaud P, Andre E, François A, Colson P, Muscatelli F, Guillon G, Desarménien M and Jeanneteau F. Neuropeptide therapeutics to repress lateral septum neurons that disable sociability in an autism mouse model. ***Cell Rep Med****. 2024 Nov 19;5(11):101781. doi: 10.1016/j.xcrm.2024.101781.*

NAPE-PLD in the ventral tegmental area regulates reward events, feeding and energy homeostasis

The N-acyl phosphatidylethanolamine-specific phospholipase D (NAPE-PLD) catalyzes the production of N-acylethanolamines (NAEs), a family of endogenous bioactive lipids involved in various biological processes ranging from neuronal functions to energy homeostasis and feeding behaviors. Reward-dependent behaviors depend on dopamine (DA) transmission between the ventral tegmental area (VTA) and the nucleus accumbens (NAc), which conveys reward-values and scales reinforced behaviors. However, whether and how NAPE-PLD may contribute to the regulation of feeding and reward-dependent behaviors has not yet been investigated. This biological question is of paramount importance since NAEs are altered in obesity and metabolic disorders. Here, we show that transcriptomic meta-analysis highlights a potential role for NAPE-PLD within the VTA→NAc circuit. Using brain-specific invalidation approaches, we report that the integrity of NAPE-PLD is required for the proper homeostasis of NAEs within the midbrain VTA and it affects food-reward behaviors. Moreover, region-specific knock-down of NAPE-PLD in the VTA enhanced food-reward seeking and reinforced behaviors, which were associated with increased *in vivo* DA dynamics in response to both food- and non-food-related rewards together with heightened tropism towards food consumption. Furthermore, midbrain knock-down of NAPE-PLD, which increased energy expenditure and adapted nutrient partitioning, elicited a relative protection against high-fat diet-mediated body fat gain and obesity-associated metabolic features. In conclusion, these findings reveal a new key role of VTA NAPE-PLD in shaping DA-dependent events, feeding behaviors and energy homeostasis, thus providing new insights on the regulation of body metabolism.



Castel J, Li G, Onimus O, Leishman E, Cani PD, Bradshaw H, Mackie K, Everard A, Luquet S, Gangarossa G. NAPE-PLD in the ventral tegmental area regulates reward events, feeding and energy homeostasis. ***Mol Psychiatry.*** *2024 May;29(5):1478-1490. doi: 10.1038/s41380-024-02427-6. Epub 2024 Feb 15.PMID: 38361126*

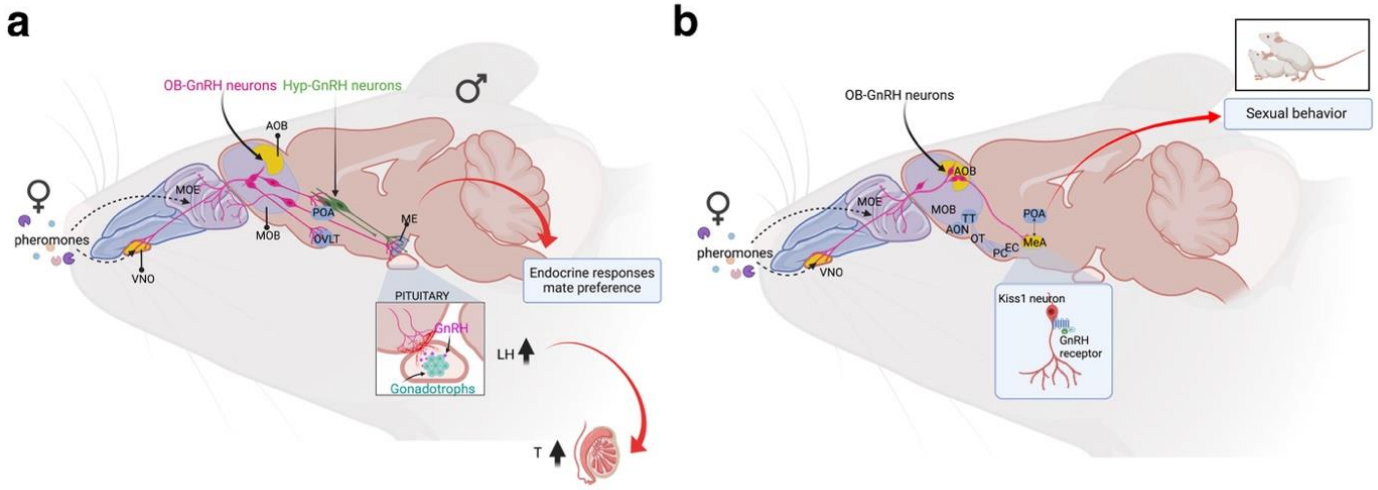
The Nose Knows: Neuroendocrine Cells That Turn Smells into Mating Cues

