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NeuroFrance 2023 – from basic neuroscience to translational discoveries



After the hindrance imposed by the COVID-19 pandemic, neuroscience research pushed forward.

NeuroFrance 2023 took place as an in-person meeting and highlighted current and future strategies for exploring the brain and its pathologies, including a strong pathway to mental health research.

Every 2 years, at the beginning of summer, NeuroFrance, the largest neuroscience conference in France, takes place. After a virtual event in 2021, it was exciting to return to an in-person conference. At the NeuroFrance 2023 edition, held in the beautiful city of Lyon, various published and unpublished data were presented, and new ideas as well as new perspectives were exchanged.

NeuroFrance is organized by the French Neuroscience Society (*Société des Neurosciences*), established in 1988, with the aim of promoting interactions between researchers from all neuroscience backgrounds. This year, the congress took place over 3 days, from 24 May to 26 May, comprising an opening ceremony, 8 plenary lectures, 35 parallel symposia and more than 200 posters. The French Club of Glial Cells and the French Society for Sleep Research and Medicine also hosted dedicated symposia during the congress. Two satellite events were organized and held before the meeting: the Glial Cell Day for Young Researchers, and the French Neuroethology Club. Additionally, two satellite workshops on translational research presented the state of the art on current topics and encouraged interactions between medical interns and young researchers from various fields. Here are some of the highlights of the NeuroFrance conference.

Plenary keynotes

Among the plenary keynotes, which were all excellent and thematically varied, Thomas Bourgeron (Institut Pasteur, Paris Diderot University) provided a comprehensive view of the complexity of the genetics of autism made by a combination of common variants

and rare variants. Such variants increase the probability of developing autism by modulating chromatin remodeling, protein synthesis and degradation, and synaptic physiology. In a recent large-scale study of more than 200,000 undiagnosed participants, his team showed that beyond the autism diagnosis, these variants were associated with a small but significant decrease in fluid intelligence, qualification level and income, as well as an increase in metrics related to material deprivation¹. He has advocated for more participative research involving autistic people and their families for better support and integration (<https://www.r2d2-mh.eu/>).

Ila Fiete (Massachusetts Institute of Technology) presented her work on how neural dynamics and connectivity constraints drive the emergence of function. From a bottom-up perspective, she developed computational models to predict how molecules and cell types influence circuits, how these circuits impact system-level dynamics and, ultimately, how they influence behavior².

Frank Polleux (Columbia University) presented his work on characterizing genomic changes that serve as human-specific modifiers of cortical development and function. Throughout evolution, the human brain has undergone cortical expansion, developed distinct physiological properties of neurons and modified synaptic development to facilitate advanced cognitive functions. Polleux elucidated the role of human-specific gene duplications as determining factors in brain development and evolution³. These genetic modifications are critical regulators of synaptic development and maturation that increase the density of excitatory and inhibitory synapses, which leads to long-lasting changes in synaptic density throughout adulthood.

Nora Abrous (INSERM, Bordeaux Neurocampus) dispelled the neuromyth about adult neurogenesis in the mammalian brain. Through her research, she clarified the distinction between developmental hippocampal neurogenesis and adult hippocampal neurogenesis. Her investigations in rats revealed that electrophysiological stimulation of adult-born neurons in the hippocampus can

enhance the precision and robustness of distant memories. This process can thus counter the natural fading of memory traces as time progresses. Abrous framed this phenomenon of adult neurogenesis as a 'Baldwin effect' that enables behavioral adaptation through non-genetic and non-hereditary means⁴. This process could also account for individual variability that extends beyond genetic diversity and opens new avenues for treating memory problems that may arise over time.

In her plenary presentation, Marion Leboyer (Paris-Est Créteil University) focused on the relationship between immune dysfunction and psychiatric disorders. She explored how specific infections are linked to an increased risk of developing psychiatric conditions. Through investigation of COVID-19 cohorts, her group observed significant correlations between people with psychotic disorders, a strong antibody response to SARS-CoV-2 (the coronavirus responsible for COVID-19), the presence of retro-transposable genetic elements (HERVs) and elevated levels of pro-inflammatory cytokines⁵. These findings suggest that SARS-CoV-2 infection did not result in severe COVID-19 among these patients but affected the expression of HERVs and cytokines. These results underscore the importance of customized therapeutic approaches in fighting infections.

