Paris Brain Institute
ICM

Synapse

The newsletter designed to connect with you

No. 34 - August 2023

Special Report

Neuroscience research benefits everyone, even the youngest

Paris Brain Institute fights against brain diseases that are often associated with old age. However, many neurological and psychiatric conditions develop in childhood: epilepsy, schizophrenia, depression, multiple sclerosis, cerebellar ataxias, dystonia, etc. Pediatric forms of these diseases are unfortunately more common than we imagine and compromise the quality of life of patients at a crucial time in their development.

Researchers and doctors are now working to change the trajectory of these diseases to avoid preventable disabilities and detect the sometimes discreet signs that predict the appearance of neurodegeneration later in life. For example, recent research has shown that Huntington's disease, which occurs between the ages of 30 and 50, is associated with brain abnormalities that occur as early as the embryonic stage.

Understanding the subtle pathophysiological that make up the foundation of a disease could help us, in the long run, to stop or delay the onset of symptoms. But that is not all: research dedicated to major cognitive and brain functions – attention, learning, memory, motivation, creativity – helps us understand under what conditions, in children, development sometimes deviates from the norm to the point of creating disorders.

This research is essential to identify the characteristics of brain diseases at different stages of life. The success of this research depends on your faithful support, for which we warmly thank you.

You will also find in this issue 2022 Institute highlights and a presentation of the foundation's accounts. We are proud to show that its management is as robust as its scientific ambition. One does not exist without the other.

Serge Weinberg
Founding Member and Treasurer
of Paris Brain Institute

Brain & Mind, a future Biocluster in neuroscience

On May 16, the President of France, Emmanuel Macron, announced that the Brain & Mind project, led by Paris Brain Institute, the FondaMental Foundation, and the Vision Institute, was named an official French 'biocluster'. The French Biocluster initiative aims to create poles of excellence with a global dimension bringing together companies, patient care, research, and disruptive innovation, with the ambition of transforming the landscape of French biomedical research. Brain & Mind will bring together more than 50 scientific, medical, and industrial partners to create an internationally renowned ecosystem for neuroscience research in France.

NeurAL programme: announcement of the winners

Launched in 2023 by Paris Brain Institute with the support of the Anne and Claude Berda Foundation, NeurAL (Neuroscience Acceleration Launchpad) is an initiation program in neuroscience dedicated to the development of therapeutic products. The successful candidates were announced last July and will benefit from personalized support as well as financial support. The first prize was awarded to the IGHOR project, which aims to develop new candidate molecules in the treatment of glioblastoma. The second prize was awarded to CicaNEURO for the design of a drug candidate with neuroprotective properties that can be applied to Parkinson's disease.

The origin of great discoveries deciphered

How is scientific research a cornerstone of discovery? What are the mechanisms at work in the brain? In his new book, Professor Yves Agid, member of the Academy of Sciences and founding member of Paris Brain Institute, addresses the process of creation in a way that is neither banal, academic or routine. There are more researchers than "discoverers" because making a discovery and inventing something new, useful, and unexpected is not easy.

Le Cerveau, machine à inventer, by Professor Yves Agid, Albin Michel, 208 pages, 20.90 euros.

SYNAPSE, Paris Brain Institute's newsletter addressed to its donors. No. 34 – 2023. Editorial Board: Jean-Louis Da Costa, Marion Doucet, Astrid Crabouillet, Isabelle Rebeix, Marie Simon, Claire Pennelle, Lauriane Gallier, Carole Clément, Aurélie Grosse, and Emma Kavcic Mondoloni. Design: Adfinitas. Printer: Imprimerie Jean Bernard. Printed: 115 000 copies. © adobestock: alphaspirit - romaset - andreaobzerova - Freedomz - Przemek Klos - Igor - peterschreiber.media - lera_efremova - New Africa / Paris Brain Institute

The Mutuelle du Médecin becomes a sponsor

Who knows more about patient concerns and the public health urgency of nervous system disorders than a physician? This is why, true to its mutualist values, the Mutuelle du Médecin has been supporting Paris Brain Institute since 2022. Not wanting to restrict their funding to a specific project, the Mutuelle du Médecin's three-year commitment provides general funding in support of all of our programs. This will provide invaluable support to our researchers, enhancing their freedom and flexibility and creating the best conditions for new discoveries.