Scientists have made an intriguing discovery about how male mice recognize potential mates. They discovered that a group of brain cells, known as GnRH neurons, and which are known to control the development of sexual organs and reproduction, are located in the olfactory bulb, which processes odors. When a male mouse detects the scent of a female, these neurons become active, triggering a hormonal response that prepares the male for mating.

Researchers have also showed that when the activity of these GnRH neurons was increased, male mice exhibited heightened interest in female scents. Conversely, reducing or removing the activity of these neurons led to diminished attraction to females. This indicates that these cells play a crucial role in helping male mice recognize potential mates and engage in mating behaviors.

This research underscores the complex interplay between chemical senses and reproductive behaviors, revealing how the brain orchestrates the intricate dance of attraction and mating.

Overall, these findings highlight the importance of GnRH neurons in regulating both fertility and social recognition in male mice, potentially offering clues about similar processes in other mammals.



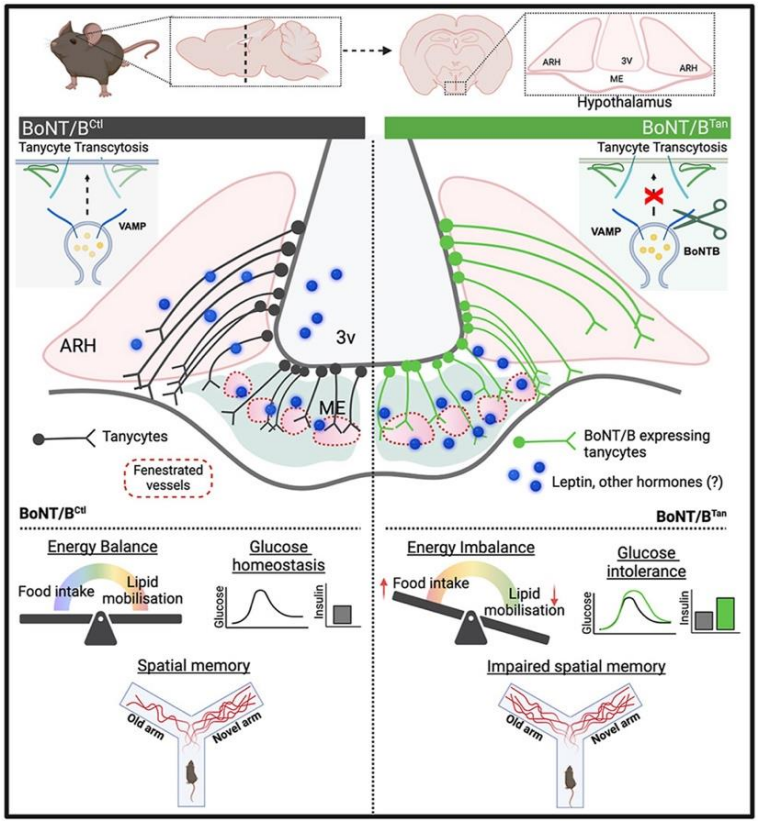
Decoster L, Trova S, Zucca S, Bulk J, Gouveia A, Ternier G, Lhomme T, Legrand A, Gallet S, Boehm U, Wyatt A, Wahl V, Wartenberg P, Hrabovszky E, Rácz G, Luzzati F, Nato G, Fogli M, Peretto P, Schriever SC, Bernecker M, Pfluger PT, Steculorum SM, Bovetti S, Rasika S, Prevot V, Silva MSB and Giacobini P. A GnRH neuronal population in the olfactory bulb translates socially relevant odors into reproductive behavior in male mice. ***Nat Neurosci.*** 2024 Sep;27(9):1758-1773. *doi:10.1038/s41593-024-01724-1.*

