



Annual Report 2019

Key Figures - 2019



Table of contents

Editorial.....	page 4
Highlights.....	page 6
A unique model.....	page 11
OUR SCIENTIFIC STRATEGY.....	page 12
Paris Brain Institute teams.....	page 14
Cellular and molecular neurobiology.....	page 16
Integrative neurophysiology.....	page 18
Cognitive neuroscience.....	page 20
Clinical and translational neuroscience.....	page 22
Neuroinformatics.....	page 24
Core facilities of the Paris Brain Institute.....	page 26
Technological advances.....	page 28
RESEARCH APPLICATIONS.....	page 30
CLINICAL RESEARCH AND CARE : patients at the heart of our priorities.....	page 34
EDUCATION AND TRAINING.....	page 40
The Paris Brain Institute, its national and international network.....	page 44
LIFE AT THE PARIS BRAIN INSTITUTE.....	PAGE 46
Sharing and passing along knowledge.....	page 47
Patronage, donations and bequests.....	page 50
Corporate social responsibility.....	Page 52
Governance.....	page 54
Financial report.....	page 57
Thank you.....	page 61

Editorial

Prof. Gérard Saillant, President of the Paris Brain Institute

“**A**t the Paris Brain Institute, we come together around shared values that are at the core of our daily activities. We share an innovative and ambitious project that bring women and men with different talents and backgrounds together, for whom sharing means progress and a means of achieving our goal towards the greater good: searching, finding, and curing. As you will discover in this 2019 Annual Report, the past year was filled with advances on a scientific, clinical and societal level. This was made possible by the many individuals involved in our project: researchers, donors, and partners, who helped carry our Institute to the forefront of research in neuroscience in Europe and abroad thanks to their work and dedication. As our Institute celebrates its 10-year anniversary, it is time to launch a new phase of our growth. We therefore decided on a change that reflects this: in 2020, ICM becomes the Paris Brain Institute. A simple name that reflects the clarity we are hoping to bring as we open to society and its neuroscience research challenges. The ICM acronym will remain, in honor of our history and our important breakthroughs on the nervous system and its diseases in the past 10 years. Our name may change, yet our research missions remain on course.

I would like to extend my sincerest thanks once again. We have gotten to where we are together, and together, we will take the Paris Brain Institute to new heights.”



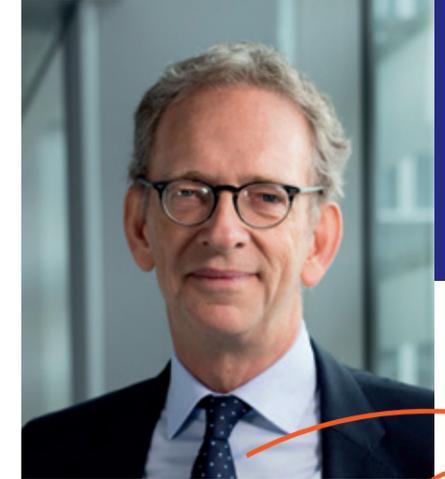
Corinne Fortin, Secretary General of the Paris Brain Institute

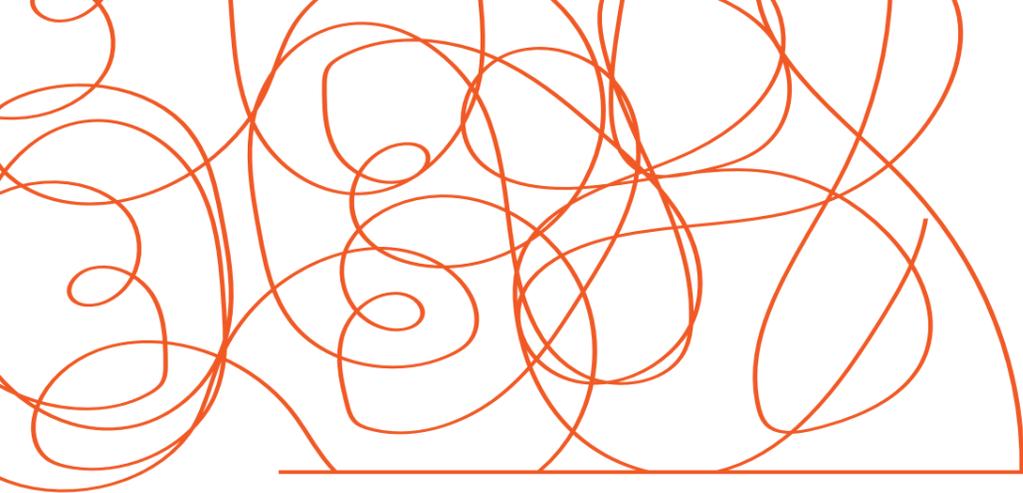
“**T**he Paris Brain Institute is a unique ecosystem at the heart of Paris. It is a prime example of a successful partnership between a private foundation and a public research unit, located in the largest neurological hospital in Europe. Since it was built, its excellence has been highlighted on numerous occasions: with the IHU program, Carnot accreditation, and more recently French Tech Seed certification, first of its kind for a research institute. This was made possible thanks to the hard work of research teams and platforms on a daily basis and with administrative support. Administrative service and support staff help design a meticulous, simple, flexible and dynamic framework that frees researchers from useless constraints and opens new funding opportunities for ambitious projects. The Institute is experiencing continued growth both on a scientific level and in terms of resources, as you will discover in this 2019 Annual Report. To stay in line with this dynamic, we must focus on applying « rigorous flexibility » to our actions. We will continue to strive towards lightening the administrative load for our researchers and remaining firm in our respect of regulations and our standards of excellence for our organization.”



Prof. Alexis Brice, Chief Executive of the Paris Brain Institute

“**2019** – what a year! Many changes took place on both a scientific and administrative level and thanks to the hard work of the Paris Brain Institute’s teams as a whole, we can be very proud of the results of this past year. The development of a new Mixed Research Unit (UMR) with our public partners and a new administration, as well as the renewal of our University-Hospital Institute accreditation following an international assessment by the National Research Agency (ANR), highlight our scientific credibility as well the financial credibility of our public-private partnership model and its results. We acquired a building located at rue du Chevaleret to grow further and improve research transfer, a sign of the Institute’s scientific, commercial, and financial growth. 2019 was also the year 13 iCRIN, neuroscience clinical research infrastructures, were designed. They are a testament to the Paris Brain Institute’s involvement in clinical research and illustrate the close proximity with the medical community at the Neuroscience Medical University Department of Pitié-Salpêtrière Hospital. 2019 was also the year of the Open Brain School certified as “training organization” which brings together all our teaching and training programs. We have cause to celebrate the advances of our research teams, with an even greater number of publications in high impact factor scientific journals, success in obtaining national and international awards and funding and especially three new ERC (European Research Council) grants, highly competitive grants that highlight the quality of our researchers’ work. Now is the time for continued effort to reach even further. We must continue to recruit talented researchers to support our dynamic and cutting-edge ecosystem. We must focus on developing new technology to have the best instruments at our disposal and achieve even greater breakthroughs. We must also look at nervous system functioning and diseases under novel angles, which requires teaming up with experts in multiple fields. Our strength lies in getting researchers to work together in an interdisciplinary manner to bring new concepts to life.”





Highlights

In 2019, the Paris Brain Institute welcomed two new team leaders: Nathalie Cartier, head of the “Gene and cell therapy” team and Jaime de Juan-Sanz, holder of the Diane Barrière Chair “Molecular physiology of synaptic bioenergetics”.

“**O**ne of the things I really enjoy about the Paris Brain Institute is the concentration of forces and means on neuroscience. The idea that all my colleagues are conducting very different research ranging from clinical trials to molecular biology, networks, and diseases is very exciting! It is a great place to learn about all the aspects of neuroscience I am not an expert in, but also to have the opportunity to help others with my knowledge of molecular neurobiology, imaging and biosensors.”

Jaime de Juan-Sanz



“**W**hy the Paris Brain Institute? Its environment, of course. Collaborations with research teams and clinicians, access to clinical research, to patients, the Clinical Investigation Center and the iPEPS. This whole ecosystem fosters research and scientific and medical advances. This energy is also very important for establishing industrial partnerships. Pitié-Salpêtrière Hospital is an international benchmark. I think the Paris Brain Institute can become an essential location in terms of neuroscience research and clinical work.”

Nathalie Cartier (Inserm)



Paris Brain Institute receives certification as part of the “French Tech Seed”

The Paris Brain Institute has just been selected and certified by the State as part of the “French Tech Seed” Fund managed by Bpifrance. This certification confirms the dynamic strategy undertaken by its iPEPS bio-incubator towards entrepreneurship, with strong field-wide expertise in neurology and psychiatry.



Visit of Raymond G. Chambers, WHO ambassador for global strategy

On April 4, 2019, the Brain Institute hosted Raymond G. Chambers, WHO ambassador for global strategy and American philanthropist, for a visit and meetings with Institute researchers. He responded to an invitation from Jean Todt, vice-president of the Paris Brain Institute. As WHO ambassador, Raymond G. Chambers aims to help this international organization bring the international community together to advance global health action within the framework of the sustainable development goals set for 2030 by the United Nations.

A Parkinson’s disease project wins the Health data hub call for projects!

The NS-Park project of the Paris Brain Institute is one of the winners of the “Health Data Hub” call for projects by the Ministry of Solidarity and Health, with the aim of facilitating interactions between producers of health data, users and citizens, with the utmost security for the development of research innovations. It is coordinated by Professor Jean-Christophe Corvol (Sorbonne University / APHP), team leader at the Paris Brain Institute and neurologist at Pitié-Salpêtrière Hospital, in collaboration with Stanley Durrleman (INRIA), team leader at the Paris Brain Institute and coordinator of the neuroinformatics center, Prof. Florence Tubach, epidemiologist at Pitié-Salpêtrière Hospital, Prof. Olivier Rascol and Dr. Maryse Lapeyre-Mestre of Toulouse University Hospital. Its aim is to provide neurologists with an instrument that predicts individual trajectories of Parkinson’s patients in order to implement appropriate preventive measures. The data from this cohort of 20,000 individuals monitored in centers dedicated to Parkinson’s disease will be linked to data from the National Healthcare Data System (SNDS) in order to improve overall patient care.

2019 Philanthropy Award: Paris Brain Institute and Euryale AM are winners!

The Paris Brain Institute and Euryale Asset Management were awarded the Grand Prize for Philanthropy thanks to their joint initiative to finance and philanthropy together: the SCPI Pierval Santé Sharing Fund.

The Paris Brain Institute receives the BFM RMC Organization Award at the BFM AWARDS

For the 15th edition of the BFM Awards, the Paris Brain Institute, represented by its founders Professor Gérard Saillant and Jean Todt, received the RMC BFM association award.



CAP’CARNOT: Carnot annual summer meeting at the Paris Brain Institute

The association of Carnot institutes organizes Cap’Carnot, a meeting of the Carnot institutes with innovation leaders, on a yearly basis. This year, the event took place at the Paris Brain Institute, also a member of the Carnot network. The 2019 edition of this meeting showcased artificial intelligence technologies applied to healthcare including biomonitoring, neuroscience research, medical diagnosis, machine learning and medical imaging.

The Paris Brain Institute partners with two university hospital research projects

Two projects in which the Paris Brain Institute is a partner are among the 15 recipients of the fourth call for projects for University Hospital Research (RHU). The COZY project, led by Dr Guillaume Canaud and involving Stéphanie Baulac (Inserm), team leader at the Paris Brain Institute, aims at developing new treatments for disharmonious overgrowth syndrome, a rare disease. The BETPSY project, led by Jérôme Honnorat, with the collaboration of Dr Agusti Alentorn of the Experimental Neuro-Oncology team, is tackling “encephalitis and paraneo-

plastic neurological syndromes caused by autoimmune reactions”. Their aim is to develop diagnostic tools for these diseases and improve patient care.

Launch of the Paris Brain Institute’s first masterclass on creativity

The Paris Brain Institute offers a wide range of training and education for neuro-experts and “neuro-curious”. Teaching benefits innovation and the individual and at the Paris Brain Institute, we believe it all starts with the brain. Organized with scientists from the Paris Brain Institute and experts from the American Society for Neuroscience, the aim of this masterclass was to uncover the secrets of creativity and introduce participants to their creative potentials and those of their colleagues.

The Symbiosis Prize for short scientific film goes to a Paris Brain Institute researcher

Nathalie Magne, post-doctoral fellow in the “Genetics and Development of Brain Tumors” team, won the Symbiosis competition with director Cyprien Bisot at the Pariscience International Scientific Film Festival for her short film “A glioma to demolish”.

The Paris Brain Institute obtains renewal and additional funding for its IHU program

The Paris Brain Institute obtained a 17-million-euro renewal of its IHU program. This renewal highlights the scientific, medical and economic efficiency of the “IHU model” implemented in 2010 following a call for projects from the Ministry of Higher Education and Research and the Ministry of Health, as part of the investments for the future program to strengthen the French attractiveness in the field of medical research. The goal is to provide France with several centers of excellence in research, care, training and technology transfer in healthcare. The Government confirms its support for biomedical research, a major issue for the country’s competitiveness, development of knowledge, innovation, and the improvement of scientific and medical practices.



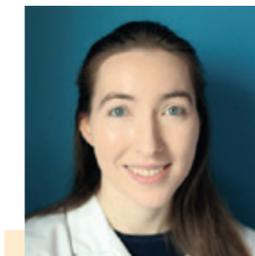
Awards and distinctions obtained by our researchers in 2019



Lamia Bouslama (Sorbonne Université) Team “Myelin plasticity and regeneration” — **Marie-Ange Bouvet-Labruyère Award**



Stéphanie Baulac (Inserm) Team “Genetics and physiopathology in epilepsy” — **Michael Foundation International Epilepsy Research Award** — **Robert Debré organization for medical research Award**



Sinead Gaubert (AP-HP) Team “Aramis: algorithms, models and methods for human brain imaging and signals” — **2019 Philippe Chatrier Award**



Claire Wyart (Inserm) Team “Spinal sensory signaling” — **Voted in as member of EMBO, the European Molecular Biology Organization**



Catherine Lubetzki (Sorbonne Université/AP-HP) Team “Remyelination in multiple sclerosis: from biology to clinical translation” — **2019 Charcot Award from the Multiple Sclerosis International Federation (MSIF)**



Julia Sliwa (CNRS) Team “MOV’IT: movement, investigation, therapeutics, normal and abnormal movement: physiopathology and experimental therapy” — **International Peter and Patricia Gruber Award from the Society for Neuroscience**



Ninon Burgos (CNRS) Team “Aramis: algorithms, models and methods for human brain imaging and signals” — **Cor Baayen Young Researcher Award**



Bassem Hassan (Inserm) Team “Brain development” — **2019 Roger de Spoelberch Award**

2019 Marie Skłodowska-Curie Actions

This year, 6 young researchers from the Paris Brain Institute were awarded a Marie Skłodowska-Curie Actions (MSCA) postdoctoral fellowship among 1,500 European laureates, with a total of 21 scholarships since the creation of the Institute. The Marie Skłodowska-Curie Actions (MSCA) scholarships are part of Horizon 2020, the EU's framework program for research and innovation. They are awarded to excellent postdoctoral researchers as well as exceptional doctoral and postdoctoral training programs.



Three ERCs for the Paris Brain Institute in 2019

Every year, the European Research Council (ERC) promotes the best scientific projects through competitive calls for projects open to all researchers from the European economic community. These grants support high-level exploratory research. According to the President of the ERC, Professor Jean-Pierre Bourguignon, "since 2007, the European Research Council has funded the most daring research projects and an independent evaluation has shown that this strategy has paid off. Researchers from across Europe are able to develop their best ideas for tomorrow's breakthrough discoveries."

In this ranking by scientific excellence, the Paris Brain Institute is continuously positioned at the forefront. Since 2012, our researchers have obtained 14 European grants for projects ranging from fundamental research to better understand the development and functioning of the healthy brain to applied research for neurological and psychiatric pathologies. In 2019, three researchers from our Institute were among the best in Europe and recipients of the ERC grant. These results highlight the quality of the research conducted at the Institute and the researchers recruited.

- **Jaime De Juan Sanz**, a young researcher who recently joined the institute as team leader, obtained an "ERC STARTING GRANT" intended to encourage projects carried out by researchers 2 to 7 years after obtaining their doctorate and dedicated to building a research team to carry out a high-level scientific project. The "SYNAPTOENERGY" project aims to identify neural energy deficits responsible for pathologies such as epilepsy.



- **Fabrizio De Vico Fallani (INRIA)**, researcher in the team led by Olivier Colliot and Stanley Durrleman, obtained an "ERC CONSOLIDATOR GRANT" for project "BCINET" dedicated to understanding and decoding connections between neurons to promote motor skill recovery after a stroke.