For more than 120 years, the Mutuelle du Médecin has been run by doctors, for doctors. Its vision of protecting and supporting doctors and their families is embedded in its deeply mutualist identity.

"Supporting health innovation, encouraging prevention, and participating in research development are among our philanthropic priorities," says Dr. Anne-Elizabeth Cabée, Chairperson of the Mutuelle du Médecin. *"Our commitment to Paris Brain Institute responds to an urgent and vital goal of improving health and aging well through the emergence of new therapies in neurology for the benefit of patients."*

Many thanks to the directors and management of the Mutuelle du Médecin for their support!

www.mutuelle.org

Science celebrated!

An event that highlights science, technology, and innovation throughout France, the Fête de la Science is aimed at all audiences and helps to promote the sharing of knowledge between scientists and citizens. Paris Brain Institute reiterates its participation for this 23rd edition (from October 6 to 16) by organizing two conferences face-to-face and digitally: one on the mechanism of creativity and the other on what happens in our brain when neurons die.

Information: www.fetedelascience.fr

YOU ARE 342 ACTIVE MEMBERS OF THE CIRCLE OF FRIENDS (WHO DONATE €10 000 OR MORE PER YEAR)*. THANK YOU FOR YOUR COMMITMENT.

* on 12/31/2022

Follow us

seen on the web

Find out more in the "News" section of our website.

- Multiple sclerosis: a new tool to reduce clinical failure
- A simple blood test can now diagnose De Vivo's disease
- Appreciation of humorous scenes is associated with specific electrical activity in the brain

videos

- July 4th conference on sleep
- May 11th Science, Art, and Culture Conference: "When the brain ruminates" with Prof. Cynthia Fleury, Chairperson of "Humanities and Health".
- Understanding leukodystrophies in two minutes with Prof. Fanny Mochel

agenda

Thursday, 21 September
World Alzheimer's Day

Thursday, 21 September
Morning open conference on Alzheimer's disease: registration required at **cercle@icm-institute.org** or by phone on **+33 (0)1 57 27 40 32**

Friday, October 6 to Monday, October 16
Science Festival 2023 at Paris Brain Institute. National program: www.fetedelascience.fr

Seeing and recording the brain to understand its functioning and failures

Prof. Stéphane Lehéricy,
Director of CENIR (Research Neuroimaging Center) of Paris Brain Institute, Head of the Department of Neuroradiology at Pitié-Salpêtrière, co-leader of the team "Mov'It: Movement, Investigations, Therapeutics. Normal and abnormal movement: pathophysiology and experimental therapeutics."

What is the CENIR?

S. L. The CENIR platform specializes in neuroimaging and neurophysiology. It offers the Institute's research teams six essential pieces of equipment for the study of brain diseases and the understanding of normal brain function: magnetic resonance imaging (MRI), PET-MRI, electroencephalography (EEG), magneto-encephalography (MEG), transcranial electrical or magnetic stimulation, stereotactic imaging, and ultrasound.

What is the purpose of this equipment?

S. L. MRI obtains multiple images of brain structure or function, PET-MRI combines simultaneously a positron emission tomography (PET) and an MRI; EEG records the electrical signals of the brain; MEG explores visual, auditory, and sensory cognitive modalities, transcranial electrical or magnetic stimuli to study excitatory, inhibitory, or plasticity phenomena associated with motor, sensory, or cognitive behavior.

Through stereotactic imaging used for deep brain stimulation in Parkinson's disease, for example, but also in drug-resistant epilepsies, three-dimensional internal structures of the brain can be identified. Transcranial-focused ultrasound is used for surgery and also to open the blood-brain barrier for more targeted and effective therapy.

How will the acquisition of a 7T MRI enhance certain projects or initiate new ones?

S. L. The Tesla 7 MRI (7T) will greatly improve image quality. At 3T, the resolution of brain images is 500 microns to 1 millimeter or 1000 microns. At 7T, we can accurately observe structures of 200 microns, or five times smaller.

> “The 7T MRI can reveal whole areas of the brain. „

The 7T MRI can reveal whole areas of the brain, that were previously difficult to map.

The precision of the images will lead to a better knowledge of the anatomy, structure, and functioning of the brain, but also a better understanding of the diseases that affect it, therefore, a more precise diagnosis as well as more targeted and more effective treatments.