Tanycytic transcytosis inhibition disrupts energy balance, glucose homeostasis and cognitive function in male mice

High-caloric diets and genetic factors disrupt body-brain communication, fueling obesity and metabolic disorders. In this study we focus on the hypothalamic tanycytes role in energy balance regulation and cognition. We used a Cre-dependent approach to express botulinum neurotoxin type B (BoNT/B) in tanycytes of adult male mice, inhibiting vesicle-associated membrane protein (VAMP)-mediated release.

In mice fed standard diets, BoNT/B expression in tanycytes blocked leptin transport into the mediobasal hypothalamus, leading to central obesity marked by increased food intake, abdominal fat, and elevated leptin levels without significant weight changes. This manipulation promoted fatty acid accumulation, causing glucose intolerance and insulin resistance, together with compensatory insulin secretion. Additionally, impaired spatial memory was observed in BoNT/B-expressing mice, associating the tanycytic function to both metabolism and cognitive regulation.

These findings highlight tanycytes crucial role in brain-periphery communication, linking their function to type 2 diabetes and cognitive decline. The tanycytic BoNT/B mouse model offers insights into disease progression from prediabetes to advanced metabolic and cognitive disorders. Recognizing tanycytic transcytosis role in hormone transport could guide novel therapies addressing metabolic and cognitive comorbidities, particularly those worsening with age.



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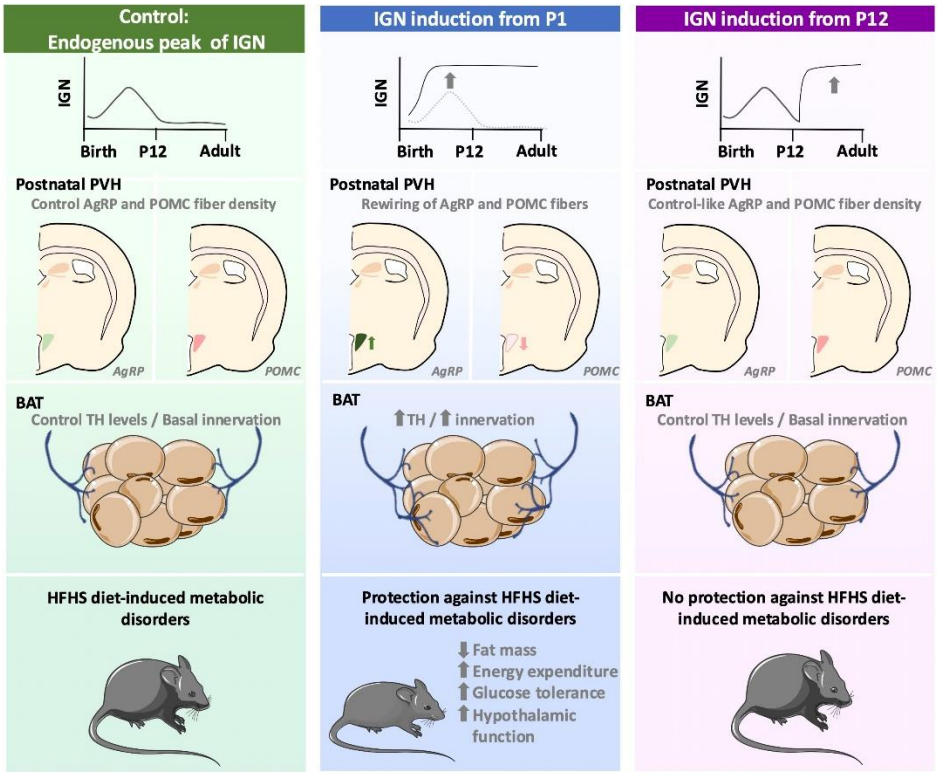
Intestinal gluconeogenesis controls the neonatal development of hypothalamic feeding circuits