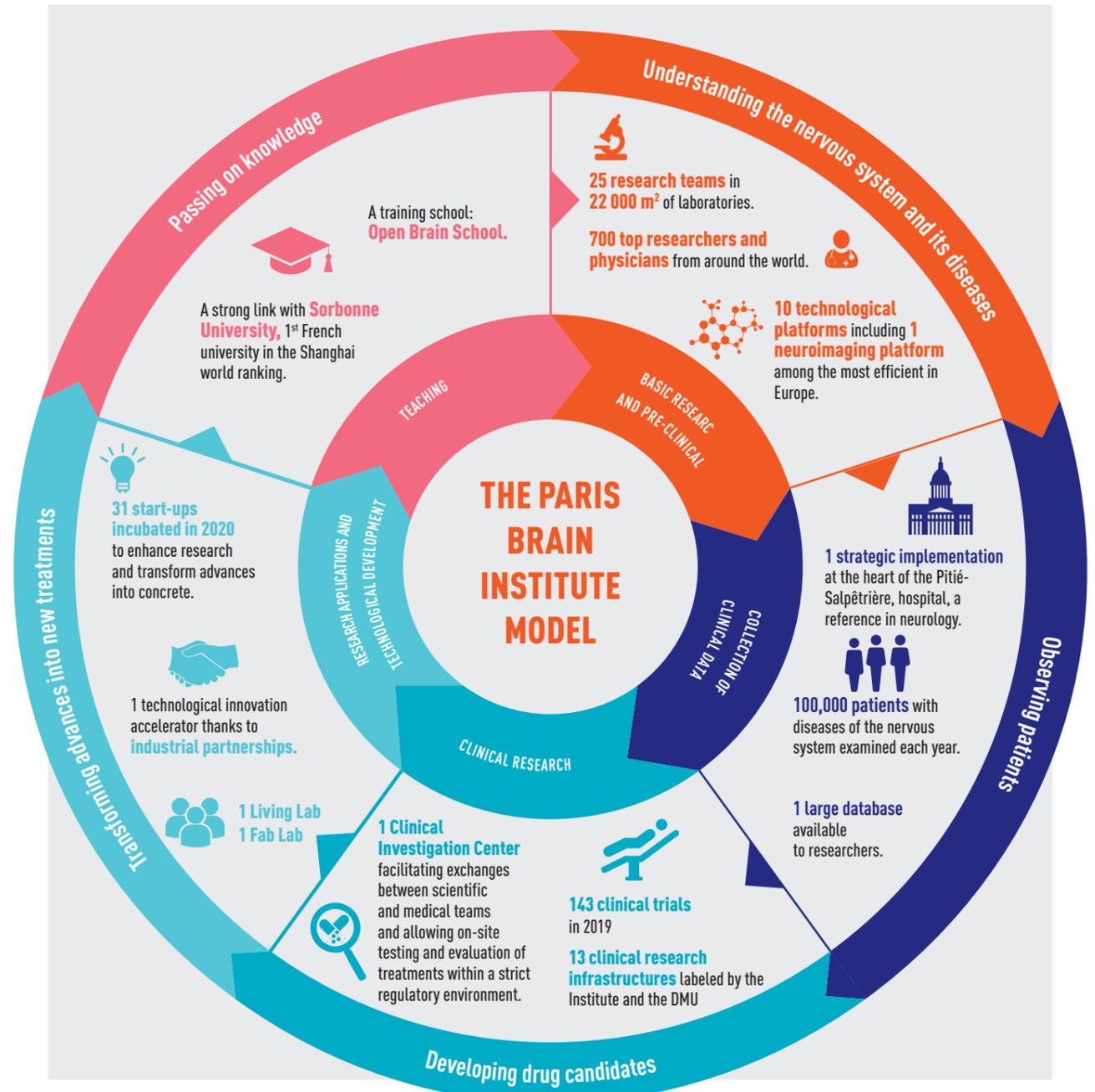
- **Daniel Margulies (CNRS)**, researcher in Richard Levy's team, obtained an "ERC CONSOLIDATOR GRANT" for project "CORTIGRAD" developed to identify and map neural networks within the cerebral cortex. Understanding the connection between these networks will allow us to study the different relationships between brain activity and behavior, and to improve our understanding of individual differences.



A unique model

Tomorrow's medical care is at the heart of today's research at Paris Brain Institute thanks to the incredible synergy between 25 research teams, state-of-the-art platforms, the Clinical Investigation Center, the Medical University Neuroscience Department and the entrepreneurial ecosystem enabled by its business incubator. Paris Brain Institute is above all a human endeavor, fueled by a community of experts who bring pas-

sion to the fight against nervous system diseases on a daily basis. A multicultural and multidisciplinary environment come together with a successful blend of private and public culture for optimal efficiency! As a joint research unit (UMR) and with its public partners (INSERM, CNRS, Sorbonne Université, AP-HP), Paris Brain Institute's governance is founded on a strong partnership between public and private stakeholders.



Scientific strategy

that addresses the challenges of brain research

**PROF BASSEM HASSAN,
PARIS BRAIN INSTITUTE
SCIENTIFIC DIRECTOR**



“The ambition of the Paris Brain Institute to become the world’s leading brain research institute depends on two main pillars that we are currently building.

The first pillar is encouraging research that questions dogma, takes risks, research that is allowed to fail and try once more, and recruiting and rewarding people who dare to challenge existing models. The major discoveries that make a difference are by definition unexpected and unpredictable. Going on charted paths with a step by step approach is still necessary to advance our understanding of a problem, yet it is rarely, if ever, the source of new paradigms. The challenges of brain diseases and their increasing cost for patients, their families and society in general show how essential it is for us to challenge existing paradigms and to rework our models.

The second pillar is creating an open environment in which people who take an interest in the brain as a whole, from molecules to networks, cognition and disease, work together to create a virtuous circle of knowledge from patients’ bedsides to a laboratory environment. At the Paris Brain Institute,

we want to break down the traditional barriers of “basic”, “translational” and “clinical” research. This outdated vision slows progress and creates obstacles to finding original and effective solutions to important problems. We also want to break down the barriers between idea-driven research and technology-driven research. Technological progress almost always creates opportunities to ask and answer new questions, reach a deeper understanding, get a clearer picture of the situation and get things done faster.

Today, the timespan between an initial discovery and its benefit to society is around 30 years. Our ambition is to cut this time in half and we strongly believe that our vision is the best way to achieve it.

RENEWAL OF THE JOINT RESEARCH UNIT OF THE PARIS BRAIN INSTITUTE

On January 1, 2019, the Paris Brain Institute entered a new mandate of its Joint Research Unit (UMR). The initial strategic choices of the Paris Brain Institute were based on specific research objectives and on a uniquely valuable environment to address challenges raised by neuroscience and its diseases. The institute has succeeded in integrating basic neuroscience research specialists and high-level clinical research expertise in one place. The UMR renewal confirms the Paris Brain Institute’s ambitious scientific and medical strategy of increasingly multidisciplinary approaches, a truly unique positioning in its field. The Paris Brain Institute is organized into 4 research domains: molecular and cellular, neurophysiology, cognition, clinical and translational. The great flexibility between these fields is a cornerstone of our scientific and medical growth. Many internal programs, including Big Brain Theory, accelerate interactions between research areas. Strengthening the robust relationship between research teams, technological platforms, clinical research through certified ICRIN centers is also a major ambition of our scientific and medical strategy.

Paris Brain Institute teams

ALS : CAUSES AND MECHANISMS OF MOTOR NEURON DEGENERATION

Séverine Boillée (Inserm)
Competitive grants received in 2019: ANR-PRC, ARLSA, SLA association

BASIC TO TRANSLATIONAL NEUROGENETICS

Giovanni Stevanin (Inserm/EPHE) and **Alexandra Durr** (Sorbonne Université/AP-HP)
Competitive grants received in 2019: Ataxia UK, Fondation Agir pour l'Audition, ARSEP, AFAF, ASL-HSP France, Association CSC,

MOLECULAR PATHOPHYSIOLOGY OF PARKINSON'S DISEASE

Olga Corti (Inserm) and **Jean-Christophe Corvol** (Sorbonne Université/AP-HP)
Competitive grants received in 2019: IDEX Sorbonne Université, France Parkinson

ALZHEIMER'S DISEASE AND PRION DISEASES

Marie-Claude Potier (CNRS) and **Stéphane Haïk** (Sorbonne Université/AP-HP)
Competitive grants received in 2019: H2020, Institut de Veille sanitaire, Fondation Jérôme Lejeune, France Parkinson, France Alzheimer

EXPERIMENTAL THERAPEUTICS OF PARKINSON'S DISEASE

Étienne Hirsch (CNRS) and **Stéphane Hunot** (CNRS)

MOV'IT: MOVEMENT, INVESTIGATION, THERAPEUTICS. NORMAL AND ABNORMAL MOTOR CONTROL : MOVEMENT DISORDERS AND EXPERIMENTAL THERAPEUTICS

Marie Vidailhet (Sorbonne Université/AP-HP) and **Stéphane Lehericy** (Sorbonne Université/AP-HP)
Competitive grants received in 2019: ANR-FLASH, GIS-IBISA, APTES, ANR-PRC, ANR-JCJC, ANR-ERA NET E-RARE, France Parkinson

CELLULAR PHYSIOLOGY OF CORTICAL MICROCIRCUITS

Alberto Bacci (Inserm)
Competitive grants received in 2019: FRM

DYNAMICS OF EPILEPTIC NETWORKS AND NEURONAL EXCITABILITY

Stéphane Charpier (Sorbonne Université), **Mario Chavez** (CNRS) and **Vincent Navarro** (Sorbonne Université/AP-HP)
Competitive grants received in 2019: ANR-PRC, IDEX Sorbonne Université, LRTCA

GENETICS AND PHYSIOPATHOLOGY OF EPILEPSY

Éric Leguern (Sorbonne Université/AP-HP) and **Stéphanie Baulac** (Inserm)
Competitive grants received in 2019: ANR-IA-RHU, AXA, FRM, ARDRM,

SENSORY SPINAL SIGNALING

Claire Wyart (Inserm)

GENETICS AND DEVELOPMENT OF NERVOUS SYSTEM TUMOURS

Emmanuelle Huillard (CNRS) and **Marc Sanson** (Sorbonne Université/AP-HP)
Competitive grants received in 2019: ANR-IA-RHU, ARTC, APHP, Cancéropôle Ile-de France, APHP, Ligue contre le cancer, IDEX Sorbonne Université, ARC, FRM

REPAIR IN MULTIPLE SCLEROSIS: FROM BIOLOGY TO CLINICAL TRANSLATION

Catherine Lubetzki (Sorbonne Université/AP-HP) and **Bruno Stankoff** (Sorbonne Université/AP-HP)
Competitive grants received in 2019: FRM, ARSEP

MYELIN PLASTICITY AND REGENERATION

Brahim Nait-Oumesmar (Inserm) and **Violetta Zujovic** (Inserm)
Competitive grants received in 2019: ANR-PRC, ARSEP

PICNIC- PHYSIOLOGICAL INVESTIGATION OF CLINICALLY NORMAL AND IMPAIRED COGNITION

Laurent Cohen (Sorbonne Université/AP-HP), **Lionel Naccache** (Sorbonne Université/AP-HP) and **Paolo Bartolomeo** (Inserm)
Competitive grants received in 2019: MSCA-IF/GF, ANR-MRSEI, ANR-ERAPerMed, FRM

FRONTLAB: FRONTAL FUNCTIONS AND PATHOLOGY

Richard Lévy (Sorbonne Université/AP-HP)
Competitive grants received in 2019: ANR-PRC, CNRS, ERC Consolidator Grant, FRC, Fondation pour la recherche sur Alzheimer, FRM

CIA: CONTROL - INTEROCEPTION - ATTENTION

Philippe Fossati (Sorbonne Université/AP-HP) and **Liane Schmidt** (Inserm)
Competitive grants received in 2019: Fondation NRJ, FRC

NEUROPHYSIOLOGY OF REPETITIVE BEHAVIORS

Éric Burguière (CNRS)
Competitive grants received in 2019: FRM, Fondation de France

MOTIVATION, BRAIN AND BEHAVIOR

Mathias Pessiglione (Inserm), **Sébastien Bouret** (CNRS) and **Jean Daunizeau** (Inserm)
Competitive grants received in 2019: ANR-PRC, Région Ile-de-France, FRM

ARAMIS: ALGORITHMS, MODELS AND METHODS FOR IMAGES AND SIGNALS OF THE HUMAN BRAIN

Olivier Colliot (CNRS) and **Stanley Durrleman** (Inria)
Competitive grants received in 2019: ERC Consolidator, ANR-JPND

EXPERIMENTAL NEUROSURGERY

Brian Lau (CNRS) and **Carine Karachi** (Sorbonne Université/AP-HP)
Competitive grants received in 2019: MSCA-IF/GF, ANR-PRC, ANR-LABCOM, FRM, CHU de Rouen

BRAIN DEVELOPMENT

Bassem Hassan (Inserm)
Competitive grants received in 2019: ANR-PRC, IDEX Sorbonne Université, Fondation Roger de Spoelberch, ARSEP

STRUCTURAL DYNAMICS OF NETWORKS

Nicolas Renier (Inserm)
Competitive grants received in 2019: MSCA-IF/GF, ANR-PRC, DIM Mathinnov, Action on hearing loss

CELLULAR MECHANISMS OF SENSORY PROCESSING

Nelson Rebola (CNRS)
Competitive grants received in 2019: FRM

GENE AND CELL THERAPIES

Nathalie Cartier (Inserm)
Competitive grants received in 2019: ELA research foundation, Fondation Jérôme Lejeune, FRM, AFSR

DIANE BARRIÈRE CHAIR: "MOLECULAR PHYSIOLOGY OF SYNAPTIC BIOENERGETICS"

Jaime De Juan-Sanz
Competitive grants received in 2019: ERC Starting Grant

Supporting research and its funding

Research institutes have developed a dynamic financial strategy to cope with the ever-changing regulations of public financial support and to adapt to the industrial environment, where new trends and new needs arise close to daily. The Department of Medical and Scientific Affairs of the Paris Brain Institute (DAMS) is home to a grants office that offers numerous services to the Paris Brain Institute community. It is proactive to help build new external collaborations with the Paris Brain Institute. With a wide range of skills, DAMS offers sourcing and engineering assistance to obtain competitive national, European and international research grants.

€18,40 million

in external competitive grant revenue in 2019

€103 million since 2012

3 prestigious ERC grants

obtained by our researchers in 2019, for a total of **14** since the creation of the Institute

ACRONYMS

AFAF : Association française de l'Ataxie de Friedreich
ANR-ERANET E-RARE : Shared European Program on rare diseases
ANR-ERAPerMed : National Research Agency - Transnational Medical Project
ANR-FLASH : National Research Agency - Research practices and open data
ANR-IA-RHU : National Research Agency - Hospital-University Research
ANR-JCJC : National Research Agency - Young Researcher
ANR - JPND : National Research Agency - Joint program in neurodegenerative diseases
ANR-MRSEI : National Research Agency - European and International Scientific Network Development
ANR - PRC : National Research Agency - Collaborative Research Projects
APHP : Assistance publique - hôpitaux de Paris
APTES : Association des personnes concernées par le tremblement essentiel
ARDRM : Association Robert Debré pour la Recherche médicale

ASL-HSP France : Association Strumpell-Lorrain / Hereditary Spastic Paraplegia-France
Association CSC : Connaître les syndromes cérébraux
ARC : Association pour la recherche sur le cancer
ARSEP : Association pour la recherche sur la sclérose en plaques
ARSLA : Association pour la recherche sur la Sclérose Latérale Amyotrophique
DIM Mathinnov : Domain d'intérêt majeur Math Innov
ELA research foundation : European leucodystrophy organisation
ERC : European Research Council
FRM : Fondation pour la recherche médicale
GIS-IBISA : Infrastructures en biologie santé et agronomie
H2020 : European Horizon 2020 Program
LRTCA : Laboratoire de recherche en technologies chirurgicales avancées
MSCA-IF/GF : Marie Skłodowska-Curie actions - Individual and Global Fellowships (Europe)

Cellular and molecular neurobiology

The teams focused on this line of research aim at deciphering the influence of genetics, dissecting the molecular machinery, establishing the role of different types of cells and understanding the complex cellular interactions in normal or pathological conditions.

A repertoire of unexplored DNA regions

A study led by Philippe Ravassard and Hélène Chevval identified the spectrum of long non-coding RNAs in dopaminergic neurons, a primary target for degeneration in Parkinson's disease. This repertoire from unexplored areas of our genome is extremely specific to dopaminergic neurons. Characterizing the non-coding repertoires makes it possible to assess the existence of an increased relationship between these risk factors and specific lncRNAs of dopaminergic neurons. If this relationship is proven, it could be a significant clue to help explain the specific vulnerability of dopaminergic neurons in Parkinson's disease.

Gendron J, et al. Scientific Reports. February 2019

An important mechanism in myelin repair within the central nervous system

When myelin, the insulating and protective sheath surrounding neurons, is damaged in the context of demyelinating diseases such as multiple sclerosis or spinal cord injuries, Schwann cells, responsible for producing myelin in the peripheral nervous system, participate in central nervous system lesion repair. Beatriz Garcia-Diaz and Anne Baron-Van Evercooren highlighted the mechanism allowing the migration of Schwann cells in the spinal cord.

Garcia-Diaz B, et al. Acta Neuropathologica. April 2019

A new therapeutic target to treat spinocerebellar ataxias?

Spinocerebellar ataxias are genetic neurodegenerative diseases of the cerebellum and brainstem that cause many motor disorders. The most prevalent form is SCA3, also known as Machado-Joseph disease. In her recent research, Nathalie Cartier-Lacave and her team discovered the crucial role of an enzyme that improves disease symptoms in mice. A European program (Erare) is underway and coordinated by Inserm at the Paris Brain Institute to confirm these results on other models of ataxia and to assess the feasibility and tolerance of a potential treatment application in patients suffering from these severe genetic pathologies.

Nóbrega C, et al. Acta Neuropathologica. June 2019

The role of lymphatic vessels in neurodegenerative diseases

The lymphatic vascular system is present in nearly all tissues. It acts as a complement to blood vessels, ensuring the evacuation of waste as well as immune surveillance within organs and tissues. However, the lymphatic vascular system is absent from the brain and spinal tissue. Laurent Jacob and Jean-Léon Thomas, in collaboration with Nicolas Renier, characterized the anatomy and functions of vertebral lymphatic vessels for the very first time. They play a role in the transportation of immune cells to lymph nodes, to which they are connected on a regional basis. The researchers developed 3D mapping of this system and its organization. They also highlighted the crucial role of these vessels in the immune response to spinal cord injury.

Jacob L, et al. Nature Communications. October 2019

The regulation of single gene determines the balance between sight and smell

Finding a compromise between the size of visual and olfactory organs is common in animal evolution, but the underlying genetic and developmental mechanisms remain unclear. A study conducted by Ariane Ramaekers and Bassem Hassan reveals that a single genetic variant that affects the development of sensory organs in *Drosophila* (fruit flies) could explain the trade-off between the size of the eyes and antenna. It may provide a fast track for behavioral change and adaptation. The gene, *eyeless / Pax6*, is also found in invertebrates and vertebrates, including humans. This discovery may highlight a general mechanism in the compromise between the sizes of sensory organs within the animal kingdom.

Ramaekers A, et al. Developmental Cell. July 2019

Anti-inflammatory effect of cannabidiol, a non-psychoactive compound found in cannabis

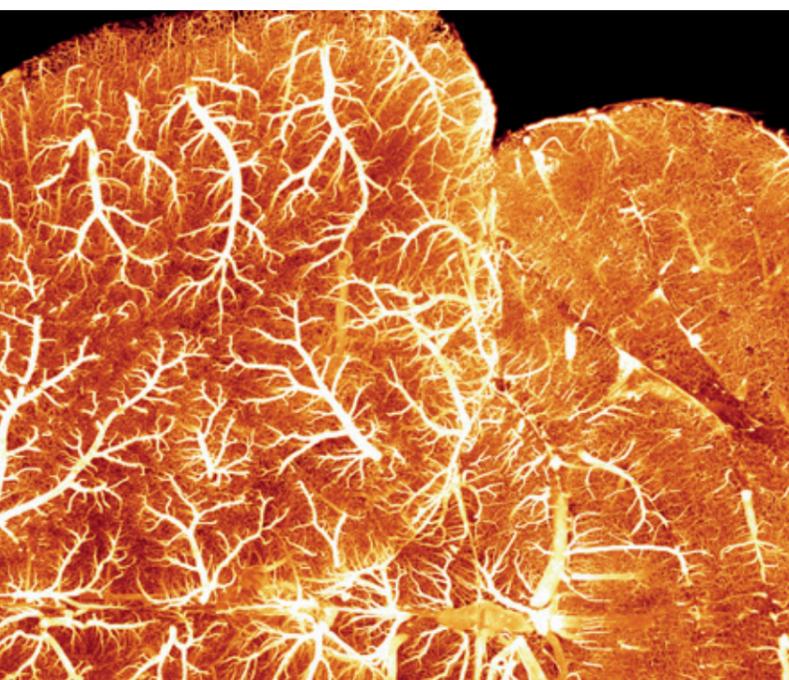
Cannabidiol (CBD), a non-psychoactive compound in cannabis, has the ability to limit immune system cell response in various pathological inflammatory contexts. Mauricio dos-Santos-Pereira and Patrick Michel, in partnership with a team in Brazil, have identified a key mechanism by which cannabidiol exerts its anti-inflammatory effects.