Alfred Fessard lecture

This year, the Alfred Fessard lecture, which serves as recognition by the French Neuroscience Society of a researcher's entire career, was given by Vincent Prévot (Lille University, INSERM) and was titled 'The Neuroendocrine Key to the Brain Aging Enigma'.

Prévot's scientific work has contributed substantially to understanding of the essential dialog between the brain and the body. Specifically, Prévot has discovered that tanyocytes, which are special ependymocytes that line the base of the third ventricle and form a bridge, via their extensions, between the cerebrospinal fluid and the hypophyseal portal circulation, serve a crucial role in neuroendocrine processes.

His recent work was on the role of neurons that release gonadotropin-releasing hormone

(GnRH) in controlling postnatal brain maturation, pre-pubertal growth and adult cognition. Noting that children born prematurely have a greater risk of developing cognitive and sensory disorders, as well as infertility, in adulthood, he has focused on congenital hypogonadotropic hypogonadism, a rare disease induced by the deficient production, secretion or action of GnRH. Of note, GnRH controls the development and functioning of male and female gonads. Thus, Prévot studied nitric oxide (a neurotransmitter that regulates the activity of GnRH neurons) and, more particularly, the enzyme that synthesizes it: neuronal nitric oxide synthase (nNOS). After rare mutations in the gene encoding nNOS were found in a cohort of patients with this disease, the therapeutic potential of nitric oxide was then tested in nNOS-deficient mice shortly after birth; the results showed that this molecule was able to reverse problems of puberty and sensory and neurological disorders⁶. Going further, Prévot launched a clinical trial with the University Hospital of Lille (France) and the Children's Hospital in Athens (Greece) to measure the effect of nitric oxide on premature children. His work, from bench to bedside, represents an exemplary and inspiring career for the entire scientific community.

Neuropeptide-induced regulation of astro-neuronal networks and behavior

Alexandre Charlet (University of Strasbourg, CNRS) chaired and began this symposium by focusing on the recent topic of the contribution of astroglia to neuropeptidergic modulations. He described his findings on the role of astrocytes in the modulation of fear behavior by oxytocin. The central amygdala is a key brain region that underlies this behavior, and it is known to be regulated by oxytocinergic inputs that promote a positive anxiolytic emotional state. The research described here showed that this takes place through a subset of central amygdala astrocytes that express oxytocin receptors, whose activation leads to astroglial-signaling-upregulating activity of nearby interneurons via activation of the N-methyl-D-aspartate receptor. These findings were confirmed in a presentation by Laura Boi (University of Regensburg) that also put forward the proposal of a key role for astroglial-gap-junction-mediated networks in oxytocin-driven anxiolysis. Another function of the gap-junction protein connexin 30 was highlighted by Nathalie Rouach (Collège de France, INSERM), who presented findings showing that the non-channel-signaling function of connexin 30 controls the structural remodeling of supraoptic hypothalamic

astrocytes known to modulate oxytocin levels and maternal behavior. The maturation of female reproductive function controlled by preoptic hypothalamic neurons that produce GnRH was then shown by Ariane Sharif (Université de Lille) to require the recruitment of astrocytes during early postnatal development. At puberty, recruited astrocytes associated with GnRH neurons release prostaglandin D₂ to stimulate neuronal electrical and secretory activity and thus participate in the induction of the first ovulation. Finally, Vinícius Elias de Moura Oliveira (Université de Liège) ended the session by describing how hypothalamic oxytocin increases aggressive behavior in virgin female rats only, whereas aggressive behavior in male rats is promoted by GnRH. In both sexes, kisspeptin originating from the periventricular hypothalamic area conversely decreases aggressive behavior. Collectively, the research presented in this symposium highlighted the emergence of a novel research field that takes into consideration neuroglial interactions in the intercellular signaling underlying neuropeptidic modulation of behavior.