Intestinal gluconeogenesis (IGN) is crucial for energy homeostasis through its signaling effects on the hypothalamus. During the neonatal period, IGN peaks alongside a leptin surge that regulates hypothalamic axonal outgrowth and peripheral autonomic innervation. This study explored the impact of the neonatal peak of IGN on the development of hypothalamic feeding circuits, adipose tissue innervation, and long-term metabolic health.

Using mice genetically engineered to overexpress *G6pc1*, the catalytic subunit of glucose-6-phosphatase, in the intestine, we induced neonatal IGN either from birth (P1) or after the endogenous peak (12 days later (P12)). In 20-day-old pups, IGN induction from P1 reorganized Agouti-related protein (AgRP) and Pro-opiomelanocortin (POMC) axonal projections to the paraventricular nucleus of the hypothalamus. It also increased tyrosine hydroxylase levels in brown adipose tissue, indicating enhanced sympathetic innervation. In adulthood, mice with IGN induction from P1 exhibited reduced fat mass, and resistance to high-fat/high-sucrose diet-induced metabolic disorders. However, none of these effects occurred when IGN was induced from P12.

This study highlights the critical role of neonatal IGN in shaping hypothalamic feeding circuits and adipose tissue innervation during a limited perinatal window. Early-life IGN induction could be a novel approach to improving metabolic resilience and preventing obesity-related disorders in adulthood.



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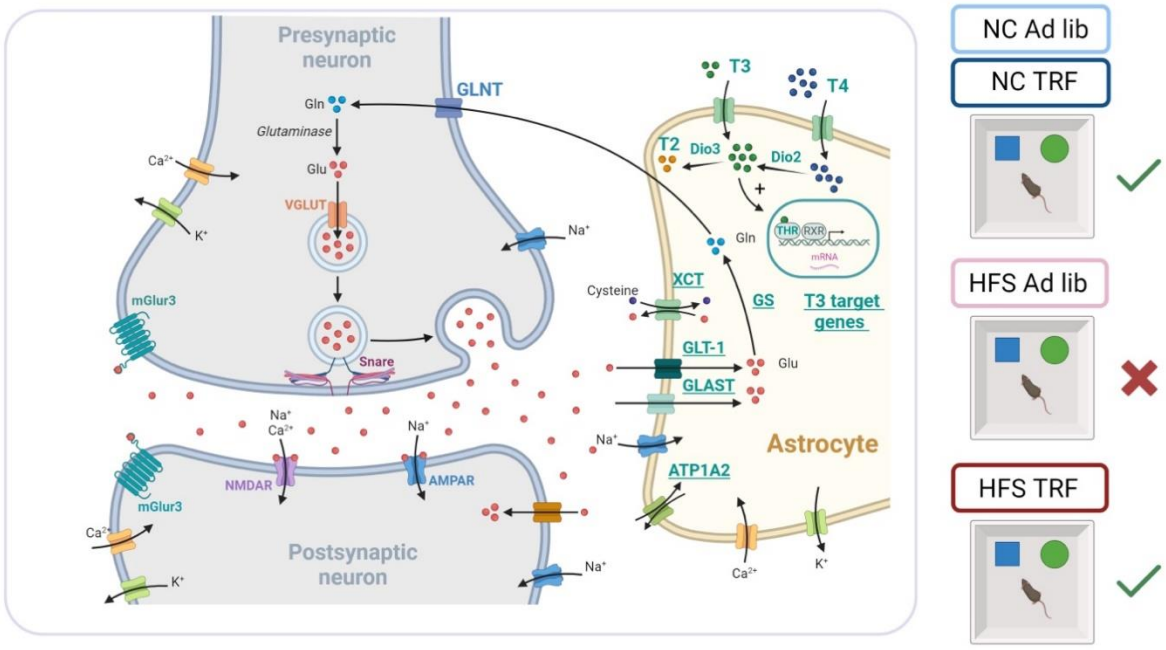
Time-restricted feeding prevents memory impairments induced by obesogenic diet consumption, via hippocampal thyroid hormone signaling.