Dos-Santos-Pereira M, et al. Glia. October 2019

Identification of genetic mutations present in brain malformations associated with epilepsy

Malformations of cortical development (MCDs) are major causes of pediatric intractable epilepsy. Surgical resection of the epileptic foci is often the only treatment option for these children with epilepsy. Stéphanie Baulac's team conducted a genetic analysis using DNA extracted from the postoperative tissue of 80 patients with MCD (collaboration with Fondation Rothschild Hospital). Results highlight the presence of so-called somatic mutations in several genes of the mTOR signaling pathway, responsible for regulating brain development, in a large subset of the cohort. Using a laser microdissection approach on pools of cells, the team found that these somatic mutations were only present in a few brain cells located within the malformation and displayed abnormal morphology. These results are part of the emerging concept that the brain is like a mosaic, with each brain cell having its own unique DNA. These discoveries offer a new genetic framework for MCD-associated epilepsy, strengthening the relationship between neuropathology and genetics and guiding towards a precision-based medical approach targeting somatic brain mutations.

Baldassari S, et al. Acta Neuropathologica. December 2019



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Integrative neurophysiology

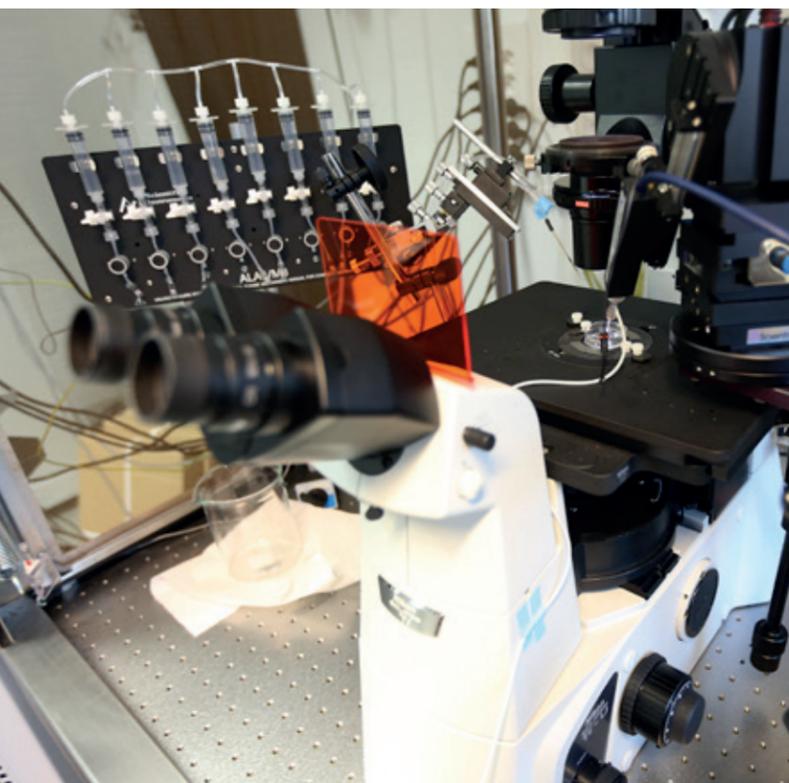
The aim of the teams in this field is to better understand the physiology of neurons and their networks under normal and pathological conditions. The approaches shared by the Institute's different teams include molecular, cellular, electrophysiological methods and optical recordings, optogenetics and the manipulation of neuronal activity through transcranial magnetic stimulation, as well as computer models that link physiological recordings amongst themselves.

Cerebral anoxia and brain resuscitation in real time from inside neurons

Stéphane Charpier's team described, for the very first time, the real-time electrical changes that occur simultaneously in neurons and an electroencephalogram during death (due to cerebral anoxia, for example during cardiopulmonary arrest) and during an attempt at resuscitation. The study found that oxygen deprivation in the brain halts synaptic activity followed by a leak in electrical current from the inside of the neurons, creating a brain wave recorded in the electroence-

phalogram referred to as a "Wave of death". This is the first time this wave has been on a neuronal scale. The team also highlighted a correlation between the shutdown of brainstem functions (where vital functions are controlled) and the neuronal process of imminent death. Re-oxygenation can reverse this process leading to a new brain wave, never previously described, called a "Resuscitation Wave". Its occurrence is accompanied by recovery of synaptic activities in the brain and electrical properties of neurons.

This wave could constitute a reliable and reproducible real-time marker of recovery of neuronal and cerebral functions as it is only observed in the event of successful resuscitation. The results obtained by this team open up new perspectives for real-time assessment of the chances of successful resuscitation in the context of cerebral anoxia. Schramm AE, et al. *Progress in Neurobiology*. December 2019



Inhibitory autapses, modulators of cortical neural network activity

A study conducted by Alberto Bacci's team found that Parvalbumin-expressing basket cells (PV cells), a major type of cortex-inhibiting neurons that play a part in several major cognitive functions, form a large number of synapses with themselves, called autapses. This auto-inhibition (autaptic inhibition) is much stronger than the inhibition that these cells exert on other neurons in the cortical network. This mechanism influences coupling between the activity of these neurons and gamma oscillations, a brain rhythm essential to sensory perception, attention, memory and other cognitive functions. Autaptic self-inhibition could therefore be an important mechanism that underlies the essential role of these cells during sensory and other major cognitive functions, with possible crucial consequences on certain cortical actions under physiological and pathological conditions.

Deleuze C, et al. *PLOS Biology*. September 2019

Quantifying brain changes in progressive supranuclear palsy

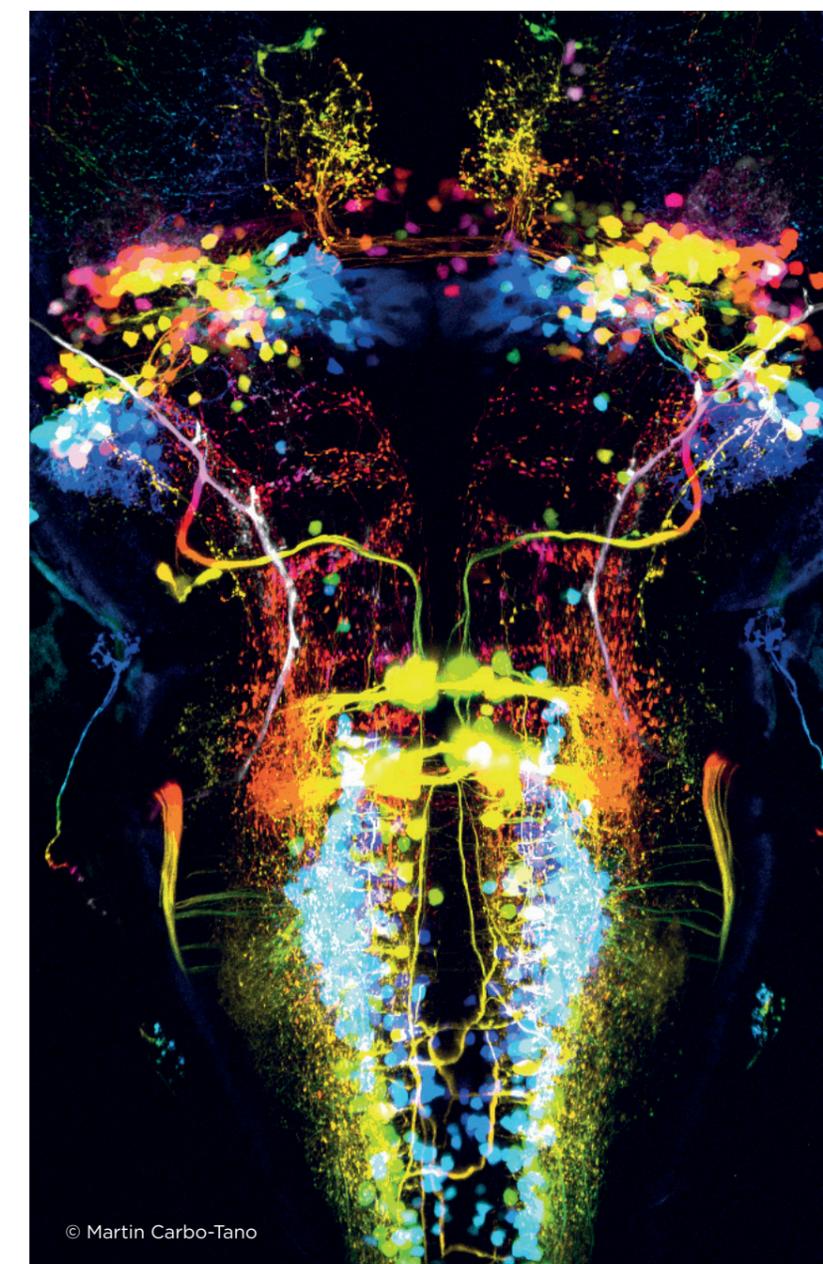
Progressive supranuclear palsy (PSP) is a clinically heterogeneous neurodegenerative disease. It causes damage to the brainstem, leading to progressive loss of balance, eyesight, speech and mobility. There is currently no treatment for this disease, and one challenge for considering new treatment strategies is to improve detection and quantification of the development of neurodegeneration in patients. A study conducted by Nadya Pyatigorskaya, Marie Vidailhet and Stéphane Lehericy highlighted the potential of using an imaging method called quantitative MRI to assess brain degeneration in PSP in a non-invasive and precise manner even in the smallest brain structures including in brainstem nuclei. This method also allows clinicians to differentiate degeneration present in PSP from that of Parkinson's disease.

Pyatigorskaya N, et al. *Movement disorders*. 2019

Beneficial effects of coffee in treating dyskinesia

A team from the neurology department of Pitié-Salpêtrière hospital (AP-HP) and Paris Brain Institute, directed by Emmanuel Flamand-Roze and Aurélie Méneret, found that coffee has beneficial effects in treating abnormal movements due to a mutation in the ADCY5 gene in an eleven year-old child.

Méneret A, et al. *Annals of Internal Medicine*. September 2019



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Cognitive Neuroscience

The teams in this field combine structural, electrophysiological and functional studies to understand the functioning of neural networks on a whole brain scale as well as their importance in the onset of specific behaviors and cognitive processes in healthy individuals and in patients with neurological and psychiatric disorders.

The dynamics of our brain activity determine our state of consciousness

Jacobo Sitt and collaborators found that signal coordination of brain activity determines state of consciousness. They highlighted the link between communication dynamics among different areas of the brain on the one hand, and the level of consciousness on the other. These results represent an important breakthrough in understanding the various states of consciousness or unconsciousness encountered in non-communicating patients, and could pave the way for unique treatments based on stimulation of patients with real-time analysis of fluctuations in brain activity.

Demertzi A, et al. Science Advances. February 2019

The first complete mapping of functional brain lateralisation

Certain processes within the brain are carried out preferentially in the right or left hemisphere of the brain. But which functions for which hemisphere? A Franco-Italian research team led by Michel Thiebaut de Schotten answers this question by creating the first complete mapping of lateralisation of brain functions. Their results are the first to show that decision-making, perception, and action as well as emotion, mostly involves the right hemisphere. Symbolic communication, on the contrary, is based predominantly in the left hemisphere.

Karolis VR, et al. Nature Communications. March 2019

First ever identification of neurons in the visual cortex that respond to faces

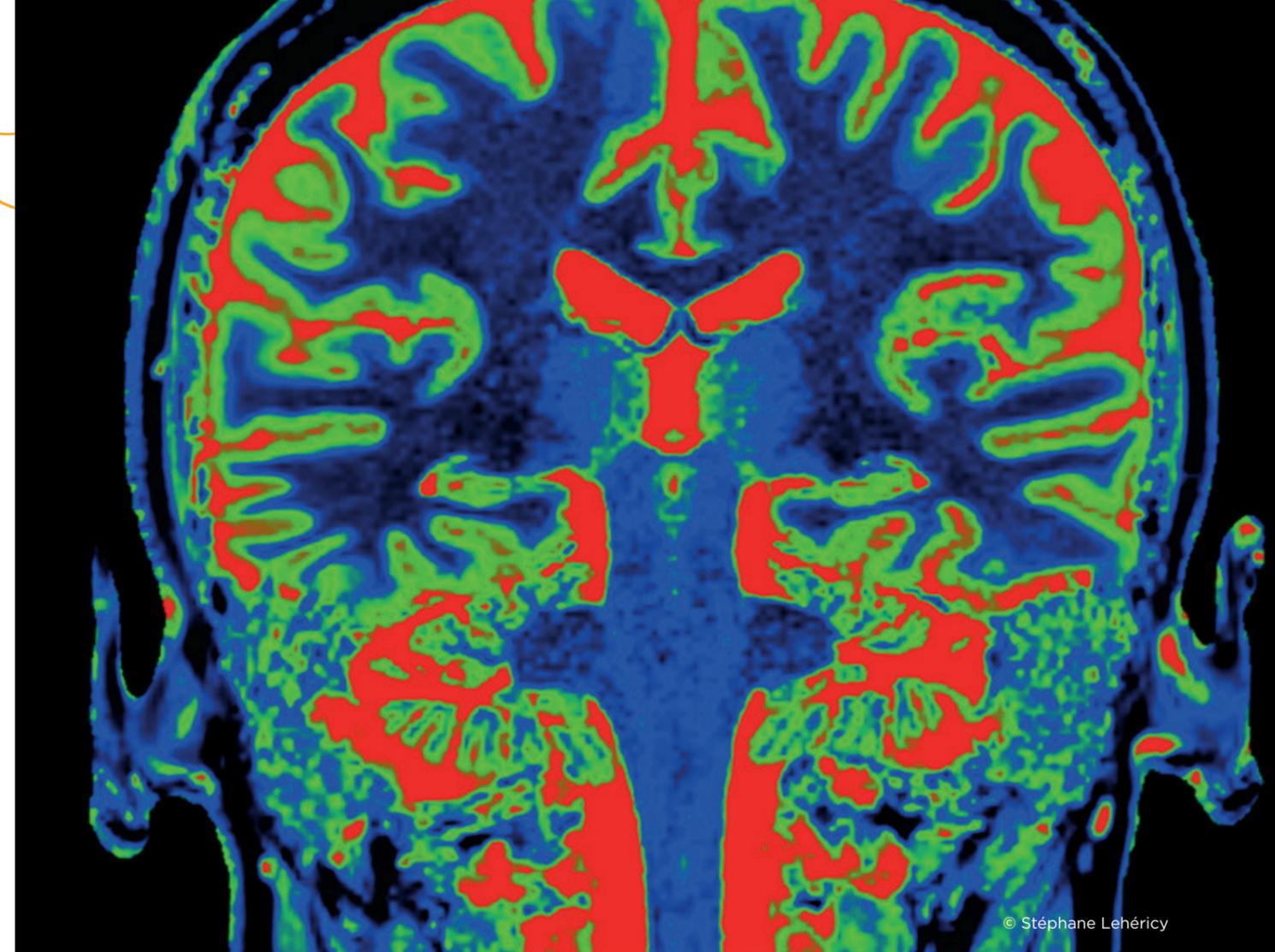
A study led by Dr. Vadim Axelrod, head of the Conscience and Cognition Laboratory at Gonda (Goldschmied) Multidisciplinary Brain Research Center at Bar-Ilan University (Israel), in collaboration with Lionel Naccache (Sorbonne University-APHP) and team at the Paris Brain Institute and at Pitié-Salpêtrière Hospital, was the first to find in humans, neurons of the visual cortex within the face fusiform area respond much more strongly to faces than landscapes or objects.

Axelrod V, et al. Neurology. January 2019

When narcolepsy makes you more creative!

Could sleeping make us more creative? Studying individuals with narcolepsy, who have specific access to REM sleep, could provide key information for understanding this phenomenon. Isabelle Arnulf's team, in collaboration with a team from the University of Bologna in Italy, highlighted the existence of greater creativity in patients with narcolepsy. The study results suggest a link between a specific sleep phase, REM sleep, and creative abilities. This important breakthrough paves the way for understanding the cognitive function of sleep and the mechanisms of creative thinking.

Lacaux C, et al. Brain. July 2019



© Stéphane Lehéricy

Is intensive sports training beneficial for our health?

Everyone hears that physical activity is good for your health, but up to what level of training can we go without damaging our brain? A study carried out by Mathias Pessiglione's team in collaboration with INSEP (National Institute of Sports, Expertise and Performance) and the French Anti-Doping Agency (AFLD) found that overly intense physical training harms brain capabilities and especially cognitive control. These results highlight that cerebral fatigue must be taken into account to prevent poor decision-making in economic, political or even judicial contexts. On a clinical level, the fatigue related to cognitive control may represent a first step in the development of burn-out, observed in all types of professional fields.

Blain B, et al. Current Biology. September 2019

Our color categorisation is not language-dependent

We use language every day to express our thoughts and the way we view the world. But to what extent does language influence our thinking? In this context, the perception of colors raises an interesting question. The colors we see form a continuous spectrum from purple to red. However, we draw boundaries between different colors: red, purple, etc. The fundamental cognitive process of categorisation refers to our ability to classify these different shades of color under nominal categories. A study by Katarzyna Siuda-Krzywicka and Paolo Bartolomeo shows that there is no correlation between our ability to name colors and our ability to categorize them. These results suggest a pre-verbal notion of colors. This novel idea is in line with experiments carried out on animals and children from four to six months who demonstrate an ability to categorise colors without the vocabulary to qualify them.

Siuda-Krzywicka, K, et al. Cell Reports. 2019

Clinical and Translational Neuroscience

The aim of clinical and translational research is to enable the development of predictive or progression markers and treatments for neurological and psychiatric diseases, from identification in simple laboratory modelling to clinical trials at the Paris Brain Institute's Clinical Investigation Center and throughout the entire Institute. Clinical and translational research increasingly involves computational neuroscience, the joint analysis of clinical and biological data, and therefore requires development of novel mathematical and statistical approaches, a field called Neuroinformatics.