The 7T MRI allows more precise targeting of the areas to be stimulated or treated, such as brain tumors, by significantly limiting the side effects.

Neuroscience research benefits everyone, even the youngest

For many, “brain diseases” evoke Alzheimer's or Parkinson's, but among the 21 pathologies studied at Paris Brain Institute, 12 of these manifest in childhood. For example, over 9 million young people in Europe are estimated to suffer from a diagnosed mental disorder. For every 1 000 children and young people in Europe, 5 are likely to have epilepsy and this figure rises to 6 in 1 000 for the USA.

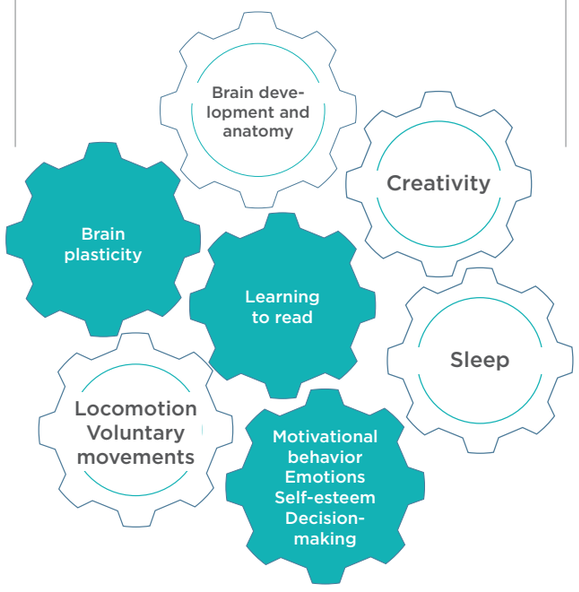
Learning, motivation, sleep... brain research affects us all!

Although the major challenge of neuroscience lies in the development of therapies to treat neurological and psychiatric diseases, understanding the functioning of the healthy brain is equally important and indispensable.

Imagine someone trying to fix a car engine without knowing how it works, what parts make it up, and how they interact with each other. It would be impossible to determine the causes of the breakdown.

This metaphor may seem simplistic, yet it illustrates well the challenge of research on the brain because, even today, all the constituents of this complex organ are not identified and some higher functions call on mechanisms still unknown.

Major brain functions



At Paris Brain Institute, researchers who study processes, such as learning to read, motivation, procrastination, and creativity, are in daily contact with other researchers or clinicians who focus their work on brain diseases.

"If fundamental research yields a result that might be relevant to a disease, it is easy at Paris Brain Institute to find the right expert to test the hypothesis."

Prof. Bassem Hassan, Scientific Director

In bilingual people, the visual cortex treats reading Latin and Chinese characters differently

Learning to read in childhood is accompanied by anatomical and functional changes in various brain regions. The work carried out at Paris Brain Institute by the "PICNIC - Neuropsychology and functional neuroimaging" team co-directed by Professor Laurent Cohen, aims to better understand the brain transformations involved in this process through functional MRI, which observes the activation of the different areas of the brain, anatomical MRI, for the study of subtle changes in the structure of white matter and grey matter, but also electro- and magneto-encephalography for the analysis over time of the circulation of information in the brain.