Obese subjects show alterations in memory processes as well as in circadian biological rhythms. This is particularly worrisome in adolescents whose brains are still maturing. The objectives of this project were at understanding the cellular and molecular mechanisms underlying the therapeutic effect of time-restricted feeding (TRF) on obesity associated memory impairments. TRF is a nutritional intervention where food intake is re-aligned to circadian rhythms without calorie restriction. We identified behavioral and hippocampal molecular circadian disruptions in our model of juvenile consumption of obesogenic (HFS) diet A 4-week TRF protocol was sufficient to prevent the alteration of circadian rhythms of food intake, respiratory exchange ratio and energy expenditure observed in mice consuming HFS diet *ad libitum* since weaning. This TRF protocol also displayed beneficial effects on hippocampal-dependent memory deficits observed in mice with unlimited access to HFS diet, independently of body fat levels. Finally, TRF also normalized part of the hippocampal translatome altered by *ad libitum* HFS diet consumption and restored the diurnal expression of genes that displayed blunted expression under *ad libitum* HFS diet. In particular, *ad libitum* HFS diet led to a reduced response of the thyroid hormone signaling pathway during memory formation that was rescued by TRF.



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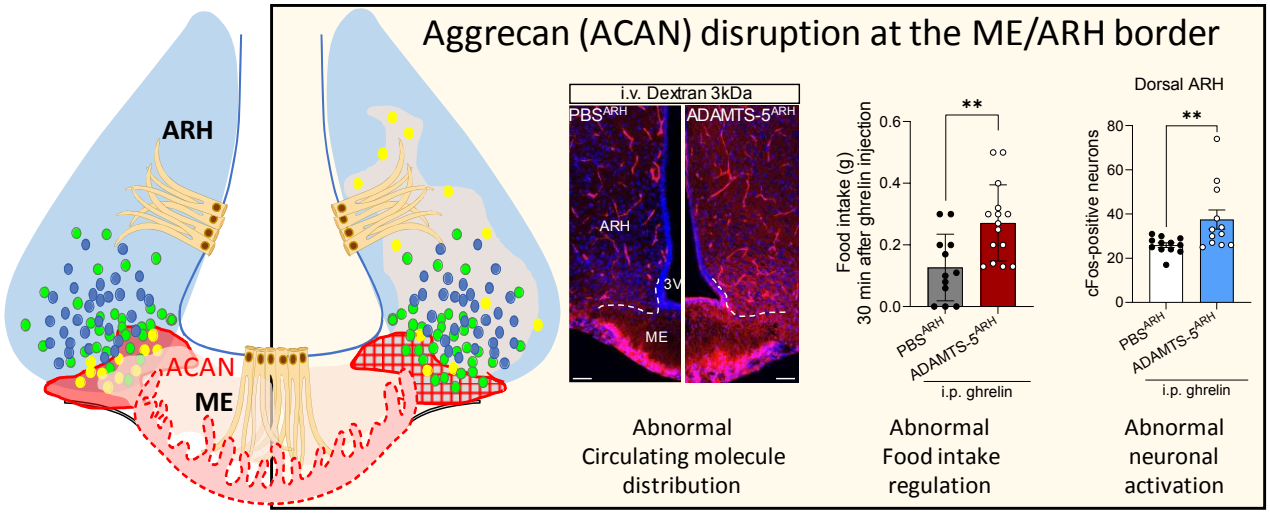
A plastic aggrecan barrier modulated by peripheral energy state gates metabolic signal access to arcuate neurons.