Diagnosing Alzheimer's disease in the preclinical phase using electroencephalography

Diagnosing Alzheimer's disease as soon as possible is essential in order to provide early treatment for patients. However, there is currently no easy-to-use technique for diagnosing Alzheimer's disease in the preclinical phase, before symptom onset. Sinead Gaubert, Federico Raimondo and Stéphane Epelbaum discovered early electrical changes in the brain measured by electroencephalography (EEG) in subjects with preclinical Alzheimer's disease within the INSIGHT-preAD cohort followed by Professor Bruno Dubois' clinical research team at the Memory and Alzheimer's disease Institute. These highly promising results suggest that EEG may be used in the coming years for early detection of preclinical Alzheimer's disease.

Gaubert S, et al. Brain. July 2019

Doc feeling: caregiver expertise contributes to improving diagnosis of patients in an altered state of consciousness

Teams from the Pitié-Salpêtrière hospital (AP-HP), Inserm and the Paris Brain Institute found that the assessment of caregivers (nurses and nursing assistants) regarding the state of consciousness of patients represents a real added value to medical diagnoses and to electrophysiology and traditional brain imaging exams. This research is based on the notion of "collective intelligence". The study, initiated by Gwen Goudard and Karine Courcoux, two nurses from the neurological intensive care unit at Pitié-Salpêtrière Hospital, involved over 80 caregivers over more than a year. It demonstrates the extraordinary motivation and enormous potential of paramedical research in the unit.

Hermann B, et al. BMJ Open. February 2019

Early spinal cord damage in individuals at risk of developing FTD/ALS

A collaborative study led by doctors Giorgia Quérin and Pierre-François Pradat from the Biomedical Imaging Laboratory (Sorbonne Université), the Neurology department of Pitié-Salpêtrière Hospital - APHP and the Paris Brain Institute highlights the existence of early spinal cord damage in subjects at risk of developing frontotemporal degeneration (FTD) or amyotrophic lateral sclerosis (ALS) as they carry a specific genetic mutation. Early brain damage before the age of 40 was found in a previous study by the PREVDEMALS cohort. These new spinal cord injuries, visible only after the age of 40, may suggest the existence of primary brain damage with subsequent diffusion to spinal structures. These results provide important information on the pre-symptomatic phase of the disease and are one step further towards developing early treatments.

Querin G, et al. Annals of Neurology. June 2019

Neurological consequences of the Zika virus finally revealed

Zika viral infection remains a global public health issue. The identified pathogen is the Zika virus, transmitted by Aedes mosquitoes. Since 2007, numerous epidemics have been recorded in Asia and Africa and more recently in Central America and South America. Researchers and doctors are very familiar with the virus yet frequency of occurrence of neurological complications, their clinical description and prognosis remain enigmatic. Teams of French researchers including Annie Lannuzel and Emmanuel Flamand-Roze of the Paris Brain Institute discovered the long-term effects of the virus. Long-term sequelae are common in Neuro-Zika and the patient's viral status upon admission may inform the prognosis. These elements must be taken into account to adapt diagnosis and management of patients with NeuroZika.

Lannuzel A, et al. Neurology. January 2019

A multimodal approach for brain-machine interface optimization

"Brain-machine interface" is a generic term that includes the ability to use brain activity for interactions with the outside world without going through muscles. It includes technologies such as neurofeedback - techniques used in neuroscience to relax, modify stress levels, or other tasks, as well as the possibility of controlling external objects using our brain, to write with our thoughts, to control a cursor on a screen, or a robotic arm, for example. If these technologies seem so powerful, why aren't brain-machine interfaces used on a regular basis? One simple reason: they don't work all the time. In fact, it is currently very complicated to use these interfaces routinely, especially in clinical practice. A study conducted by Marie-Constance Corsi and Fabrizio De Vico Fallani shows how a multimodal approach for brain-machine interface optimization could be of interest. Optimization of these brain-machine interfaces suggests that they may be used in clinical practice in the coming years, for example in motor imagination for motor skills recovery after a stroke.

Corsi MC, et al. Int J Neural Syst. February 2019

Towards diagnosis of predisposition to Alzheimer's disease using a blood test

The diagnosis of a person at risk of developing Alzheimer's disease is a major challenge in view of the increase in the number of cases expected in the coming years due to extended lifespans. Currently, detection of amyloid plaques in the brain using imaging (positron emission tomography) is a first step towards this diagnosis given that the presence of these lesions constitutes an increased risk of developing Alzheimer's disease. At the Paris Brain Institute, the team led by Marie-Claude Potier in collaboration with clinician and neurometabolism researcher Fanny Mochel identified a biological blood profile 99.4% correlated to the presence of amyloid plaques in the brains of subjects included in the INSIGHT study led by Pr Bruno Dubois at the Paris Brain Institute and IM2A.

Xicota L, et al. EBioMedicine. September 2019

Neuroinformatics

Neuroinformatics for tomorrow's research and medicine

Medical research generates billions of data and the advancement of technologies only increases the number and the complexity of the data collected, be it genetic, imaging or biological. Faced with the challenges of this growing increase in data, scientists must develop the tools and methods necessary to analyze and make the most of it.

The Center for Neuroinformatics at the Paris Brain Institute aims at developing shared instruments and methods to manage and analyze all types of neuroscience data. It enables all scientists, whatever their field, to contribute to and benefit from interoperable databases and a shared portfolio of methods and instruments for analysis.

One of the main assets of the Paris Brain Institute is the ability to collect large amounts of medical and biological data of all types and to know how to "give them a voice" thanks to powerful statistical calculation tools and the collaboration of many players: researchers, engineers, doctors, computer scientists and technicians. Several multidisciplinary projects combining genomics, neuroimaging, clinical observations and data science are underway and focus on the effective use of artificial intelligence. They constitute a great hope in improving our understanding of the brain and its diseases, diagnosis, and assistance in developing tailored treatment.

Neuroinformatics center expertise

Data analysis

The center for neuroinformatics offers expertise in biostatistics, mathematical modeling, and machine learning for the analysis of multimodal data for use by teams at the Paris Brain Institute.

Data management

Implementation of standardized processes for neuroscience data organization of various types: genomics, electrophysiology, imaging, clinical, etc

Software development

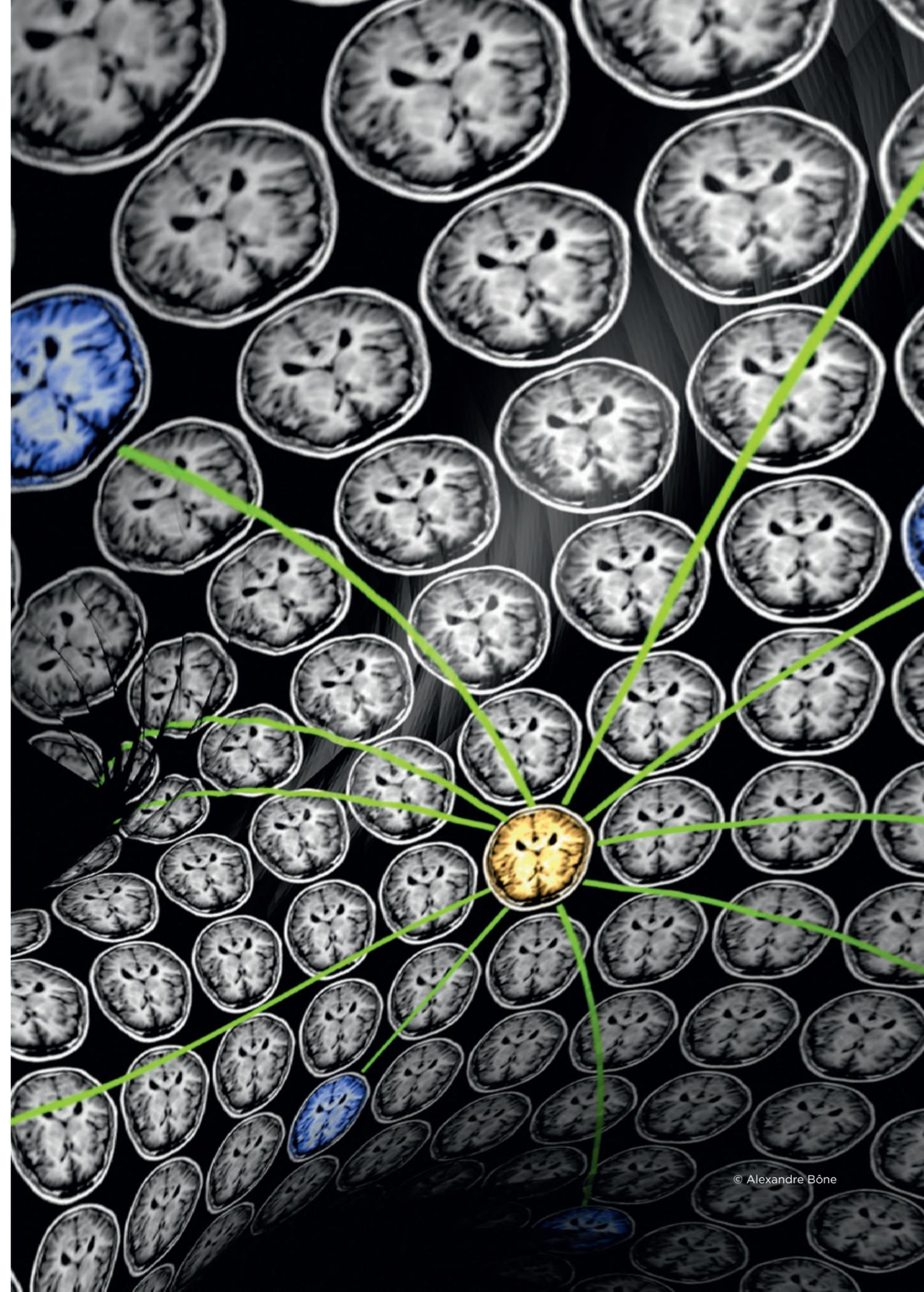
Software for structuring and indexing heterogeneous data sets as well as data processing and analysis tools.

Scientific computing

Management of servers and computing clusters dedicated to scientific data

Training & communication

The center for neuroinformatics develops a full range of training programs on statistical analysis and modeling methods and software for Paris Brain Institute teams. It also organizes events to bring the scientific community together around neuroinformatics issues and promote its activities on a regular basis.



Core facilities of the Paris Brain Institute

The progress and quality of science depends as much on technological progress as it does on good ideas. At the Paris Brain Institute, researchers and core facility managers work together to continuously monitor technological advances to offer the most advanced equipment and techniques operated by highly competent staff to move brain research forward.

Beyond providing innovative equipment, the mission of the core facilities at the Paris Brain Institute is to pool skills and provide services and expertise for the entire scientific community: Institute research teams, external scientific teams, incubated companies and outside companies as well.

Basic equipment is distributed according to research areas and their scale of analysis: molecular exploration, cellular exploration, imaging, preclinical

functional exploration, functional exploration, bioinformatics and banks.

The main activities of the Paris Brain Institute are three-fold:

- Supplying equipment and services from project design to results analysis;
- Maintaining cutting-edge technological research and development in each area of expertise;
- Training for equipment use or implementing techniques.



10 CORE FACILITIES AND BIOBANKS



iGenSeq
Next generation sequencing of RNA and DNA



iVector
customized lenti, adenovirus, Crispr



CELIS
Screening, cell culture, iPSC, electrophysiology



Histomics
processing of histological animal and human material



ICMQuant
conventional fluorescence microscopy, microscopy confocal laser scanning, bi-photonic microscopy, confocal rotating disk microscopy or transmission electron microscope



PhenoPark
Preclinical functional exploration, behavioural analyses, surgery, electrophysiology



CENIR
Center for NeuroImaging Research:
3T MRI, PET-MRI, TMS, MEG-EEG, Gait analysis



ICONICS
Databases and Datawarehouse, Genomics, Bioinformatics and Biostatistics



PRISME
cognitive and social evaluation in ecological conditions and virtual reality



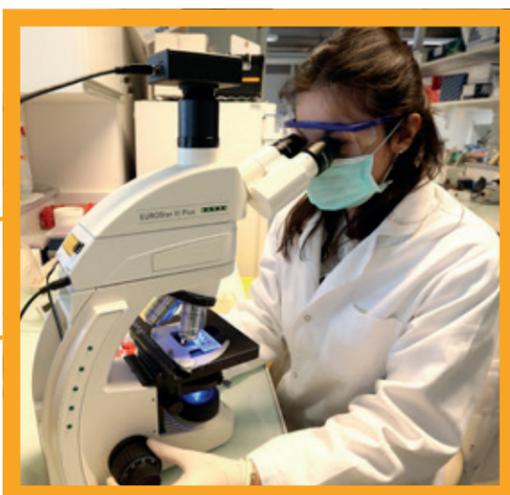
Biobanks
biological resource collection, DNA, plasma, cells, brain tissue

Technological advances essential to scientific research

Updates in the organization of our technological core facilities

A new organization has been implemented for the Paris Brain Institute's technological core facilities. Expert committees of Paris Brain Institute researchers have been set up for each core facility to ensure that we are always at the forefront of what technology has to offer to science. We are also moving towards simplifying interactions between core facilities and the other services of the Paris Brain Institute to reduce administrative burden on core facility staff so that they can devote themselves even more to developing their core facility activities.

Throughout 2019, core facility managers worked to put new core facility websites online, always with the aim of increasing visibility for the incredible activity of our core facilities and the expertise of staff who work there.



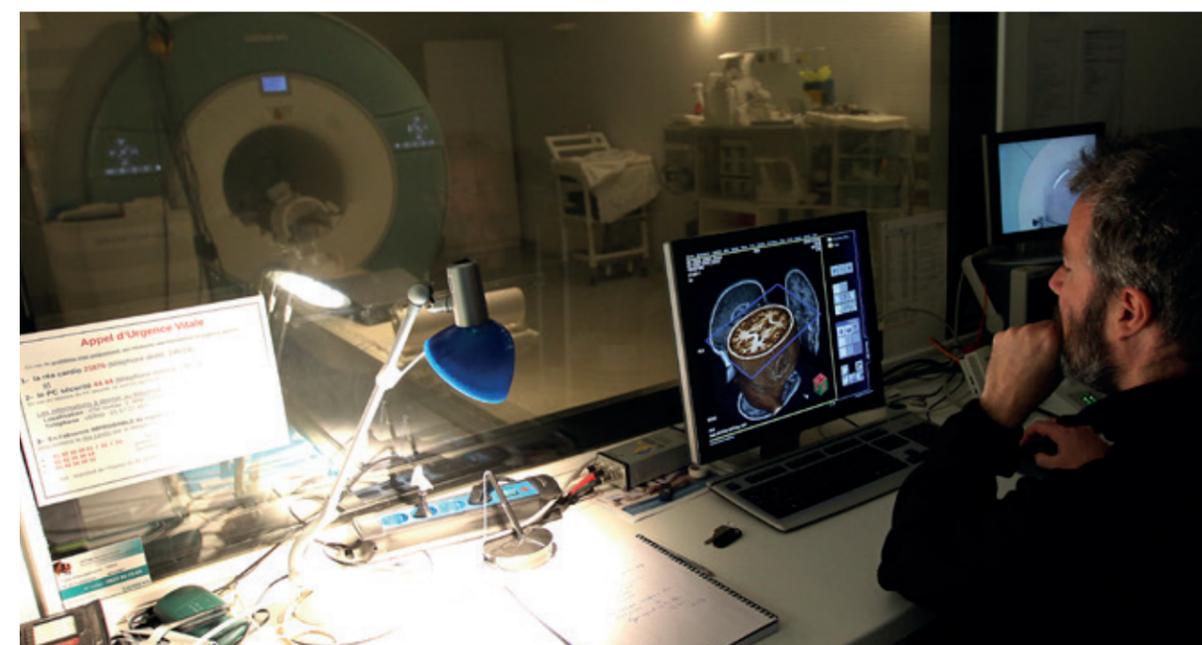
New cutting-edge equipment

To remain at the forefront of what technology can offer to scientific and medical research, a priority for the Paris Brain Institute is to acquire expert equipment to support work of its entire scientific community.

In 2019, the Paris Brain Institute acquired the Nova-seq 6000 ILLUMINA, the world's most powerful short fragment DNA sequencer, for the iGenSeq core facility. The DNA and cell bank has equipped itself with two new nucleic acid extraction machines.

A collaborative project with Nikon has enabled a three-year loan of a high-resolution imaging system for high-content analysis. This system allows high-speed acquisitions using confocal or wide field mode as well as tailored acquisition and analysis protocols, for different 2D / 3D cell culture models.

The Paris Brain Institute's Neuroimaging Research Center (CENIR) has acquired a high-intensity focused ultrasound treatment system (HIFU) for patients with essential tremor. The first treatments in France are set to begin in 2020.



A publication in Nature on the development of the Coelacanth skull thanks to the 11.7T MRI core facility

The Latimeria coelacanth is a deep-sea animal related to terrestrial vertebrates. Since its discovery 80 years ago, the study of coelacanths has yielded important information about the evolutionary changes in vertebrates that led to the appearance of tetrapods. It is the only current vertebrate to share anatomical characteristics with the fossil forms of the Devonian (-410 to -360 million years), ancestors of terrestrial vertebrates, and especially a skull divided into two portions by an intracranial joint. Thanks to the work of Mathieu Santin on the ultra-high-field MRI core facility (11.7 Tesla) at the Paris Brain Institute, 3D images of coelacanth heads were obtained. In addition to this unique instrument, we also used our specific skill set for the analysis of these types of samples. We were able to generate a 3D image, in their entirety, of two of the six models of the study, in particular the juvenile stage of the coelacanth. These images were then integrated into a structure segmentation model to analyze its anatomical characteristics. These results provide novel information on the origin of coelacanth skull features and create new research perspectives on the evolution of the vertebrate skull.

Source : Dutel H, et al. Nature. 2019

PRISME core facility involved in a study conducted by Mathias Pessiglione's team on neurocognitive consequences of physical overexertion published in Current Biology

A study carried out by Mathias Pessiglione (Inserm), team leader at the Paris Brain Institute, in collaboration with INSEP (National Institute of Sports, Expertise and Performance) and the French Doping Control Agency (AFLD) found that overly intense physical training harms our brain capabilities, especially when it comes to cognitive control. The study is a good illustration of how PRISME can explore all facets of human behavior, in this case by combining physical effort and cognitive performance, in coordination with CENIR to study the neurobiological correlates of these cognitive mechanisms.

Source : Blain B, et al. Current Biology. Septembre 2019

Launch of research protocols in collaboration with manufacturers

The SPAST industrial protocol (Pathmaker Neuro-modulation Inc, Boston) is a randomized, controlled, double-blind study aimed at evaluating a new medical device for the treatment of lower limb spasticity after a stroke.