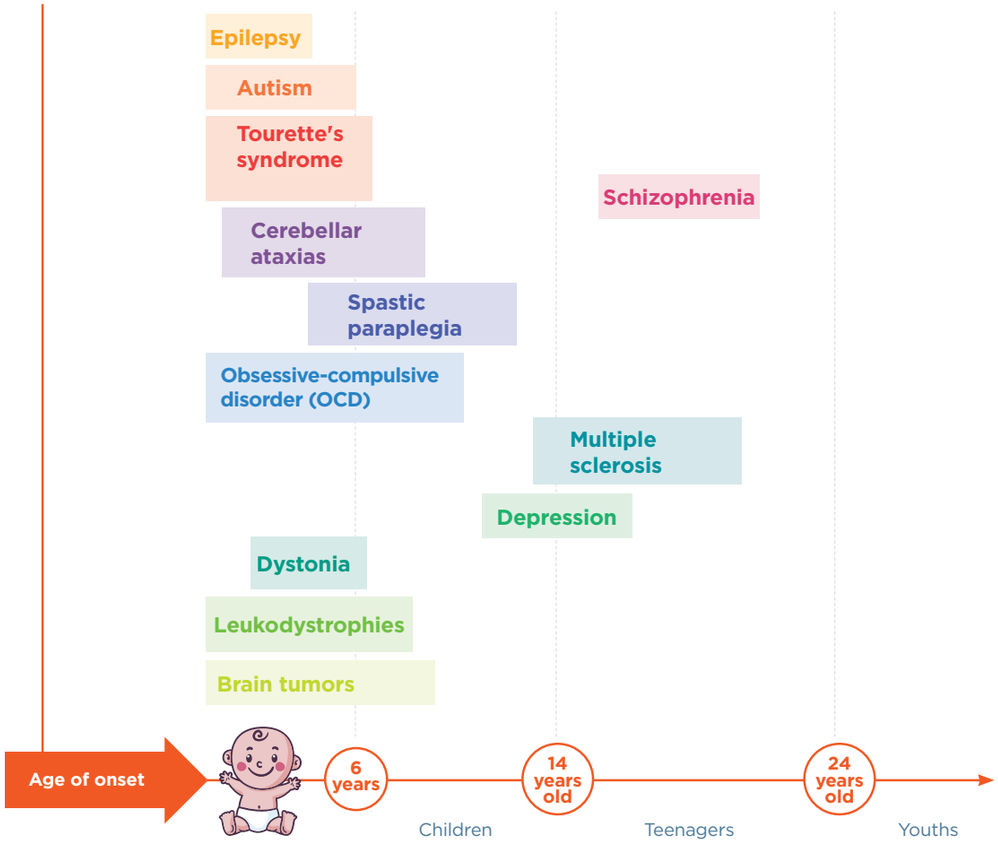
Nearly half of humanity speaks more than one language and many adults can read and master multiple writing systems. How does the visual cortex adapt to the recognition of words written with different characters? To answer this question, using high-resolution 7T functional MRI, researchers showed that the brain area of reading (the Visual Word Form Area or VWFA) is actually composed of tiny cortical areas sensitive to word perception. These are equally activated when reading English and French, two languages written in the Latin alphabet. However, in English-Chinese bilinguals, certain cortical areas react specifically to Chinese ideograms and also seem to be involved in face recognition. Learning several writing systems could therefore shape the visual cortex to the point that certain groups of neurons specialize in reading an alphabet.

Reading, whether in words or music, involves new skills for which our brains are not innately equipped. However, the great plasticity of this organ allows it to be modified to accommodate these new capacities: some regions acquire new functions and on a larger scale and collaboration networks develop between remote regions.

Prof. Laurent Cohen, neurologist, team leader at Paris Brain Institute

This work opens avenues towards better understanding of the difficulties of learning to read for some children.

Research on infant, child, and teenage diseases at Paris Brain Institute



Pediatric neurological and psychiatric diseases are varied, from epilepsy to movement pathologies such as dystonia, Tourette's syndrome, and obsessive-compulsive disorders (OCD).

Did you know that 20 to 40 babies are born each week in Europe suffering from leukodystrophy; 9 million young people in Europe have a mental health disorder with anxiety and depression accounting for over half the cases, and 1 in 100 people worldwide are thought to have autism, with symptoms usually appearing in early childhood ?

Although the cause of some of these diseases is known and treatments exist, diagnosis often remains difficult because of the heterogeneity of symptoms. For others, however, there are no effective treatments yet.

This is why researchers at Paris Brain Institute are focusing their efforts on finding the causes of these diseases, identifying diagnostic biomarkers, and developing new therapies.

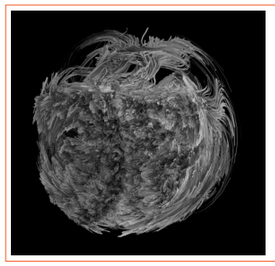
Atypical juvenile forms of Parkinson's disease

Although age is the major risk factor for developing Parkinson's disease with a prevalence of 2% in people over the age of 80, this disease can appear in young children in the case of hereditary family forms.

The "Molecular Physiopathology of Parkinson's Disease" team, co-led by Professor Jean-Christophe Corvol, coordinated an international study that identified new mutations at the origin of an atypical juvenile form of Parkinson's disease associated with intellectual disability in children aged 11 to 16 years.