The arcuate nucleus of the hypothalamus (ARH) contains neurons vital to the maintenance of energy homeostasis that sense blood-borne metabolic hormones, signal changes in metabolic state and orchestrate the appropriate adaptive response. Despite the juxtaposition of the ARH with the median eminence (ME), a circumventricular organ devoid of a typical blood-brain-barrier, only a few ventral ARH neurons have direct access to blood-borne molecules extravasating into the ME parenchyma due to the existence of a dorsolateral diffusion barrier of unknown nature. Here, Laura Kuczynski-Noyau, Sixtine Karmann, and colleagues show that the deposition of aggrecan, a perineural net proteoglycan, by ARH neuropeptide Y (NPY) neurons create a peculiar ventrodorsal diffusion gradient. Fasting triggers additional aggrecan deposition more dorsally, reinforcing the diffusion barrier, particularly around NPY neurons adjacent to ME capillary loops that enter the ARH and become fenestrated under food deprivation. Genetic or aggrecanase-mediated disruption of aggrecan deposits results in the unregulated diffusion of blood-borne molecules, including ghrelin, into the ARH and impairs the physiological response to refeeding. Our findings reveal the molecular nature and plasticity of the previously unexplained ME/ARH diffusion barrier, and indicate a novel physiological role for this perineural net in hypothalamic metabolic hormone sensing and, thus, energy homeostasis.



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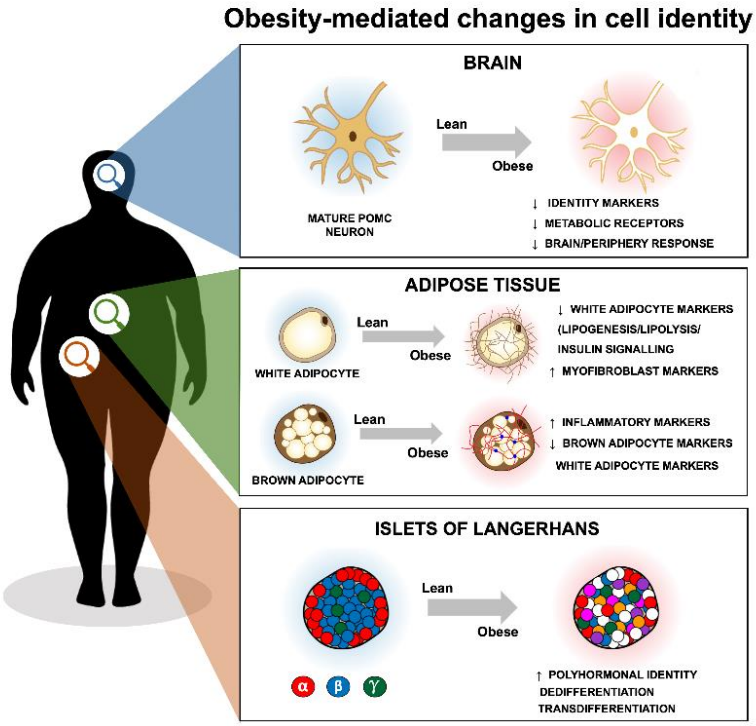
Single cell tracing of Pomc neurons reveals recruitment of 'Ghost' subtypes with atypical identity in a mouse model of obesity

The paper explores the complex relationship between obesity and the hypothalamus, a region rich in diverse neurons that regulate behaviour and metabolism. These neurons play a critical role in monitoring the body's energy needs through crosstalk with peripheral signals. Contrary to the traditional view that neural diversity in the hypothalamus is fixed after development, the evidence presented challenges this idea.

Using state-of-the-art lineage tracing and single cell profiling of hypothalamic pre-opiomelanocortin (Pomc) expressing neurons in adult mice, we have uncovered 'ghost' neurons characterised by minimal expression of both the key identity marker Pomc and several other markers that define this neuronal population.