The GAIN industrial protocol (MindMaze, Lausanne) aims at evaluating a virtual reality device in motor recovery of the upper limb after a stroke.

Research Applications



FRENCH TECH SEED

By creating the “Deeptech fund”, a public investment fund of 400 million euros focused on the “seed” sector (i.e. the first stage of entrepreneurship after exiting the research project stage), the Public Investment Bank (BPI) aims to promote the development of a greater number of entrepreneurial projects based on highly innovative science. These “deeptech” projects are meant to allow the proliferation of breakthrough innovation throughout France. In order to detect these young yet promising technologies in the most organized way, the BPI relies on a limited number of structures with experts both in science and in the support of innovative companies. They carry “French Tech Seed” certification and are responsible for detecting and qualifying innovations of very young companies, following which the BPI grants seed funding of up to 250,000 euros to build the project. The Paris Brain Institute is currently the only French organization certified for its expertise in the field of neuroscience entrepreneurship and represents a sign of recognition and a true asset for both the start-ups it supports and its entrepreneur researchers.

BY ALEXIS GENIN,
RESEARCH AND TECHNOLOGY OFFICE DIRECTOR



2018 marked the launch of “Made @ ICM” initiatives, namely the development of health products produced by or enabled by the Paris Brain Institute. The following year, 2019, saw the development of the first innovative small treatment molecules with France’s best medicinal chemists. At the same time, the Institute decided to invest in a new building to accelerate medical technology development --- this is a true change of scale, with soon to be three separate sites for the iPEPS incubator. The Healthtech Hub will be organized around three sites: The initial incubator at the heart of the Paris Brain Institute building, mainly for young companies developing drugs research-accelerating instruments; a space dedicated to digital health, hosted at Station F; and by the end of 2020, a new building halfway between the Paris Brain Institute and Station F, made possible by the support of the City of Paris and Ile-de-France. This unique space will welcome entrepreneurs from all horizons in an environment that is both modern and green, built around a skylight in a large central agora. Beyond quality of life, essential to the creativity of researcher-entrepreneurs, an integrated service offer will strengthen the relationship with the hospital environment by allowing access to the Institute’s platforms - and especially to its LivingLab - and will support innovators towards clinical research with the help of “Neurotrials” experts... while facilitating even greater access to financing and investments. We are counting on an extraordinary year and cannot wait to present the next output of this great idea machine!

Research Applications in 2019

BIOTECH medical drug gardeners

2019 was marked by an increasing number of partnerships with industrial healthcare players in France and abroad. The Paris Brain Institute has established a collaboration with manufacturer Nikon to develop robotic microscopes allowing high-speed “subcellular” imaging capable of reaching the depths of neuron functioning. Another collaboration was initiated with a French SME to assess the protective potential of novel small molecules that may help fight Parkinson’s disease. A new experimental model was developed by researchers at the Institute for this project, using a small worm called *C. Elegans* whose neurons carry the alterations found in the disease.

Several patents were also filed during the year, one of which is to protect a drug with promising effects for treating neurological dysfunctions linked to strokes.

The “sleeping beauties” project to assess the treatment potential of small molecules was strengthened by the creation of new strategic partnerships with medicinal chemistry research institutes. Several families of molecules were assessed using cellular models of pathologies such as Parkinson’s disease or multiple sclerosis. Screening of over 2,000 compounds was also carried out to assess the ability of these compounds to kill glioblastoma cells (a highly aggressive brain tumor). Several promising mole-

cules have been identified, one of which is, very interestingly, highly toxic for tumor cells and not for healthy cells. In 2020, these molecules and many others will be protected by patents and offered to various partners to secure the funding to continue their development.

MEDTECH Medical technologies designed for patient needs

2019 was an important year for the development of “user-centered” technology products. Throughout the year, and in interaction with the physical and rehabilitative medicine department of Pitié-Salpêtrière hospital and the support of Medtronic and HappyNeuron by SBT Human(s) Matter, engineers and designers reflected with caregivers and patients on solutions to improve care and self-sufficiency of patients suffering from brain injury, especially following a stroke. Various solutions were drawn up including:

- DocFeeling (project led by Dr Benjamin Rohaut): collaborative application to facilitate monitoring of the state of consciousness of intensive care patients by medical teams;
- Au fil des mots (project led by Agnès Weill Chounlamounry): rehabilitation support application to facilitate improvements in pronunciation and lexical memory of stroke patients;
- BRO (project led by the physical and rehabilitation medicine team): appli-

cation to help patients cook using the “kitchen” tool to stimulate memory and help them regain their independence.

The LivingLab (collaborative innovation organization) and the Workshop (rapid prototyping platform) also created a panel of services to facilitate the “user-centered” innovation process of start-ups and large groups. For example, the LivingLab was able to support Roche group employees within the framework of an intrapreneurial program in designing a professional mediation solution for those suffering from invisible illnesses. On its end, the Workshop supported the prototyping of a robot designed by a start-up to facilitate interaction with those suffering from neurodegenerative diseases.



NEUROTRIALS Proof through clinical research

2018 was dedicated to creating and structuring the NeuroTrials team. 2019 then saw the development of interactions with industrial partners in the field of drugs and medical devices. In this framework, NeuroTrials supported the clinical development of a French SME that plans to use its technology for fine characterization of gait disorders (observed in many neurodegenerative illnesses). NeuroTrials also advises another young European company focused on researching a metabolic approach to Charcot’s disease to “reposition” a drug already used for other purposes. Discussions are also underway to develop gene therapy for Huntington’s disease based on the research of a team leader from the Institute. Finally, 2020 will see the launch of a “phase II” clinical study offering a new option to treat patients with acute optic neuritis. The drug candidate, developed by another young European company, presents interesting neurotrophic and neuroprotective properties. NeuroTrials brings these partnerships its ability to identify the best clinical trial design to quickly demonstrate product effectiveness, ensures patient protection with regulatory authorities,

and manages the test procedure. The perfect integration of NeuroTrials within the Paris Brain Institute ecosystem and its proximity to expert clinicians is a major asset in supporting the healthcare industry for clinical development of neurology and psychiatry products.

IPEPS Full-fledged entrepreneurship

iPEPS, the Paris Brain Institute’s innovative business incubator, is located at the heart of the Institute as well as at STATION F, the world’s largest startup campus. Since 2012, the incubator has supported roughly fifty young innovative companies in developing their technology.

In 2019, the incubator operated the “Pfizer Innovation France” endowment fund’s first acceleration program. Four startups in the digital health field benefited from the support and resources of the incubator, as well as the expertise of the leader in the pharmaceutical industry. Building on the success of this first edition, which allowed these start-ups to project themselves more rapidly both towards their market and on an international level, a second edition will take place in 2020 with the renewal

of this unprecedented partnership. 2019 was also the year of renewed trust by the Ile de France Region with funding for the continued development of incubator services and partnership between the Paris Brain Institute and STATION F. Several of the incubated companies have taken important steps in their development: WeFight and its virtual companion Vik



raised an investment of 1.8 million euros, and Neurallys accelerated the development of its connected implant thanks to a new investment of 750,000 Euros.

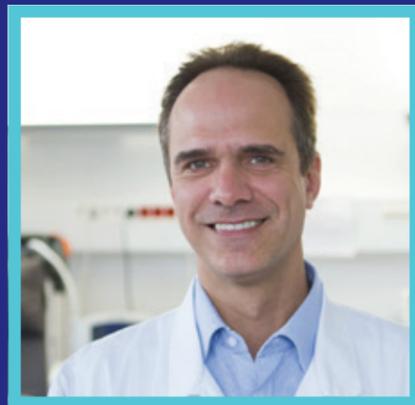
Bioserenity, formerly incubated at the Institute, is the only healthcare startup to join the Next 40, an index created by the French government in September 2019 to track 40 French start-ups with very high potential. Finally, six new companies joined iPEPS, including HealthyMind (a virtual reality solution for pain management) and Cairn Biosciences from San Francisco to develop new drugs against addiction.



Clinical research and care



Patients at the heart of our priorities



BY PROF JEAN-CHRISTOPHE CORVOL, DIRECTOR OF THE CLINICAL INVESTIGATION CENTER AT THE PARIS BRAIN INSTITUTE AND PROF JEAN-YVES DELATTRE, PARIS BRAIN INSTITUTE MEDICAL DIRECTOR AND DIRECTOR OF THE NEUROSCIENCE MEDICAL-UNIVERSITY DEPARTMENT AT THE PITIÉ-SALPÊTRIÈRE HOSPITAL



At the Paris Brain Institute, everything is implemented to develop synergies between clinical and scientific fields, supported by our Institute, the clinical investigation center, and Pitié-Salpêtrière hospital group. For years, a major effort has been underway to structure clinical research within hospital services by providing Paris Brain Institute thanks to the IHU program. We can now consider our Institute as the driving force of clinical neuroscience research on the Pitié-Salpêtrière site.

In 2019, we officially launched iCRIN, the clinical research infrastructure of the Paris Brain Institute, to further this structuring of clinical research. We can now give clinical teams the means to work in a better environment as well as establish the culture of the Paris Brain Institute and its translational research in hospital departments. Other tools have also been implemented or developed to promote clinical research: NeuroTrials, now including a support unit for clinical research development, Neurocatalyst, and the Big Brain Theory program that brings clinicians and researchers together on breakthrough research projects.

This progress in our organization has led to significant results in 2019. These include the start of several industrial therapeutic trials testing innovative therapies in rare neurodegenerative diseases such as anti-sense oligonucleotides in Huntington's disease and amyotrophic lateral sclerosis, or anti-tau antibodies in progressive supranuclear palsy (2 trials completed in 2019). In addition, NeuroTrials has signed its first contracts with companies for the development of medical devices in gait assessment, for the treatment of pain in virtual reality, and for an innovative drug in optic neuritis. In terms of academic studies, the NS-PARK cohort coordinated by the Paris Brain Institute has been selected as one of the 10 Health Data Hub pilot projects, also demonstrating the Brain Institute's commitment to data sharing in the spirit of "open science".

The challenge ahead, and one in which we can keep improving, is to increase our inclusions in clinical trials. For each patient that enters our clinical services, we must be able to help them "here and now", using available treatments, as well as offering participation in clinical trials for innovative treatments to increase our understanding of diseases and their treatment.

CIC 2019 BY THE NUMBERS: 143 CLINICAL TRIALS IN 2019

SLEEP DISORDERS	1
EPILEPSY	1
NEURO-VASCULAR	2
NEUROPSYCHIATRY	3
TRAUMATIC BRAIN INJURY	3
PSYCHIATRY	6
COGNITIVE NEUROSCIENCE	6
ALS	8
NEUROGENETICS	16
DEMENTIA	19
NEURO-ONCOLOGY	20
MULTIPLE SCLEROSIS	23
MOVMENT DISORDERS	35

The Neuroscience Medical-University Department (DMU)

The Nervous System Diseases Hub at Pitié-Salpêtrière hospital was recently renamed as the Neuroscience Medical-University Department (DMU) in line with a reorganization of AP-HP Sorbonne Université hospital departments.

The 13 new medical-university departments replace the 24 old hubs of Pitié-Salpêtrière-Charles Foix hospital group and the university hospitals of eastern Paris (Saint Antoine, Tenon, Trousseau, Rothschild), now united as a single hospital system: Sorbonne University / AP-HP. Beyond activity management and human resources, that remain under the help of the MUD, the development of these new departments aims at improving their services, optimizing healthcare channels and developing teaching and research.

Organization of the Neuroscience Medical-University Department

The Neuroscience Medical-University Department includes 13 services or departments, for a total of 34 functional units. It is made up of 4 pillars:

- “Neurology” (Saint Antoine and Salpêtrière);

- “Adult Psychiatry - Addictology” (Saint Antoine, Tenon, Salpêtrière, Charles Foix);
- “Physical medicine rehabilitation, Follow-up rehabilitation care (MPR-SSR)” (Rothschild and Salpêtrière);
- « Neurophysiology-neuropathology “ (Saint Antoine, Salpêtrière, Charles Foix).

The Neuroscience DMU has the considerable advantage of having a very strong thematic consistency and backing by very large research institutions (Paris Brain Institute, Institute of Myology), and of being part of the Paris Brain Institute, the only Neuroscience IHU in the country. The integration of new units is an opportunity. By strengthening the adult psychiatry-addiction and MPR-SSR units, it becomes possible to develop a true “pillar-based strategy” for the fields of “adult psychiatry” and “MPR”, alongside the already-large “Neurology” pillar.

The department has 541 beds and spots, 249 medical staff and 1054 paramedical and administrative staff. The DMU also takes part in 14 rare disease reference centers (including 8 as coordinator or constitutive center) and 2 rare cancer reference centers (coordinators).

“The main goal of the DMU is to bring “care” and “academics” (teaching and research) together within medical and nursing teams. They enrich each other. A second goal is to extend the “patient care” aspect to the period preceding and following hospitalization, which explains the importance granted to the “healthcare channels” group.”

Prof Jean-Yves Delattre, director of the Neuroscience Medical-University Department and Paris Brain Institute’s Medical Director.



The 13 Clinical Research Infrastructures (iCRIN) at Paris Brain Institute

The aim of iCRIN infrastructures is to develop interactions and knowledge-sharing between team members of the Neuroscience Medical-University Department and Paris Brain Institute research teams. The winners of this call for projects received “Clinical research infrastructure of the Paris Brain Institute” certification paired with funding to develop their project within the hospital. A call for projects was launched in Spring 2018 in hospital units for medical and paramedical teams. Projects were assessed by the Scientific Advisory Board of the Paris Brain Institute on criteria including expertise, performance, quality, visibility of the structure. 13 projects were selected with an official launch in 2019, backed by Paris Brain Institute’s Clinical Investigation Center.

The launch of the iCRINs now makes it possible to support numerous clinical research projects in the clinical services of the Neuroscience Medical University Department directly or indirectly linked to the Paris Brain Institute. This adds to the Institute’s historical partner services new prospects for collaboration with other services at the Pitié-Salpêtrière Hospital (sleep, neurosurgery) but also at Saint Antoine (psychiatry, neurology, addictology), Rothschild Hospital (rehabilitation) and Tenon Hospital (outpatient psychiatry). The Paris Brain Institute’s Clinical Investigation Centre team coordinates this activity by organising monthly meetings with the iCRIN referents for each theme to share experience, set up common procedures and report activity indicators. These meetings with iCRIN referents, mostly project managers or clinical study technicians, are also intended for training sessions. These meetings are also an opportunity to take stock of the different missions of the iCRIN referents and to exchange on their possible difficulties in order to offer them adequate assistance.

ALZHEIMER’S DISEASE

Coordinator: Richard LEVY (AP-HP/Sorbonne Université)

In collaboration with the Institute of Alzheimer’s and Associated Diseases (IM2A), this project aims to: identify novel cognitive markers and bring together specific populations of patients; develop clinical applications by increasing preclinical and clinical trials and proof of concept studies. To do so, we group and monitor patient cohorts suffering from neurodegenerative diseases. Their clinical, biological and neuroimaging data will be organized in a database.

PARKINSON’S DISEASE AND MOVEMENT DISORDERS

Coordinator: David GRABLI (AP-HP/Sorbonne Université)

The iCRIN specialized in Parkinson’s disease and movement disorders benefits from a partnership between the team led by Olga Corti and Jean-Christophe Corvol and the team led by Marie Vidailhet and Stéphane Lehericy. Its two main objectives are to identify biomarkers of disease severity, its progression and response to treatment, and to decipher the pathophysiological mechanisms underlying behavioral and motor control disorders in rare movement disorders.

AMYOTROPHIC LATERAL SCLEROSIS (ALS)

Coordinator: François SALACHAS (AP-HP)

The ALS center in Paris is one of the largest in Europe, both in terms of new patients and patients treated. It collaborates with several members of Séverine Boillée's team at the Paris Brain Institute. The ALS iCRIN is composed of four main pillars: elucidating ALS triggering and identifying biomarkers; understanding propagation of motor neuron dysfunction; discovering why compensation mechanisms for innervation remain in some patients; and studying the effect of opening the blood-brain barrier with focused ultrasound in ALS.

NEUROLOGICAL INTENSIVE CARE

Coordinator: Sophie DEMERET (AP-HP)

The neurological intensive care unit is a structure with extensive experience in the management of patients with acute disorders of the peripheral nervous system and / or the central nervous system. Its activity focuses on four major pathologies: categorization and monitoring of consciousness disorders in collaboration with Lionel Naccache's team; diagnosis and treatment of status epilepticus with the team led by Stéphane Charpier and Vincent Navarro; early diagnosis of encephalitis; and the development of a large clinical database in myasthenia gravis.

NEUROSURGERY

Coordinators: Carine KARACHI (AP-HP/Sorbonne Université) and Alexandre CARPENTIER (AP-HP/Sorbonne Université)

Nearly all of the clinical activities of the neurosurgery department have research programs with Paris Brain Institute teams and platforms. iCRIN aims to ensure the development of multimodal databases for future clinical trials. There are five main lines of research: identification of morbidity and mortality predictors in brain tumor and aneurysm patient cohorts; novel deep brain stimulation targets and brain-machine interfaces; opening of the blood-brain barrier in various neurological pathologies; novel treatment approaches for meningiomas; ex vivo human tissue for cellular electrophysiology.

NEUROGENETICS

Coordinator: Alexandra DURR (AP-HP/Sorbonne Université)

The NEUROLOP clinical research center, including reference centers for rare diseases from the Genetics department of the hospital and Paris Brain Institute teams, aims at deciphering phenotypes associated with genes involved in neurogenetics pathologies such as spinocerebellar ataxia and Huntington's disease; is involved in clinical, imaging, biological and genetic data research; innovative treatment trials in small rare disease cohorts; and the transition between neurodevelopmental defects and programmed neuron loss in adulthood in neurogenetic diseases in collaboration with basic research.

NEURO-ONCOLOGY

Coordinator: Ahmed IDBAIH (AP-HP/Sorbonne Université)

The partnership between the neuro-oncology department and a dedicated research team, led by Marc Sanson and Emmanuelle Huillard at the Paris Brain Institute, as well as a tumor bank (Onco-neurotek), a preclinical treatment research group (Gliotex, led by Ahmed Idbah) and National Cancer Institute certification for early phase clinical trials and innovative treatments makes it possible to reach for the following goals: accelerating transfer of laboratory innovations into clinical applications by identifying novel biomarkers and testing innovative treatments, including areas that have yet to be explored.



STROKES

Coordinators: Yves SAMSON (AP-HP/Sorbonne Université) and Charlotte ROSSO (AP-HP/Sorbonne Université)

The Stroke iCRIN has the following objectives: participation and coordination of randomized controlled trials, use of Big data to build a dynamic prognosis model of stroke outcome; identification of novel structural and functional markers of stroke sequelae; development of innovative treatment approaches in rehabilitation, such as non-invasive brain stimulation techniques and playful and innovative rehabilitation strategies (serious games, neurofeedback) or drug treatments.