This study resulted in the first identification of mutations in the PTPA gene. These mutations lead to a deficiency of the enzyme PP2A, which is very abundant in the brain and acts in particular on α-synuclein, a protein that accumulates and forms aggregates in the brain of patients with Parkinson's disease.

These results, beyond the identification of new mutations, open new avenues of research on the role of PTPA and PP2A proteins in more typical forms of Parkinson's disease, paving the way towards new therapies targeting these biological mechanisms.



A new treatment for leukodystrophies

Leukodystrophies are a group of rare genetic disorders that affect the central nervous system. A phase II/III clinical trial, coordinated by Professor Fanny Mochel, researcher at Paris Brain Institute, showed that leriglitazone can reduce the progression of certain symptoms, and above all, reduce the risk of developing the brain form of the disease associated with premature death.

Improving our understanding of Tourette's syndrome to pave the way for new treatments

Tourette's syndrome often occurs during childhood and results in chronic motor and sound tics frequently associated with different disorders: attention-deficit hyperactivity disorder, obsessive-compulsive disorders, panic attacks, etc.

Clinicians find that symptoms improve significantly in adolescence in the majority of cases and even disappear spontaneously in 30% of patients. However, significant and troublesome disorders persist in 30% of adult patients.

The monitoring of a cohort of 60 patients aged 13 to 18 years, through regular clinical examinations, brain imaging (MRI), or behavioral tests for 18 months, can identify biomarkers characteristic of the disappearance of symptoms that may constitute new therapeutic targets to be tested.

Dr. Yulia Worbe

"Symptoms, depending on their severity, can have a major impact on the schooling and social integration of young patients. Our study could lead to the identification of new methods to treat people with this syndrome and represents an immense hope of relieving them and allowing them to lead a normal life."

Share your experience

What to do when confronted with hereditary disease?

A genetic cause of a disease does not only concern the patient, but also his/her family. When a patient undergoes a genetic analysis, the doctor must inform the patient (and his/her parents for minors) that the family will have to be notified if a genetic abnormality is detected (French law of July 7, 2011).

Diagnosis of certain genetic diseases may allow the establishment of preventive measures, treatment, and in some cases, the possibility of special care during pregnancy.

What subjects or conditions would you like to read about in future issues of Synapse?

Email us your suggestions. Your subject may be covered in a special report in one of our upcoming issues.

contact@icm-institute.org

Status epilepticus: discovery of new inflammatory markers

Aurélie Hanin and Professor Vincent Navarro (Sorbonne University, AP-HP), in collaboration with Yale University, have shown a disruption of innate immunity in a rare form of epilepsy. This discovery could improve patient care.

Unlike epileptic seizures that last only a few seconds or minutes, status epilepticus corresponds to neuronal hyperactivity that persists for several hours or days. When this event occurs without a rapidly identifiable cause and in people without a neurological history, we speak of new-onset refractory status epilepticus (or NORSE). A rare event, this is a medical emergency that requires intensive care because it can cause serious neurological complications.

NORSE may appear in response to an infection or the development of a tumor. But in half of the patients, it is cryptogenic, that is to say, its origin remains unknown. To address this lack of data, Aurélie Hanin, a post-doctoral researcher, in collaboration with Professor Vincent Navarro's team, recruited a cohort of 61 NORSE patients. Of these, 51 had a cryptogenic NORSE.

The researchers assessed the clinical condition of the patients at the end of resuscitation and then looked for the presence of inflammatory markers in the blood and cerebrospinal fluid.

> **“ A rare event, this is a medical emergency that requires intensive care because it can cause serious neurological complications. „**

The same data were collected on a cohort of 37 patients with status epilepticus of known causes, and 52 control patients.

The team showed that the concentration of several cytokines – small proteins that attract inflammation cells – was higher in patients with epilepsy compared to controls. In subjects with a cryptogenic NORSE, the increase in these cytokines was also correlated with a poor prognosis.

These results suggest the involvement of a disruption of innate immunity in the occurrence of NORSE and its consequences. They also confirm the value of anti-inflammatory therapeutic strategies directed specifically against one or more cytokines in these patients: intervening very early could prevent irreversible neuronal damage.

How do our tastes influence our creativity?

Alizée Lopez-Persem, Emmanuelle Volle (Inserm), and their colleagues from the FRONTLAB team show how individual preferences influence the speed of emergence of new ideas, as well as their degree of creativity.