Unlike classical Pomc neurons, 'ghost' neurons have unique molecular properties that make them undetectable by standard neuroanatomical techniques and promoter-based reporter mice used in Pomc research. These atypical neurons also display different functional properties. Notably, the number of 'ghost' neurons increases in diet-induced obese mice without the involvement of neurogenesis or cell death, suggesting a potential adaptability of neuronal identities in response to obesity-related stimuli.

This study highlights how changes in adult neuronal identity maintenance may be closely linked to maladaptive hypothalamic functions in obesity. It also suggests the potential for identifying molecular targets that modulate neuronal identity as a treatment for obesity and metabolic disorders.



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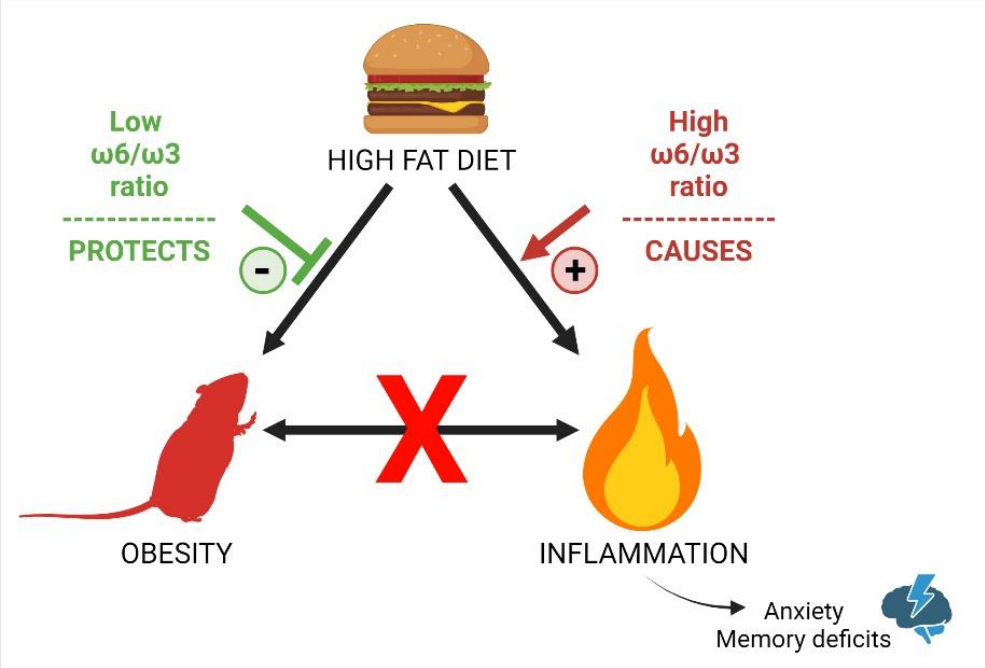
Dietary fatty acid composition drives neuroinflammation and impaired behavior in obesity

Nutrient composition in obesogenic diets may influence the severity of disorders associated with obesity such as insulin-resistance and chronic inflammation. Here we hypothesized that obesogenic diets rich in fat and varying in fatty acid composition, particularly in omega 6 (ω6) to omega 3 (ω3) ratio, have various effects on energy metabolism, neuroinflammation and behavior. Mice were fed either a control diet or a high fat diet (HFD) containing either low (LO), medium (ME) or high (HI) ω6/ω3 ratio. Mice from the HFD-LO group consumed less calories and exhibited less body weight gain compared to other HFD groups. Both HFD-ME and HFD-HI impaired glucose metabolism while HFD-LO partly prevented insulin intolerance and was associated with normal leptin levels despite higher subcutaneous and perigonadal adiposity. Only HFD-HI increased anxiety and impaired spatial memory, together with increased inflammation in the hypothalamus and hippocampus. Our results show that impaired glucose metabolism and neuroinflammation are uncoupled, and support that diets with a high ω6/ω3 ratio are associated with neuroinflammation and the behavioral deterioration coupled with the consumption of diets rich in fat.