ORTHOPEDIC SURGERY

Coordinator: Hugues PASCAL-MOUSSELDARD (AP-HP/Sorbonne Université)

The clinical project of the Pitié-Salpêtrière orthopedics department focuses on three main topics: genetic causes of idiopathic scoliosis in collaboration with Claire Wyart's team at Paris Brain Institute; establishing a systematic database of pre- and postoperative neurological state for all patients in the spinal unit; developing various prospective analysis protocols that create a pathway between neuroscience and sports surgeries or spinal cord injuries.

ADULT PSYCHIATRY

Coordinator: Bruno MILLET (AP-HP/Sorbonne Université)

The Psychiatry iCRIN offers a multimodal approach combining brain stimulation with drug therapy or psychotherapy. It represents a strong interface between clinical services and Paris Brain Institute and more specifically with the team led by Philippe Fossati and Liane Schmidt. Two lines of research are currently under exploration: development of pragmatic trials in stress dysregulation disorders such as post-traumatic stress; and exploring network neuromodulation in psychiatric and addiction disorders.

TRAUMATIC BRAIN INJURY

Coordinator: Éléonore BAYEN (AP-HP/Sorbonne Université)

Novel approaches to integrate multimodal data are crucial for monitoring brain vulnerability, individual pathways and the evolution of head trauma (TBI). This iCRIN aims to structure and develop a large prospective cohort of individuals affected by a head trauma, multimodally explored (clinic, radiology, physiology) and to develop modeling of multimodal results, including by using statistical learning techniques.

MULTIPLE SCLEROSIS

Coordinators: Catherine LUBETZKI (AP-HP/Sorbonne Université) and Bruno STANKOFF (AP-HP/Sorbonne Université)

The Multiple Sclerosis iCRIN is focused on translational development of remyelination strategies to prevent progression of disability; development of new imaging tools to assess strategies for repair in patients with MS; development of treatments targeting the immune system; detection and understanding of multiple sclerosis symptom pathophysiology, and development of new connected instruments for a more precise assessment of disability progression.

SLEEP

Coordinator: Isabelle ARNULF (AP-HP/Sorbonne Université)

In the rapidly evolving field of physiology and sleep medicine, this iCRIN focuses on improving the description of the semiology of these disorders, their genetics, neurophysiological and brain imaging markers and the best course of treatment. It also aims to understand the mechanisms of normal sleep and dreaming; to determine whether certain brain functions (including memory and emotions) are related to REM sleep; to study preclinical neurodegeneration and implement neuro-protective treatment trials in patients with the early signs of Parkinson's disease and Lewy body disease.

Education and training



BY ALEXANDRA AUFFRET
DIRECTOR OF MEDICAL AND
SCIENTIFIC AFFAIRS

This past year saw the official launch of the Paris Brain Institute training school, known as the Open Brain School. What we know about the brain and how it works can be applied to much more than the fight against neurological and psychiatric diseases.

The brain is, in itself, the very essence of who we are. Nearly every aspect of our daily life is directly related to neuroscience. Much of the training that exists in the area of continuing education could benefit immensely from neuroscience-based knowledge and several Paris Brain Institute training programs have already been the subject of case studies that highlight the beneficial pedagogical results of their innovative approaches. The need for continuous training keeps growing. Business schools are among the key players that capitalize on this trend with innovative Master's degree

programs in administration and business, in finance, and more.

To seize this opportunity, the Institute began teaching neuroscience to people outside of the research field this year, while developing training for highly qualified professionals in the clinical and research fields.

In 2019, the first Master Class dedicated to creativity for non-experts began and the Brain Bee program created for high school students with an introduction to neuroscience and its pathologies was launched.

2019 was the first "Open" year for this young training organization, a fantastic impulse to make Paris Brain Institute discoveries accessible to the public!
openbrainschool.com

EXECUTIVE MASTER CLASS: WHAT NEUROSCIENCE TEACHES US ABOUT CREATIVITY

Together with Paris Brain Institute scientists and guest experts from the American Society for Neuroscience of Creativity, we developed a tailor-made course aimed at demystifying creativity and uncovering our own creative potentials and those of our colleagues. The program, designed by Dr. Emmanuelle Volle, welcomed ten participants.

Potential for bringing neuroscience and the various educational fields together.

To pass down and share knowledge at national and international level, the Paris Brain Institute created a training school, the Open Brain School, with the ambition of becoming a new international leader in neuroscience-based training. The Open Brain School is organized around 4 pillars with major advances in 2019:

PILLAR 1: PROMOTING SCIENTIFIC EXCELLENCE

PROGRAMME INTERNATIONAL BRAIN BEE

The program is an international neuroscience competition for high school students. Brain Bee's mission is to help students learn more about the brain and its basic functions, neuroscience research, and misconceptions about brain disorders. The Paris Brain Institute hosted the French National Brain Bee competition for the first time in April 2019. Seung-Bin Joo, winner of Brain Bee France 2019, took part in the international competition (IBB) in Daegu, South Korea.

INTERNATIONAL iMIND MASTER

The iMIND master's program is an international and interdisciplinary two-year program. Designed in collaboration with Sorbonne Université and renowned foreign universities (University of Vienna, TUM, KU Leuven, Trinity College), this master's program is the first of its kind specially dedicated to neurodegenerative diseases, one of today's major societal challenges.

PILLAR 2: PROMOTING CLINICAL RESEARCH

THE MOVE

The Move is an innovative simulation-based training program that uses mime to teach medical students neurological semiology, otherwise known as the expression of neurological diseases. This program is a remarkable example of educational innovation, the pedagogical benefits of which have been the subject of several publications and is now approved by the College of Teachers of Neurology (the highest authority for neurology education in France) for distribution to all French universities. The third edition was held in 2019 with the participation of teams from London, Dublin, Lisbon, Rennes, Lille, Bordeaux and Paris universities.

PARAMEDICAL PROGRAM

A set of programs has been implemented to promote paramedical research with article writing workshops, coursework in English, training in research reasoning, two thesis grants, and the organization of meetings between international peers.

PILLAR 3: ENCOURAGING INTERDISCIPLINARITY

BRAIN TO MARKET SUMMER SCHOOL

The "Brain to Market" summer school is an annual program combining translational neuroscience and entrepreneurial training through intensive training to encourage new projects, new initiatives and new approaches to neurological pathologies. 2019's fifth edition was focused on rehabilitation after a stroke, with an innovation value chain in close collaboration with the Living Lab and activities carried out by iPEPS.

SELF CONFIDENCE & LEADERSHIP TRAINING

A leadership and self-confidence program implemented in collaboration with XX initiative. This intensive program helps develop leadership skills and mastery of communication tools. Since 2019, 46 women (doctoral students, post-doctoral students, researchers, clinicians, support staff) have benefited from the program.

MASTERCLASS FOR RESEARCHER CAREER DEVELOPMENT

Throughout the year, the Medical and Scientific Affairs Department offers various training sessions to Paris Brain Institute researchers to improve transdisciplinary skills such as management, communication, and grant-writing.

CREATIVITY MASTERCLASS

Together with Paris Brain Institute scientists and guest experts from the American Society for Neuroscience of Creativity, we developed a tailor-made course aimed at demystifying creativity and uncovering our own creative potentials and those of our colleagues. The program, designed by Dr. Emmanuelle Volle, welcomed a dozen participants.

WHAT'S NEXT?

- Maintaining and developing Open Brain School by integrating all of the institute's programs and initiatives, including clinical workshops, open training in neuroscience and management
- Continue working towards program recognition by officially integrating them into training courses (STARE, currently on a voluntary basis, will become a teaching unit by 2020) and by obtaining program certification.
- Developing pillar 4 intended to implement novel teaching methods (virtual reality programs) to create new development opportunities with the world of EdTech.



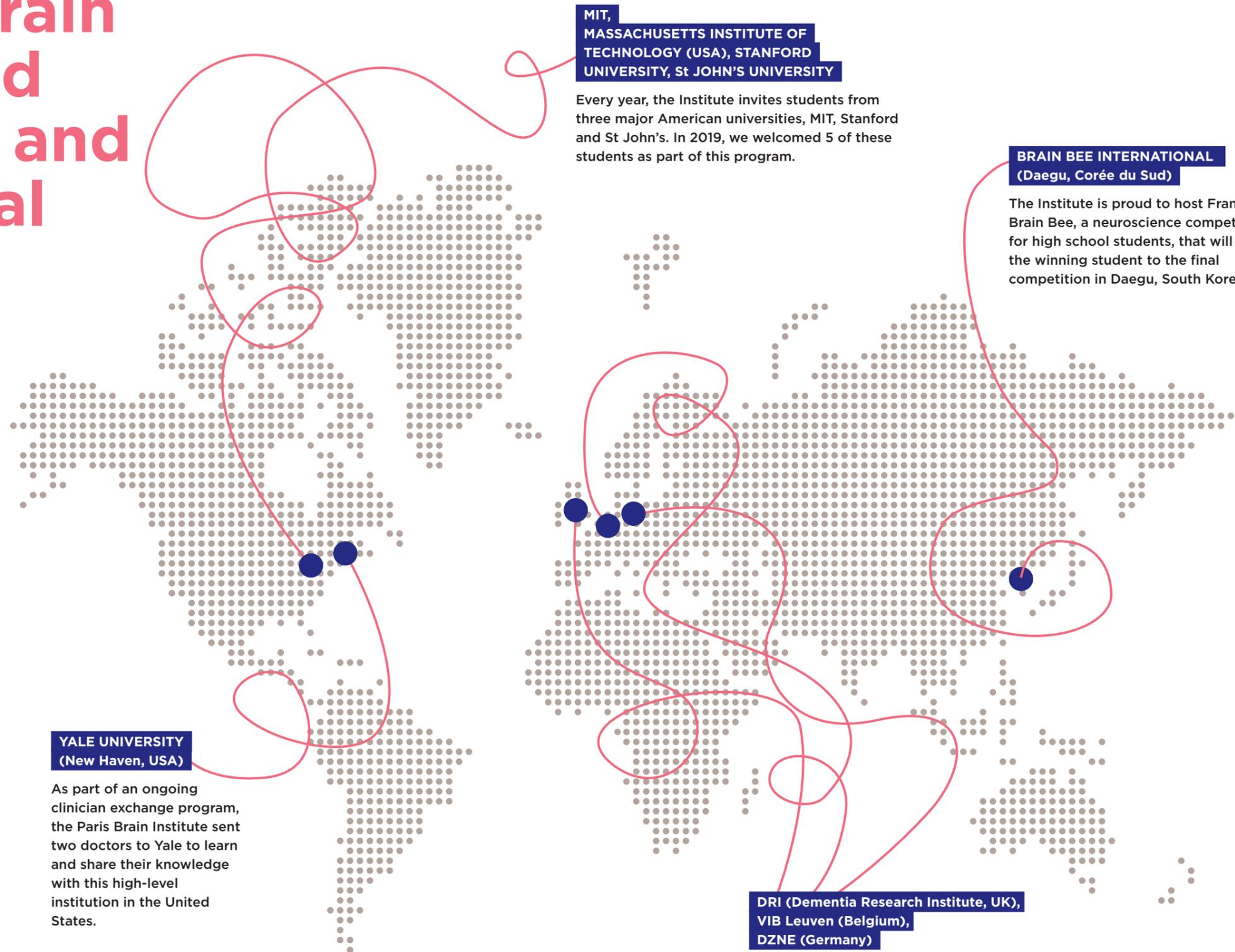
The Paris Brain Institute and its national and international network

Our diversity and close ties with our collaborators around the world are a driving force to improve our work and make it more efficient. Our institute brings together individuals from 43 countries, committed to advancing brain research.

Each year, the Paris Brain Institute cooperates with hundreds of institutes in various ways. In 2019, we collaborated with institutions from 12 different countries to obtain national, European and international funding. Our researchers also published articles with collaborators from over 1,000 different institutions.

The Paris Brain Institute Open Brain School welcomed more than 65 participants from abroad to participate in its various training programs and exchange opportunities.

To foster debates and discussion, our scientific conferences continue to bring together the world's best researchers. In 2019, the Institute proudly organized international conferences on an almost weekly basis!



MIT, MASSACHUSETTS INSTITUTE OF TECHNOLOGY (USA), STANFORD UNIVERSITY, ST JOHN'S UNIVERSITY

Every year, the Institute invites students from three major American universities, MIT, Stanford and St John's. In 2019, we welcomed 5 of these students as part of this program.

BRAIN BEE INTERNATIONAL (Daegu, Corée du Sud)

The Institute is proud to host France Brain Bee, a neuroscience competition for high school students, that will send the winning student to the final competition in Daegu, South Korea.

YALE UNIVERSITY (New Haven, USA)

As part of an ongoing clinician exchange program, the Paris Brain Institute sent two doctors to Yale to learn and share their knowledge with this high-level institution in the United States.

DRI (Dementia Research Institute, UK), VIB Leuven (Belgium), DZNE (Germany)

These three institutes have launched a task force with the Paris Brain Institute to develop a new European network of excellence on neurodegenerative diseases.

Life at the Paris Brain Institute

Sharing and passing along knowledge about the brain and its pathologies

The Paris Brain Institute's communication aims at developing the Institute's notoriety, visibility, and attractiveness in France and abroad.

To do so, we build strong relationships with the media, set up partnerships, communication campaigns, events and joint actions with our academic partners (INSERM, CNRS, AP-HP, Sorbonne University, INRIA ...).

As we strive to take up the major challenges of better understanding the functioning of the brain and treating nervous system diseases, the Paris Brain Institute communicates to:

- Promote its experts and the results of their work so that they can benefit from international funding opportunities and support;
- Encourage recruitment of the best research-wide experts in order to foster never-ending innovation and novel skills;
- Share reports on scientific and medical advances at the Paris Brain Institute for donors and further engage them;
- Share and pass along knowledge to as many individuals as possible.

In addition, as a high-level research and teaching institution, the Paris Brain Institute is committed to informing as many people as possible. That's why every year, the Institute hosts creative and educational events.

The research carried out at the Paris Brain Institute benefits from resources from our donors, companies, partner organizations and foundations and the events they host for the benefit of the Institute year after year and with renewed passion. We extend our sincerest thanks.

Our actions in 2019

Support from our partners

TOUR DE FRANCE AUTO OPTIC 2000
- PIERRE MOREL, from 29/04 to 04/05

THE TOMATO AGAINST
DYSTONIA, from 30/5 to 2/06

LE VENDOME 80 RALLY, on 7, 8 & 9/06

HEROES RACE, on 23/06

ICM MX INTERNATIONAL, on 1/07

CLASSIC DAYS, on 6 & 7 /07

FÉE RARISSIME, on 13, 14 & 15/09

RACE FOR DIVERSITY, on 19/09

LES ECHOS GOLF TROPHY, on 26/09

PARIS 20K, on 13/10

UN CIRCUIT POUR LE CERVEAU, on 12/10

EVEN VIP PETANQUE
COMPETITION, on 30/10

MUSIC PASSION PARKINSON, on 16/11

SOGNO DI CAVALLINO, on 12/11

SOLIDAIR'S,

BCG CHARITY DAY BGC, on 09/11

LION'S CLUBS

ROTARY CLUBS

UN PIED DEVANT L'AUTRE, on 23 & 24/11

BOURG LA RUN, on 9, 10 & 11/11

Events and programs to inform and raise awareness of challenges surrounding brain research

LES OPEN BRAIN BAR

The Paris Brain Institute has created a recurring "meet-up": Open Brain Bar, friendly meetings dedicated to medical innovation and the future of healthcare (in partnership with Sciences & Avenir Magazine and Le Figaro). These events reach audiences outside of the Paris Brain Institute perimeter and are aimed at concerned citizens who are curious about understanding the implication of science in their daily lives. The goal of these evenings is to reach a younger audience and raise their awareness of the major societal challenges generated by neurological diseases.

OBB 2019

OPEN BRAIN BAR # 10: "What comes after a stroke? Post stroke rehabilitation »

OPEN BRAIN BAR # 11: "Technologies and neuroscience: a marriage of reason"

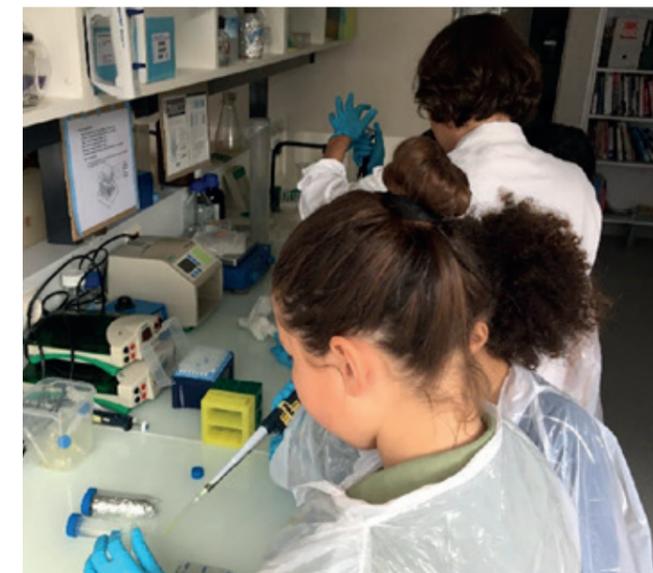
OPEN BRAIN BAR # 12 - in partnership with Groupe EDF Foundation and Sorbonne University: "When emotions speak up ..."

OPEN BRAIN BAR # 13 - in partnership with international scientific film festival PARISCIENCE: "Novel technologies in neuro-genetics: perspectives and limitations ..."



BRAIN WEEK

Each year in March, Brain Week is coordinated by the society for neuroscience. It is an opportunity for Paris Brain Institute to open its doors and to offer unique interactions with researchers, clinicians, engineers & technicians of the institute through workshops and conferences. An educational and fun itinerary gives visitors an opportunity to discover the brain and how it works.



DESTINATION RESEARCH LAB

As part of the project led by Inserm, we hosted 2 primary school classes (CE2 and CM1) and opened the doors to our laboratories. A one-of-a-kind opportunity to approach the world of science and healthcare research.



FUTURE RESEARCHERS

In partnership with INSERM and the Paris school district, the Paris Brain Institute research teams welcome students from middle school and high school every year. This initiative allows its young participants to take a deep dive into research one Wednesday per month and to take part in projects.