What drives us to develop new ideas rather than settling for familiar methods and processes? Creativity is based on complex mechanisms that we are just beginning to understand and in which motivation plays a central role. It is a key skill for adapting to change, but also for bringing it about.

> **“ Creativity is based on complex mechanisms that we are just beginning to understand and in which motivation plays a central role. „**

Emmanuelle Volle's team believes that creativity has three fundamental dimensions: exploration, which is based on personal knowledge and allows us to imagine possible options; evaluation, which consists of gauging the qualities of an idea; and selection, which allows us to choose the idea that will be verbalized.

To understand the interrelationships between these three dimensions, the researchers replicated them in a computer model that they then confronted with actual human behavior. Through the PRISM platform of Paris Brain Institute, 71 participants were invited to take free association tests, which consist of matching words in the most daring way possible. They then had to assess how much they liked these associations of ideas, and whether they seemed relevant and original.

The results of the study indicated that subjective evaluation of ideas plays a role in creativity: researchers observed a relationship between the speed of production of new ideas and the level of appreciation of these ideas by participants. In other words, the more we like the idea we are about to formulate, the faster we propose it.

Another discovery: this assessment is based on the combination of two subjective criteria – originality and relevance – whose importance varies according to the individuals depending on their experience and personality... and probably their environment.

The model designed by the team predicted the speed and quality of the participants' creative proposals, which highlights the mechanistic nature of the creative impetus. In the future, the researchers hope to define different creativity profiles. Do you have different creative preferences if you are an architect, software engineer, illustrator, or technician? What environments promote creativity or inhibit it? We may one day be able to answer these questions!

Paris Brain Institute: a multidisciplinary ecosystem to further scientific and medical innovation in neuroscience

Founded in 2010, Paris Brain Institute is a scientific and medical research center of international excellence, located in Paris within the Pitié-Salpêtrière hospital center, the largest center for nervous system diseases in Europe. Its innovative model brings together patients, doctors, researchers, and entrepreneurs in one place with a common goal: to understand the brain and accelerate the discovery of new treatments for nervous system diseases. The Institute today includes a network of more than 800 experts, within 24 research teams, 10 cutting-edge technology platforms, a clinical investigation center, multiple educational programs, and more than 2000 m² dedicated to the incubation of start-ups.

STRATEGY AND AMBITIONS

Since its creation, Paris Brain Institute's strategy has focused all its attention on patients. It's ambition is nourished by the daily scientific, technological and medical challenges that must be met in order to further innovation in neuroscience research and treatment

GOVERNANCE

Located within the Pitié-Salpêtrière Hospital (AP-HP), Paris Brain Institute is built on the association of a joint research unit (Sorbonne University, Inserm, and CNRS) and a private foundation of public interest, the ICM Foundation.

The governance of the Institute, through its board of directors, which brings together founding members, experienced professionals from various fields, and ex officio members, reflects the strong partnership forged between the public and the private sectors. It ensures that our scientific objectives are matched with appropriate resources and monitors the effectiveness of management.

In its annual report, Paris Brain Institute reports on its mission and results to provide complete transparency to its partners and donors.

The annual report of Paris Brain Institute is available on the Institute's website: institutducerveau-icm.org

2022 KEY FIGURES

826 experts at the Institute
24 research teams
10 technology platforms
5 fields of research
1 technological innovation development unit (TIDU)

564 publications in international scientific journals
8 patent applications filed in 2022
32 incubated start-ups

€11.6M in competitive grant income
€23.6M from individual, foundation and corporate donors and planned giving

PROMISING SCIENTIFIC PROGRESS

In 2022, the teams of researchers and clinicians of Paris Brain Institute made over 550 discoveries, published in leading scientific journals and platforms. Below are some of their findings:

- Deciphering a direct dialogue between the intestinal microbiota and the brain.
- Highlighting the beneficial effect of ketamine on resistant depressions.
- Promising results from a clinical trial on spino-cerebellar ataxias.
- Development of a new mathematical model to decipher the organization of the brain and its functioning in time and space.
- Identification of molecular profiles of primary lymphomas of the central nervous system, predictive of the prognosis of evolution and the risk of recurrence.
- Identification of a key brain region, the anterior cingulate cortex, in the procrastination process, and development of an algorithm for predicting this behavior.
- Highlighting a link between creativity in real life, the organization of semantic memory, and brain connectivity.
- Identification of the role of a transcription factor in the molecular mechanisms controlling the inflammatory response in the brain.