Glial cells' contributions to neurodevelopment

The role of microglia throughout the lifespan was first considered in this symposium with the research of David Munro (University of Edinburgh) showing that deficiency in microglia affects other brain cells only mildly during youth but results in major dysregulation at later life stages, which suggests that microglial cells provide resilience against detrimental brain changes that occur during aging. Claudia Pascqualini (Gustave Roussy) presented her work on the development of microglia-sufficient brain organoids from induced pluripotent stem cells and how this can improve understanding of the role of innate immunity in the progression of the brain to pediatric cancer. The genesis of a heterogeneous subpopulation of astrocytes was then shown by Karine Loulier (University of Montpellier, INSERM) to originate not only from the pallium but also from the sub-pallial area. The different astroglial populations mentioned showed considerable variability in terms of molecular signature, structural organization, localization, and number and subtype of cells generated. Martine Cohen-Salmon (Collège de France, CNRS) focused on the perivascular end of the astrocyte, showing how deletion of the astrocytic membrane protein MLC1 causes the rare disease megalencephalic leukoencephalopathy with subcortical cysts (MLC). Loss of MLC1 function causes defects in the postnatal

maturation of perivascular astrocyte coverage, as well as in vascular smooth muscle cell contractility, neurovascular coupling and parenchymal cerebrospinal fluid flow. These defects in development of the gliovascular unit are primary events in the pathogenesis of MLC and represent therapeutic targets for this disease. Shayan Moghimiyyiroozabad (Collège de France) closed this session by touching on the functional heterogeneity of oligodendrocytes. The findings presented here indicate the occurrence of non-redundant subpopulations of oligodendrocytes that seem to be genetically defined. A general take-home message here is the complexity of postnatal brain development, as it includes not only neurons but also all types of glial cells, organized into spatially and temporally distinct subpopulations.

The microbiota's contribution to socioemotional impairment in psychiatric disorders

Sylvie Rabot (Université Paris-Saclay, INRAE) began this symposium by presenting her findings on how the gut microbiota affects brain function and behavior. She highlighted the finding that only a limited number of microbiota-produced metabolites have the potential to affect emotional behavior. Her studies demonstrated that excessive indole production by the gut microbiota is associated with anxiety and depression-like behaviors in rodents, with the vagus nerve mediating these effects. In humans, evidence from a case-control study of the French NutriNet-Santé cohort also revealed a positive correlation between the urinary biomarker 3-indoxylsulfate – which reflects the gut microbiota's indole production – and recurrent depressive symptoms⁷. Consequently, these insights indicate that assessing the gut microbiota's composition and metabolic activities could prove pivotal in the prevention and therapeutic management of emotional disorders.

Jérome Becker (University of Tours, INSERM) presented the impact of perinatal exposure to a maternal Western diet on the socioemotional behavior of offspring. Female mice received a Western diet, which constituted a large intake of processed foods notably enriched with fats and sugars. This regimen was initiated 1 week before mice were mated and continued until weaning. The offspring derived from these mice showed greater weight gain, accelerated development, hyperactivity and social interaction deficits in early postnatal period than control offspring of mothers fed a healthy diet. Transfer of fecal matter between mice exposed to a Western diet and those exposed to a healthy

diet in adulthood also reproduced these behavioral changes. Becker's results confirm the critical effect of maternal nutrition on neurodevelopment and suggest that early exposure to a Western diet could be a risk factor for autism spectrum disorder. A presentation by Laetitia Davidovic (Institute of Molecular and Cellular Pharmacology, CNRS) further demonstrated that the microbial metabolite *p*-cresol selectively induces core behavioral signs of autism spectrum disorder in mice. The study found that social behavior deficits caused by *p*-cresol are dependent on alterations in the composition of the microbiota. These findings suggest potential therapeutic interventions for autism spectrum disorder, such as targeting the microbiota and *p*-cresol production⁸.

Advances in signaling and treatments for inflammatory pain syndromes

Nathalie Vergnolle (Digestive Health Research Institute, INSERM) led off this symposium by presenting recent progress in potential treatments for visceral hypersensitivity and chronic pain, fields that are often inadequately studied or considered. She drew attention to peripheral factors that stimulate the nociceptors in the gut and further cause central sensitization in patients with inflammatory bowel disease (or in models of inflammatory bowel disease). She emphasized that microbial factors, epithelial factors, ion channels, thrombin and immune-based mediators are strategic targets for mitigating visceral pain.