SCIENCE, ART & CULTURE CONFERENCES

- "Large Network Geometry" by Etienne Ghys
- "Researchers of the possible: Claude Bernard & Paul Bert" by William Rostene
- "Prospects for Alzheimer's and Parkinson's disease" by Yves Agid, Bruno Dubois and Jean-Christophe Corvol
- "Temporal mirror & innovation" by Mathias Fink
- "Smartosphere meetings: Mental health in the digital age"
- "Why take an interest in the brain to understand human psychology?" By Lionel Naccache
- "Is artificial intelligence more logical, geometric or empirical" by Stéphane Mallat

S3ODEON

The Paris Brain Institute has partnered with the general public information initiative led by S3Odéon, intended to help citizens gain a better understanding of the future of healthcare research. On the stage of the Odéon theater in Paris, the best experts in their respective fields present the latest advances in healthcare science and medicine. This, too, is the role of our Research Institute: promoting better knowledge sharing between Science, Healthcare and Society.



Patronage, donations and bequests

The support of our donors, individuals, companies, foundations and organizations, is essential to help the Paris Brain Institute strengthen its research programs, recruit the best scientists, attract young talent and make state-of-the-art equipment available to them.

Bequests, donations and life insurance: powerful discovery accelerators for research.

Thanks to the generosity of women and men who have chosen to pass along all or part of their estate to the Institute, bequests, donations and life insurance amounted to 1.7 million euros in 2019, an increase of 116% compared to 2018. This resource is strategic for our research work. It also highlights that an increasing number of individuals have perceived the high-quality research within our institute, a public interest foundation with an inheritance tax exemption, that places the Paris Brain Institute among the leading neuroscience institutes worldwide and put their trust in it.

Bequests to the Institute to us are varied in nature: life insurance contracts, real estate (houses, apartments), money, deeds Whatever its form, everything we receive is, above all, the transmission of a story that we know how to collect with the utmost respect.

Faced with the considerable challenges of brain research, an increasing number of individuals contact us each year with the desire to include the Paris Brain Institute in their will or as a beneficiary of their life insurance contract. Carole Clément, testator relationship manager, is available to answer their question and in contact when necessary with our notary, an inheritance expert, with whom an appointment can be arranged for tailored advice. Visits to the Institute are also offered for testators who wish to learn more about how research takes place there. This is a special time for those who decide to go forward with their plans for transmission.

Please reach out to Carole Clément for information on bequests, donations or life insurance (+33 (0)1 57 27 41 41 or carole.clement@icm-institute.org).

Fundraising

In 2019, fundraising efforts geared towards the public at large was very important. With over € 7.7 million raised and thanks to the support of its donors, the Paris Brain Institute can count on growing financial resources to support the teams working on a daily basis to advance our understanding of the brain, help finance the purchase of technological material and equipment that is essential to cutting-edge research, and contribute to the proper functioning of the building, the heart of the research ecosystem. To reduce its costs and allocate a larger share of donations to the Institute's social missions, donors are welcome to make their donations online or to switch to ongoing support by direct debit, thereby saving on postage and printing costs.

Fundraising efforts take place throughout the year, with mail and e-mail campaigns. These actions are carried out with measure and remain essential to the achievement of the Institute's funding objectives. Four times a year, the Donors Journal is published and sent to loyal donors. It is a true meeting place for those who wish to stay informed of the latest advances in neuroscience and gain a



better understanding of the work carried out by our researchers. The end of the year remains the fundraising highlight, notably with the Découvreurs d'Espoir campaign in November. For the second year in a row, comedian Guillaume de Tonquédec was the sponsor of this major event that brought together over 10,000 donors, all driven by the hope of quickly finding new treatments for brain diseases.

As a Public Interest Foundation, Donations to the Paris Brain Institute, a Public Interest Foundation, are 66% income tax-deductible, 75% tax-deductible for Tax on Real Estate Fortune, and 60% corporate tax-deductible.

The Donor Service can be reached at +33(0)1 57 27 47 56 or contact@icm-institute.org

Patronage: philanthropy to help research

The Circle of Friends of the Paris Brain Institute brings together the institute's patrons and major donors. Throughout the year, circle members may take part in private laboratory visits, scientific and cultural conferences and meetings with researchers.

The Circle's Office can be reached at +33(0)1 57 27 40 32 or cercle@icm-institute.org

Committed and generous patrons

In 2019, the Paris Brain Institute is proud to have been able to count on the support of particularly generous patrons and a growing number of patrons as well. The Janssen Horizon Fund and AXA

joined the ranks of the Institute's patrons. Janssen Horizon is committed to supporting a research project on gene therapy for neurodegenerative diseases for a total of 3 years. AXA will contribute to the funding of a program focusing on rare refractory childhood epilepsies over 2 years. Watchmaker Richard Mille offered, once again, to sell a creation to benefit the Paris Brain Institute and made an exceptional contribution to supporting Institute researchers.

Events in support of research

On October 16th, 2019, thanks to FIAC and director Jennifer Flay, the Paris Brain Institute organized the 9th edition of its "Art and Science" breakfast honoring the work of Dr Benedetta Bodini and Prof Bruno Stankoff on multiple sclerosis. During this matinee, hosted by Natacha Polony, dancers Alexia Giordano and Mehdi Kerkouche and a jazz ensemble led by singer Anne Ducros, actress Evelyne Bouix and artist Georges-Pascal Ricordeau translated the hope created by the research carried out at the Paris Brain Institute on this disease through their performance. 120 guests, alongside the Founding Members of the Institute, showed great generosity during the matinee and generated an important amount of donations.

The Paris Brain Institute was also fortunate to be one of the two beneficiaries of the President's Barrel auction during the prestigious Hospices de Beaune sale on November 17th, 2019. Basketball player Tony Parker agreed to sponsor the Paris Brain Institute during this event, during which € 130,000 were raised in support of the institute's research.



CIRCLE OF FRIENDS OF THE PARIS BRAIN INSTITUTE

Lily Safra,
Honorary President of the Circle of Friends of the Paris Brain Institute

Lindsay Owen-Jones,
Honorary President of the Circle of Friends of the Paris Brain Institute

Gérard Saillant,
President of the Paris Brain Institute

Jean Todt,
Vice-President of the Paris Brain Institute

Maurice Lévy,
Co-President of the Paris Brain Institute Campaign Committee

David de Rothschild,
Co-President of the Paris Brain Institute Campaign Committee

Jean-Luc Allavena,
Cédric de Bailliencourt,

Jean Burelle,
Sylvain Héfès,
François Henrot,
Jean-Philippe Hottinguer,
Eddie Misrahi,
Margaux Primat

Christian Schmidt de la Brélie,
Sophie Seydoux,
François Thomé,
Serge Weinberg,

Members of the Campaign Committee on December 31st, 2019

AMBASSADORS

Michèle Yeoh, Actress
Jean Reno, Actor

Corporate social responsibility: a major challenge for the Paris Brain Institute

A sustainable approach at the Paris Brain Institute

We are all directly or indirectly affected by the ecological crisis whether it is due to climate change, pollution of natural areas, or the collapse of biodiversity, and we will be even more greatly affected in the future. In this context, the Paris Brain Institute has been involved in a sustainable approach since its opening. Several actions were launched by Management including recycling, which allowed us to recover nearly 32 tons of waste in 2018, or procedures to save energy, water, and more. As part of a commitment to corporate social responsibility (CSR), Management encourages the Green Team initiative in its information, awareness and reflection process.

The Green Team brings together several dozen individuals within the institute and hopes to get people thinking about sustainability and develop practices to anticipate the inevitable changes to come. The Green Team is preparing a series of seminars that will address the multiple facets of

the ecological crisis as well as ways to deal with it and limit its impact as much as possible. It also hopes to set up concrete actions at the Paris Brain Institute centered on the fight against waste, lowering the use of disposable materials and limiting CO2 emissions due to air transport. These actions are at their starting point and the Green Team is in contact with several bodies of the Paris Brain Institute including the Social and Economic Committee, the Ethics Committee and the Health, Safety and Environment (HSE) Unit to develop these actions further.

The Paris Brain Institute ethics committee in 2019

The Ethics Committee of the Paris Brain Institute (COMETH-ICM) is responsible for fostering new ideas on the ethical and deontological questions raised by scientific and medical research as it is implemented within the Institute. Its mission is also to help all research staff at the Paris Brain Institute act in accordance with ethical standards, by

facilitating reflection on their own practice and by contributing to general reflection based on pioneering experiences. During its first year, it focused primarily on consulting with staff to define future priorities, the structuring of its response to queries and how to communicate on its missions.

Ethics and professional conduct queries

The COMETH-ICM can respond to queries or initiate discussion on problems requiring special consideration to find the best course of action. When it examines a file, after having verified eligibility with regard to its missions, the committee works in compliance with the strictest conditions of impartiality and confidentiality. When the file requires specific expertise, independent experts are asked to provide their analysis. The experts involved sign a form to verify the independence of their judgment as well as a confidentiality agreement. Based on their conclusions and the committee's own analysis, the COMETH-ICM issues an opinion that is shared with the issuer of the query.

COMETH issued 6 opinions in 2019. Three of the queries came from general management or unit management at the Paris Brain Institute, and three came from research personnel. The issues submitted by the management teams pertain to questions about the opportunity for industrial partnership due to the nature of the company's activity, and the issue of multiple contracts per researcher. The 3 opinions were taken into account by the relevant departments. Two research teams contacted COMETH-ICM regarding tensions when research results were published. Another query was a request for an opinion from the ethics committee of the coordinating institution, to meet the request of partner institutions within the framework of a European project on a subject unconsidered by regulatory ethics committees (reuse of post-mortem biological samples). The COMETH-ICM opinion allowed the project to start.

Communication and training

COMETH participated in two course units of the iMIND (international Master in Neurodegenerative Diseases) Master2 program at Sorbonne University: "Brain to Market Summer School" (Regulatory and ethical aspects of data sharing) and "Novel technologies applied to human pathologies" (Ethical aspects in predictive genomics, iPS use and data sharing).

From January 2020, COMETH will participate in monthly training of new Paris Brain Institute members, on the basis of the Institute code of ethics.

Gender equality: the contribution of neuroscience

Despite being a country internationally renowned for facilitating the career of women with the appropriate infrastructure and specific legislation, France is not any better in providing equal opportunities to women and men. In an article published in the journal *Nature Human Behavior*, Violetta Zujovic, and Christiane Schreiweis, members of the XX Initiative committee of the Paris Brain Institute, explain how a neuroscientific approach could more effectively combat gender inequalities. The publication warns of the impact of cognitive biases, beyond our control but deeply rooted in our mentality. Unconscious prejudice and stereotypes have a powerful influence on almost all of our choices.

The Paris Brain Institute's XX initiative committee, involving researchers and experts in neuroscience, offers a roadmap in several stages. Their recommendations highlight an essential first step: the realization that implicit shortcuts, resulting from existing prejudices, impact our decision-making. To facilitate this individual and collective awareness, a quantified assessment of gender inequality in terms of salary or level of responsibility is necessary. The impact of this committee and its neuroscientific approach introduced a year and a half ago underscores the importance of combining concrete action with national policy. The committee will organize a symposium on "gender bias: science and actions" in 2020, open to all, and practical workshops presenting tools to revise our own prejudices and know how to assess our own values and skills. A neuroscience-based approach can now be a major driver to change the way we think and our behaviors.



Paris Brain Institute's governance

The Board of Directors regulates, through its deliberations, the affairs of the Institute. It decides on the strategic orientations proposed by the Director General. He votes the budgets and approves the accounts. It is chaired by Professor Gérard Saillant, President of the Paris Brain Institute and composed of 15 members divided in 4 colleges: founders, qualified personalities, full members (INSERM, CNRS, Sorbonne University, AP-HP) and Friends of the Foundation.

THE BOARD OF DIRECTORS

MEMBERS OF THE BOARD OF DIRECTORS COLLEGE OF FOUNDERS

- **Gérard Saillant**, Professor of Orthopaedic and Traumatological Surgery, President of the Paris Brain Institute
- **Jean Todt**, President of the FIA, Vice-President of the Paris Brain Institute
- **Serge Weinberg**, President of Weinberg Capital Partners, Treasurer of the Paris Brain Institute
- **Jean Glavany**, Former Minister
- **Jean-Pierre Martel**, Lawyer

COLLEGE OF QUALIFIED PERSONALITIES

- **Philippe Ménasché**, Professor of Thoracic and Cardiovascular Surgery
- **Richard Frackowiak**, Emeritus Professor at University College London
- **Elisabeth Tournier-Lasserre**, Professor of medical genetics at Université Paris Diderot

COLLEGE OF FULL MEMBERS

- **Gilles Bloch**, representative of the Institut National de la Santé et de la Recherche Médicale (INSERM)
- **Bernard Poulain**, representative of the Centre National de la Recherche Scientifique (CNRS)
- **Bruno Riou**, representative of Sorbonne Université
- **Erik Domain**, representative of the Assistance Publique – Hôpitaux de Paris (AP-HP)

COLLEGE OF THE FRIENDS OF THE FOUNDATION

- **Maurice Lévy**
- **Christian Schmidt de la Brélie**
- **David De Rothschild**

PUBLIC COMMISSIONER

- **Philippe Ritter**

COMMITTEES OF THE BOARD

SCIENTIFIC ADVISORY BOARD

The Scientific Advisory Board (SAB) assists the Board of Directors or the CEO on the main orientations, programmes or scientific approaches of the Institute. It is composed of the best international experts in neuroscience. Every 5 years, the Paris Brain Institute, as a joint research unit (in French UMR), is assessed on the quality of its research, its organization, its strategy and its five-year scientific projects. The teams' research projects are evaluated by the SAB, whose mission is to advise the Institute and assist it in defining its general orientations. After exchanges and discussions, the SAB submits an opinion that is taken into account to build the dossier submitted for evaluation by the High Council for the Evaluation of Research and Higher Education (HCERES).

- **Michael Shelanski** - President of the CSI, Columbia University, New York, USA
- **Dimitri Kullman** - ION, University College of London, UK
- **Gabor Tamas** - University of Szeged, Hungary - Peter Brown - University of Oxford, UK
- **Brad Hyman** - Massachusetts Alzheimer Disease Research Center, USA
- **Stephen Hauser** - UCSF Sandler Institute, San Francisco, USA
- **Bill Richardson** - University College of London, UK
- **Helen Mayberg** - Center for Advanced Circuit Therapeutics, USA
- **Christian Buchel**, University Medical Centre Hamburg-Eppendorf - Department of Systems Neuroscience, Germany
- **Arnold Kriegstein** - UCSF, San Francisco, USA
- **Masud Husain** - University of Oxford, UK
- **Michael Heneka** - DZNE, University of Bonn, Germany

AUDIT COMMITTEE AND APPOINTMENTS AND REMUNERATION COMMITTEE

- **Serge Weinberg**, Chairman of the Audit Committee
- **Claire Giry**, Chairwoman of the appointments and remuneration committee, by delegation from Gilles Bloch
- **Jean Glavany**, Former Minister
- **Jean-Pierre Martel**, Lawyer

COORDINATION COMMITTEE OF THE FOUNDATION WITH ITS PUBLIC PARTNERS

- **Gérard Saillant**, President of the Paris Brain Institute
- **Gilles Bloch**, Representative of the INSERM
- **Bernard Poulain**, Representative of the CNRS
- **Bruno Riou**, Representative of Sorbonne Université
- **Erik Domain**, Representative of AP-HP

THE ETHICS AND DEONTOLOGY COMMITTEE

The Paris Brain Institute Ethics and Deontology Committee was established with the dual responsibility of contributing to the ethical conduct of research and the compliance to the ethical rules of the trades that contribute to its production. It is composed of 12 members including 7 Paris Brain Institute collaborators and 5 qualified external personalities

FOUNDERS

- **Gérard Saillant**, Professor of Orthopaedic and Traumatological Surgery, President of the Paris Brain Institute
- **Jean Todt**, President of the FIA, Vice-President of the Paris Brain Institute
- **Yves Agid**, Honorary Professor of Neurology and Neuroscience
- **Luc Besson**, Film Director
- **Louis Camilleri**, CEO of Ferrari
- **Jean Glavany**, Former Minister
- **Maurice Lévy**, Chairman of the Executive Board of Publicis Groupe, Co-Chair of the Paris Brain Institute Friends Committee
- **Olivier Lyon-Caen**, Professor of Neurology, former Director of the Nervous System Diseases Centre of Pitié-Salpêtrière University Hospital
- **Jean-Pierre Martel**, Lawyer
- **Max Mosley**, Former President of the FIA
- **Lindsay Owen-Jones**, Honorary President of L'Oréal, Honorary President of the Paris Brain Institute Friends Committee
- **David de Rothschild**, President of the Executive Board of Rothschild Bank & Co., Co-Chair of the Paris Brain Institute Friends Committee
- **Michael Schumacher**, Formula 1 Driver
- **Serge Weinberg**, President of Weinberg Capital Partners, Treasurer of the Paris Brain Institute

THE PARIS BRAIN INSTITUTE ASSOCIATION OF FRIENDS

- **Lily Safra**, Honorary President, President of the Edmond J. Safra Philanthropic Foundation
- **Gérard Saillant**
- **Jean Todt**
- **Lindsay Owen-Jones**
- **Maurice Lévy**
- **David de Rothschild**
- **Jean-Pierre Martel**
- **Serge Weinberg**

THE MANAGEMENT COMMITTEE (CODIR)

Decisions are taken by the Director General on the basis of the CODIR members' recommendations.

- **Pr Alexis Brice**, Prof Alexis BRICE
Chief executive of the Paris Brain Institute and the Mixed Research Unit (UMR)
- **Prof Jean-Yves DELATTRE**
Medical Director
- **Prof Bassem HASSAN**
Scientific director and Deputy Director of the UMR

- **Corinne FORTIN**
Secretary General of the Paris Brain Institute and the Mixed Research Unit (UMR)
- **Jean-Louis DA COSTA**
Director of Communications and Development

In addition, the Support functions management Committee (CODIS) pilots several institutional and transversal projects

4 ADVISORY COMMITTEES

They issue opinions and recommendations in their area of expertise.

THE SCIENTIFIC AND MEDICAL STEERING COMMITTEE (COPIL)

The Scientific and Medical COPIL enables researchers to participate in decision-making on scientific issues and financial issues that impact research.

THE TEAMS' COUNCIL

The teams' council, made up of the Director General and all the team leaders (25 in 2019), meets once a month. It is consulted on the scientific policy, the budgetary aspects and the means to be implemented in the UMR.

THE LABORATORY COUNCIL

The mission of the Laboratory Council is to advise the UMR management on the life of the UMR, the scientific policy, the budgetary and human resources policy, and all other questions related to the life of the UMR. The members of the laboratory council are elected by their college (5 colleges in 2018). The number of representatives is proportional to the number of members of the college (15 members in 2018).

THE COMMITTEE ON GENDER EQUITY

The Paris Brain Institute, according to the recommendations of an internal collective, the XX initiative, approved by the Scientific Advisory Board and the executive committee has formalized in 2018 a new advisory committee: the Committee for equity between men and women.