AWARDS AND COMPETITIVE CALLS FOR PROJECTS

In 2022, 18 projects obtained funding from the French National Research Agency (ANR), a success rate of 40%. Two research teams have been certified by the Fondation pour la Recherche Médicale (FRM) and more than 10 researchers have been awarded prestigious prizes, such as the CNRS Bronze Medal, the Richard Lounsbery Prize, the "Young Investigator" prize from FENS and EJN and, under the aegis of the Institut de France, the Allianz Foundation Prize and the NRJ Foundation's Scientific Grand Prize for Neurosciences.

2022 HIGHLIGHTS

2022: A PIVOTAL YEAR TO PREPARE FOR CHANGE

2022 was a year of change and laying the foundations for the years to come. The first change will be the evaluation of the Institute's joint research unit (UMR) by the High Council for the Evaluation of Research and Higher Education (Hcéres), in 2023, anticipating its renewal on January 1, 2025. The preparation of this important step gave rise in 2022 to a collective reflection on the future of the research teams. The proposals formulated were evaluated by the Institute's Scientific Advisory Board, which is composed of renowned international scientific personalities, to guarantee the excellence of the application submitted to Hcéres. The process of evaluating research teams is a core element in the life of Paris Brain Institute. The renewal of the unit will also be accompanied by the arrival of a new CEO in 2025.

SOON, TWO NEW RESEARCH TEAMS

Launched in the spring of 2021, a multi-thematic call for applications resulted in 2022 in the selection, from 259 applications, of two young scientists to form and lead two new research groups: Dafni Hadjieconomou, currently a researcher at Imperial College in London (United Kingdom), and Nikolaos Karalis from the Friedrich Miescher Institute for Biomedical Research in Basel (Switzerland). At Paris Brain Institute, Dafni wil develop a projet on the physiology of the plasticity of the brain-gut axis and Nikolaos will explore the combinatorial neuromodulation of mental states.

A YEAR OF KEY INVESTMENTS

In 2022, Paris Brain Institute made significant technological investments as part of the development plan. It signed a contract with Siemens Healthineers to purchase a MAGNETOM TERRA 7 Tesla MRI, one of the world's most powerful magnetic resonance imaging technologies for humans. This equipment, as well as a latest-generation Tesla MRI 3, also acquired, will have the particularity of being dedicated to both research and treatment. The Institute has scheduled the purchase of a STED super-resolution microscope, which pushes the boundaries of brain imaging exploration, a Neuro-Omega device, which accurately records beta waves, the abnormalities of which are characteristic of motor disorders in Parkinson's disease, and HD-MEA equipment, which will increase the analysis capabilities of the electrophysiology platform tenfold.

INNOVATING FOR NERVOUS SYSTEM HEALTH

In 2022, an ambitious “Innovation 2030” plan was developed. Firstly, the creation of technological innovation development units (TIDUs) should make it possible to accelerate the placing on the market of concrete solutions addressing urgent health needs, through the development of industrial partnerships. The first TIDU, Genov, was created in November 2022 and is developing gene and cell therapy strategies. The second acceleration tool is the "NeurAL launchpad". It aims to validate promising start-up projects and support their launch. In 2022, the iPEPS incubator also celebrated its 10th anniversary and welcomed nine new start-ups. It has also managed two start-up acceleration programs in collaboration with major pharmaceutical companies: Impact Santé Mentale (with Janssen, Eisai, Otsuka, AXA, and France Biotech) and Realize (with AstraZeneca digital solutions in the field of oncology). The Institute's innovation activity was also marked by the signing of 59 new industrial contracts, the filing of eight patent applications, the protection of four software programs, and the integration of five projects into the “Sleeping beauties” program, thanks to which 207 molecules were evaluated for their therapeutic value.

TRANSMITTING RESEARCH KNOWLEDGE

Paris Brain Institute conducts many teaching activities, notably through its training program, the Open Brain School. These activities were marked in 2022 by a special focus on e-learning, in particular through the Medtech Generator & Accelerator (MGA) program, carried out with the Imagine Institute and the Vision Institute, and accompanying in their growth the “medtech” start-ups in the fields of neuroscience and genetic diseases. Another highlight of the year was the launch, with the C-Brains consortium, of a call for tenders for five thesis scholarships, demonstrating our drive to increase our international appeal. To foster bridges between clinical care and research, the invited paramedics across the Pitié-Salpétrière hospital to discover the research conducted at the Institute.