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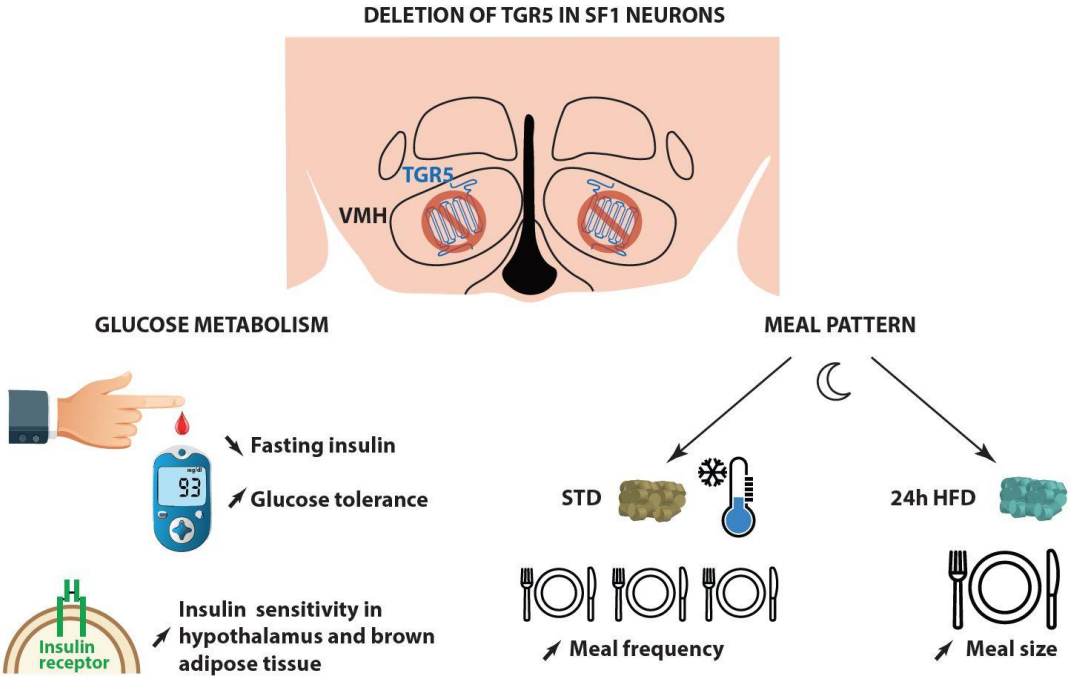
TGR5 receptors in SF1-expressing neurons of the ventromedial hypothalamus regulate glucose homeostasis

Steroidogenic factor-1 (SF1) neurons in the ventromedial hypothalamus play essential roles in regulating energy balance and glucose homeostasis. The bile acid receptor Takeda G protein-coupled receptor 5 (TGR5), which is expressed in the hypothalamus, controls some of the effects of bile acids on food intake and body weight through mechanisms that are not yet well understood. In this study, we utilized a genetic approach alongside metabolic phenotyping and molecular analyses to examine the impact of TGR5 deletion in SF1 neurons on energy balance and glucose metabolism.

Our findings indicate that TGR5 in SF1 neurons does not significantly affect food intake or body weight under standard chow conditions. However, it does play a role in the adaptive feeding response to acute exposure to cold or a high-fat diet without altering energy expenditure. Importantly, TGR5 in SF1 neurons appears to inhibit glucose metabolism, as the deletion of this receptor enhances whole-body glucose uptake and improves insulin signaling in both the hypothalamus and brown adipose tissue. These results provide new insights into the role of neuronal TGR5 in metabolic regulation, demonstrating that TGR5 in SF1 neurons promotes satiety by altering meal patterns in response to metabolic signals, while also influencing whole-body insulin sensitivity.



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