Several missions and actions of this committee have already been proposed and validated by the Management. The first step is to inform as many people as possible about the existence and the effect of gender bias in decision-making, in the behaviour adopted between colleagues but also in the way of approaching clinical research on mixed populations. These trainings will have for main goal a general awareness. Coordination with human resources management will improve the work environment and optimize research.

- Key actions were or will be carried out for the career of women at the institute, juniors or seniors, so that a men/women ratio is respected: A workshop on leadership for young women scientists was set up with a first session in February 2018 and a second one in October 2018. These trainings will be organized on a yearly basis.
- Management Committee recommendations have been made to increase the number of women becoming team leaders as part of the Paris Brain Institute Joint Research Unit Renewal and for more new teams led by women to be recruited.
- The committee will ensure that more women are integrated into the various committees and councils of the institute.

In addition, the committee for equity between men and women coordinates its activities with other national committees, participates in meetings on this subject and communicates its action plan to other universities (Bordeaux, Caen).

Financial report

Rigor and transparency at the core of our actions

The breakthroughs and actions of the Paris Brain Institute are carried out with the utmost transparency. "Trusted donation" certification was granted to the Paris Brain Institute-ICM Foundation in November 2010 and renewed in October 2019. This accreditation certifies that the Institute's activities are in line with the committee's principles: statutory functioning and selfless management, rigorous management, quality of communication and fundraising actions and financial transparency.

Fundraising

2019 fundraising revenue stands at € 17 million.

In 2019, main new sponsorship agreements signed were:

- Janssen Horizon
- AXA SA - Axa Bank - Thellie
- Bolloré Group
- UNIM
- Fonds Saint Michel
- Roger de Spoelberch Foundation

The Circle of Friends of the Paris Brain Institute brings together donors who have been involved since the early days of the Paris Brain Institute adventure with large donations (€ 10,000 + annually). This Circle was created to specifically thank major donors, individuals, companies and foundations, who have stepped up for Institute since 2008. Membership criteria for the Circle of Friends have changed and now include solely donors with donations of a minimum of € 10,000 over a single year and no longer over several years as was the case before. Following this change in criteria, the Circle brings together 559 donors. In 2019, the Circle was co-chaired by Mr. Maurice Lévy and Mr. David de Rothschild, Founding Members of the Paris Brain Institute.

In order to increase its resources, the Paris Brain Institute continued its fundraising campaigns in 2019.

The Paris Brain Institute is particularly grateful and extends its sincerest thanks to loved ones who have organized in memoriam fundraisers for the benefit of the Institute.

In-kind patronage and sponsorship

Many companies have given us their support by offering their expertise in their respective fields or by donating products free of charge. This section also includes artists or collectors who have donated works of art sold for to benefit the Paris Brain Institute.

The Paris Brain Institute-ICM Foundation has benefited from in-kind patronage as part of its PR actions and at-large fundraising efforts, namely:

- media slots with: Air France, ReedExpo/FIAC, ZenithOptimedia, Richard Mille, TFI, Klesia
- products and services free of charge: International Automobile Federation, Publicis Group, Orrick Rambaud Martel, IDEC, ANACOFI



2019 Financial situation

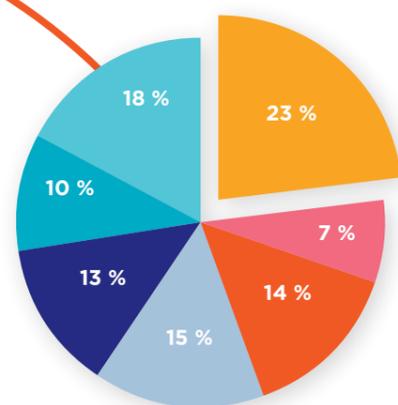
2019 SOURCES OF FUNDS

Research project funding is characterized by a variety of funding sources with a long-term perspective in order to produce knowledge and major neuroscience breakthroughs.

2019 resources amounted to € 58.3 million, including € 48.1 million in revenue for the year and € 10.2 million in the carry-over of resources allocated and not used in previous years. Revenues for the financial year mainly amount to revenue from fundraising (€ 17.3 million), either from the general public (€ 13.4 million), or from companies and private foundations (€ 3.9 million).

They also include:

- Revenue from technological platform activities (€ 5.3 million) and from research collaborations with industrial partners (€ 3.50 million),
- Public and private grants (€ 8.4 million)
- Funding for the "IHU program" (€ 7.6 million).
- Other revenue (leases, rebilled expenses, financial products, etc.) (€ 6 million)



Resources

- Funds collected from the general public
- Funds collected from businesses and private foundations
- Public and private subsidies
- Revenue from platform activity and industrial partnerships
- Funding of the "IHU Program"
- Other revenue (leases, rebilled expenses, financial products, etc.)
- Carry-over of previous resources

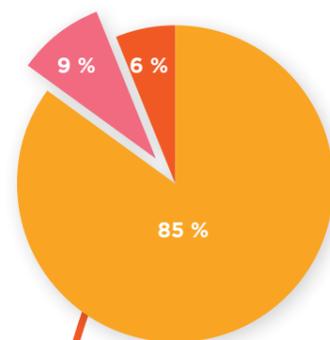
2019 APPLICATIONS OF FUNDS

Total 2018 applications of funds amounted to € 58.3 million: € 43.4 million used in 2019 and € 12.6 million to be used later with allocated resources. The total dedicated to social missions amounted to € 36.8 million, representing 85% of the total applications for the 2019 financial year. Social missions of the Paris Brain Institute include:

- Research programs;
- Technological platforms;
- Scientific leadership and implementation of international alliances;
- Incubation of innovative companies.

Funding for research projects is mainly dedicated to diseases of the nervous system and spinal cord injuries. Technological platforms (neuroimaging, vectorology, genotyping sequencing, cell culture, histology and bioinformatics) support these projects. Fundraising and communication costs correspond to the costs incurred to collect funds from individuals (donations and legacies) and private companies and foundations (patronage and sponsorship actions), as well as PR actions. They represent 9% of applications.

Operating costs represent support staff expenses (general secretariat, finance, human resources, legal, IT and logistics) amounting to 6% of total applications for the financial year. Commitments on allocated resources (€ 12.6 million) are donations from companies or foundations received during the year that will be used later for specific multi-year privately or publicly funded (ANR, etc.) research programs.



Applications

- Social missions
- Fundraising and communication costs
- Operating costs

Allocation of funding collected from the general public

Sources of funding collected from the general public used in 2019 amounted to € 13.4 million. In summary, out of € 100 of resources collected from the general public, € 72 were used to finance social missions and investments, € 22 were used to cover fundraising and communication costs and € 6 were used to cover Paris Brain Institute operating costs.

BILAN 2019

ASSETS (M€)	2018	2019
NET FIXED ASSETS	56	65
ACCOUNTS RECEIVABLE	65	67
TOTAL ASSETS	121	132

LIABILITIES (M€)	2018	2019
ASSOCIATION FUNDS	57	51
FINANCIAL YEAR INCOME	-0,2	1,7
DEDICATED FUNDS	13	15
DEBT	34	41
DEFERRED INCOME	18	24
TOTAL LIABILITIES	121	132

COMMENTS

Total investments made by the Paris Brain Institute since its opening amount to € 46 million dedicated mainly to technological platforms that support research. Investments for the year amounted to €15.7 million.

They include:

- Scientific investments: Acquisition of a latest-generation sequencer (€800K) and scientific materials and equipment (€1 238K);
- The acquisition of scientific computing storage capacity and computing clusters (€1 042K).

Net fixed assets amounted to € 65.2 million. As of December 31, 2019, cash flow amounted to € 42.5 million. Paris Brain Institute associative funds amount to € 56.1 million. They include equity for € 47.9 million supplemented by investment grants of € 4.6 million. Nonexpendable endowment amounts to € 1.2 million. At the end of the financial year, dedicated funds (funds remaining to be committed to multi-year programs) amounted to € 15 million.

Reserve policy

When it was created in 2006, the Paris Brain Institute-ICM Foundation received an endowment of € 11.7 million, of which € 1.2 million were nonexpendable. Thanks to rigorous budget management, the Paris Brain Institute-ICM Foundation has achieved an income-expense balance for 4 years, thereby avoiding drawing on its reserves. Furthermore, the policy of the members of the board of directors in terms of investment is extremely cautious. The Paris Brain Institute's cash is invested in marketable securities (capitalization contract signed with leading banking institutions, guaranteed in capital and 100% in euro funds).

Voluntary in-kind contributions

Volunteering:

The Paris Brain Institute benefited from hours of volunteer work during the year, especially for communication activities and events. Estimated volume is 1.2 FTE, or on the basis of an hourly minimum wage, an amount of € 32k.

In-kind sponsorship:

The Paris Brain Institute Foundation-ICM has benefited from in-kind patronage as part of its PR actions and at-large fundraising efforts, namely:

- media slots with: Air France, ReedExpo/FIAC, ZenithOptimedia, Richard Mille, TF1, Klesia
- products and services free of charge: International Automobile Federation, Publicis Group, Orrick Rambaud Martel, IDEC, ANACOFI

The Paris Brain Institute is particularly committed to maintaining its level of excellence and has implemented internal and external control to guarantee its thorough and efficient management, notably as a member of the Trusted Donations Charter Committee and by hiring an independent auditor.

Trusted Donation

The breakthroughs and actions of the Paris Brain Institute are carried out with the utmost transparency. "Trusted donation" certification was granted to the Paris Brain Institute Foundation in November 2010 and renewed in October 2019. This accreditation certifies that the Institute's activities are in line with the committee's principles: statutory functioning and selfless management, rigorous management, quality of communication and fundraising actions and financial transparency.



2019 expenditure statement (in €)

APPLICATIONS	2019 Applications	2019 Allocation of resources raised from the general public by application	RESOURCES	2019 Resources collected	2019 Resources collected and used
			Carryover of resources collected from general public not allocated/used at start of fiscal year		0
1. Social Missions "Actions directly carried out"	36 789 347	6 915 234	1. Resources collected from the general public	13 421 644	13 421 644
Research programs	24 579 082	2 551 114	Unallocated monetary donations	11 100 612	11 100 612
Technological research platforms	8 670 672	2 385 582	Allocated monetary donations	640 644	640 644
Research applications and incubator	2 141 065	974 409	Unallocated bequests and other gifts	1 680 388	1 680 388
Other social missions	1 398 528	1 004 127	Allocated bequests and other gifts	0	0
			Other revenue from general public generosity	0	0
2. Fundraising costs	4 049 693	2 907 634	2. Other private funds	12 225 792	
Cost of appeals to the generosity of the general public	3 686 834	2 647 105	Patronage	3 906 739	
Costs related to private fund canvassing	362 699	260 414	Partnerships	4 490 303	
Communication costs	160	115	Private subsidies	3 828 750	
			3. Subsidies and other public financial support	13 267 802	
3. Institutional operational costs	2 608 348	802 857	4. Other products	9 200 655	
			Financial products	517 319	
			Services rendered	5 324 739	
			Other products	3 358 597	
I. TOTAL APPLICATIONS	43 447 388	10 625 725	I. TOTAL RESOURCES	48 115 894	
II. PROVISIONS	555 076		II. CARRYOVER OF PROVISIONS		
III. PLEDGES ON ALLOCATED RESOURCES	12 634 148		III. CARRYOVER OF ALLOCATED RESOURCES UNUSED IN PREVIOUS FISCAL YEARS	10 171 300	
			IV. VARIATION OF ALLOCATED FUNDS COLLECTED FROM THE GENERAL PUBLIC		- 14 940
IV. FISCAL YEAR SURPLUS	1 650 582		V. INSUFFICIENT FISCAL YEAR RESOURCES		
V. GRAND TOTAL	58 287 194		VI. GRAND TOTAL	58 287 194	13 406 704
Share of fixed assets acquired during the fiscal year financed by collected funds		3 041 300	TOTAL APPLICATIONS FUNDED BY FUNDS COLLECTED FROM THE GENERAL PUBLIC		13 406 704
Neutralisation of provisions for depreciation of fixed assets financed by collected funds		- 260 321	BALANCE OF FUNDS COLLECTED FROM THE GENERAL PUBLIC NOT ALLOCATED/USED BY END OF FISCAL YEAR		0
TOTAL APPLICATIONS FINANCED BY FUNDS COLLECTED FROM THE GENERAL PUBLIC		13 406 704			
EVALUATION OF VOLUNTARY IN-KIND DONATIONS					
"Social missions Fundraising costs Operational costs Total"	32 859		"Volunteering In-kind services In-kind donations Total"	32 859	

Thank you

MAJOR PATRONS

- Elisabeth Badinter
- Maria Rosa Bemberg
- Dominique, Alexandre et Joy Desseigne
- FIA FOUNDATION FOR THE AUTOMOBILE AND SOCIETY
- FONDATION BETTENCOURT SCHUELLER
- FONDATION GROUPE EDF
- FONDATION EDMOND J. SAFRA
- FONDATION LILY SAFRA
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- HSBC FRANCE
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- Richard Mille
- OCIRP
- ORRICK RAMBAUD MARTEL
- Lindsay Owen-Jones
- PUBLICIS
- RACE OF CHAMPIONS
- Édouard et Martine de Royère
- Michael Schumacher
- Jean Todt et Michelle Yeoh
- 1 anonyme

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- Famille Jan Aron
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- FONDATION AREVA
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- M. et Mme Alain Joly
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- Maurice Lévy
- Christiane Laborie et Roger Lionnet
- Alain Mallart - GROUPE ENERGIPOLE
- Dominique et Danièle Mars
- ORACLE
- PATHÉ
- PHILIPPE FOUNDATION, INC.
- Christian Poquet
- RATP
- David de Rothschild
- SCHNEIDER ELECTRIC

- Claude Sfeir
- Dominique Vizcaino
- Serge Weinberg
- 1 anonyme

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- ACCOR
- ACCURACY
- AMAURY MEDIA
- Benoît André
- Christine André
- Yvon André et Annette Gellé
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- ASSOCIATION CLUB DES 20 km DE PARIS
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- CAMPENON BERNARD CONSTRUCTION
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- Rena et Jean-Louis Dumas
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- Henri Dura
- Cécile et Christophe Durand-Ruel
- ELIVIE

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- Emilio Ferré
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- FONDATION PLENUM
- FONDATION MARIE-ANGE BOUVET-LABRUYÈRE
- FONDATION ROGER DE SPOELBERCH
- FONDS DE DOTATION JANSSEN HORIZON
- FONDS DE DOTATION LIONS CLUB LYON DOYEN
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- FONDS SAINT MICHEL
- Dimitri et Maryvonne Fotiadi
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- Jean-René Fourtou
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- GROUPE ROUSSELET
- Mina Gondler
- GROUPE EMERIGE
- GROUPE G7
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- Jean-Jacques Lestrade
- LES AMIS DE CAPUCINE
- LIGUE DE FOOTBALL PROFESSIONNEL
- LILLY
- Georges Louvriot
- Pascal Olivier et Ilana Mantoux
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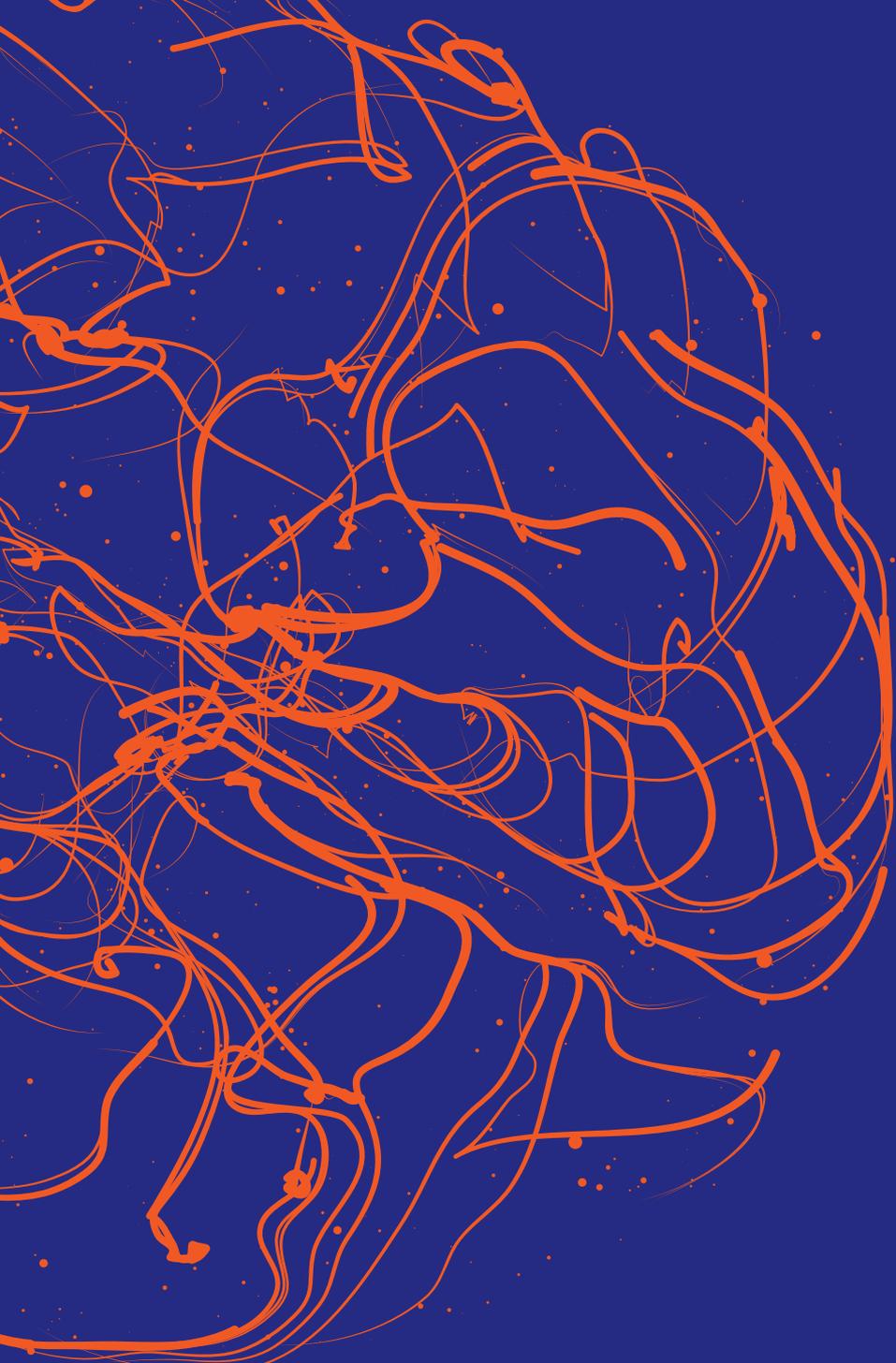
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