Cédric Peirs (University of Clermont Auvergne, INSERM) then went on to probe deeper into the microcircuits that distinguish inflammatory pain from neuropathic pain. Hanns Ulrich Zeilhofer (University of Zurich) shed light on the dorsal horn circuits associated with inflammatory hyperalgesia. Nicolas Cenac (Digestive Health Research Institute, INSERM) introduced the concept of using bacterial lipopeptides that contain γ -aminobutyric acid as potential future treatments for visceral pain. Concluding the session, Sarah Mountadem (University of Clermont Auvergne) underscored the crucial role of astrocytes in maintaining chronic pain and central sensitization, mediated through astrocyte-produced elements and receptors and/or channels. It is therefore clear that there is an urgent need to better understand inflammatory and neuropathic pain and search for appropriate treatments.

Workshop on sleep and rhythms: from the clinic to basic research

This workshop, coordinated by Christelle Peyron (University of Lyon, CNRS), Laure

Peter-Derex (McGill University) and Ouria Dkissi-Benyahya (University of Lyon, INSERM), was devised with the following three key objectives: (1) elucidate the mechanisms that underpin the regulation of alertness states; (2) identify the primary sleep disorders that stem from dysfunctions in the systems of wakefulness, sleep and circadian regulation; and (3) understand the connection between neurodegenerative diseases and sleep disorders. After a cross-sectional description of the major fields in the area of sleep and biological rhythms presented by Christina Schmidt (University of Liège), Jean-Arthur Micoulaud-Franchi (University of Bordeaux) presented the pathophysiological aspects of sleep and reflected on how to classify these disorders. On the basis of the hypothesis that most symptoms stemming from the central nervous system allow better understanding of the place of sleep dysfunctions in mental disorders, Micoulaud-Franchi identified 34 different symptoms among the 53 diagnostic criteria of the DSM-5 for the nine main disorders of the 'Sleep-Wake Disorders' section⁹. This work aims at a better understanding of the complexity of sleep and wake disorders, promoting research linking symptoms architecture to relevant biological, psychological and sociocultural factors.

Géraldine Rauchs (University of Caen-Normandie, INSERM) then tackled the question of whether sleep dysfunction is a risk factor that leads to neurological diseases by showing a complex bidirectional link between sleep and neurodegenerative diseases¹⁰. Her group showed that fewer than 6 hours sleep per night favor the development of Alzheimer's disease by exacerbating the amyloid- β (A β) burden¹¹, which in return decreases the quality of sleep by reducing the amplitude of delta frequencies during slow-wave sleep, as well as theta rhythm during rapid-eye-movement phases¹². Sleep apnea was also shown to favor neuroinflammation and reactive gliosis, leading to increased deposition of A β peptide and an elevated risk of dementia. Thus, it was hinted that early polysomnography may help in evaluation of the A β burden, making the results of sleep analysis an early biomarker for the progression of Alzheimer's disease.

Meeting of the local committees of Brain Awareness Week

Simultaneously organized in a hundred countries globally, Brain Awareness Week (BAW) aims to raise public awareness of the importance of brain research. BAW represents an opportunity for many researchers

to meet the public and present advances and highlights of their findings, challenges in understanding the brain and implications for society. In France, BAW has been held in March of every year since 1999, and it is coordinated by the Society of Neurosciences. In 2023, more than 600 events took place in more than 120 cities in France. Therefore, NeuroFrance also represents a unique opportunity for the leaders of the various local committees to meet, review their activities and discuss new projects to launch.

In conclusion, NeuroFrance 2023 was a huge success, finally allowing the French scientific community to meet in person once again. A social event at the Hard Rock Cafe also allowed informal interactions, as science extends beyond the routine of reading papers, doing experiments, tuning into Zoom discussions and remaining desk-bound to write grants or papers. NeuroFrance 2023 was therefore a privileged opportunity to gain perspective on neuroscience research topics and open up to new collaborations. Once again, NeuroFrance has showcased the pivotal role of basic research in identifying novel therapeutic targets and presented new translational approaches, promising substantial advancements in the understanding and treatment of mental health. We look forward to the next exciting NeuroFrance meeting in Montpellier, 14–16 May 2025!

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Competing interests

The authors declare no competing interests.