COMMUNICATING SCIENCE TO THE PUBLIC

Paris Brain Institute is committed to providing the public with the means of understanding the state of play and the major research topics / questions in the field of neuroscience. In 2022, it created “Dans le coin du Ciboulot”, a new podcast aimed at young audiences, explaining the main functions of the brain.

The Institute also hosted several conferences during the year (‘the Science, Arts et Culture’ series or the ‘Matinales’ series for donors, etc.) or one-offs (Brain Week, Science Festival, etc.). All these conferences are available for replay on the Institute's YouTube channel.

Once again this year, Paris Brain Institute was able to count on the generous support of our new or returning donors, or newly invested support in its cause. For example, Olivier Goy, an inspiring ambassador, facilitated a major fundraising appeal during the Art-Science breakfast held in partnership with the inaugural edition of Paris+ par Art Basel.

Paris Brain Institute thanks all its donors and supporters, who contribute on a daily basis to the excellence of research carried out in its laboratories and to advancing the fight against diseases of the nervous system.

2022 FINANCIAL SITUATION

INCOME STATEMENT BY NATURE AND FUNCTION (ISNF) AND REVENUE AND EXPENDITURE ACCOUNT (REC)

As a preamble, it should be noted that due to the change in the accounting calendar for closing the ICM Foundation's financial statements, the 2022 financial year only concerns the first nine months of 2022.

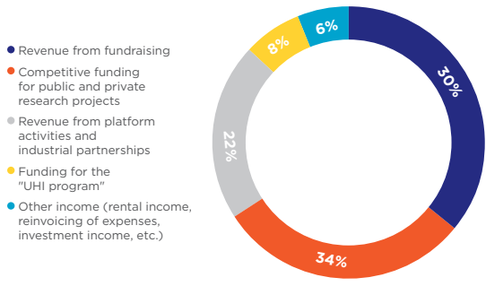
2022 REVENUE BY NATURE

Research project funding is typically diverse in terms of sources of funding, with a long-term perspective in order to produce knowledge and key neuroscience breakthroughs.

2022 revenue amounted to €52.9M. It includes €39.6M in revenue for the year and €13.3M carried forward from resources allocated and not used in previous years. Revenue for the year corresponds to fundraising revenue (€12M, or 30%), which themselves consist of donations (€7.9M, or 66%), bequests and donations (€2.6M, or 22%), and sponsorship (€1.5M, or 12%).

2022 revenue also includes:
- Revenue from technology platform activities (€6.9M) and research collaborations with industrial partners (€1.7M);
- Public and private grants (€13.3M);
- Funding for the University Hospital Institute (IHU) program (€3.2M).
- Miscellaneous revenue (rental revenue, reinvoicing of expenses, investment revenue) (€2.4M).

2022 revenue breakdown

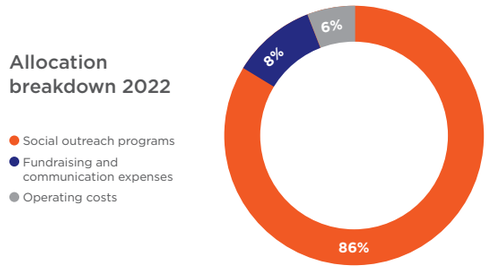


2022 ALLOCATIONS BY FUNCTION

The overall total of 2022 expenditure amounts to €55.8M: €39.9M used in 2022 and €15.9M to be spent later on the allocated resources. In 2022, the amount of allocations devoted to **social missions** amounted to €34.1M, representing **86%** of total ISNF allocations.

Paris Brain Institute's social outreach programs include:
- research programs;
- technology platforms;
- scientific activities and the development of international partnerships;
- incubation of innovative companies.

Allocation breakdown 2022



Funding for research projects is mainly allocated to nervous system diseases and spinal cord injuries. The technology platforms (neuroimaging, vectorology, genotyping sequencing, cell culture, histology, and bioinformatics) support these projects.

Fundraising and communication expenses correspond to the expenses incurred to raise funds from individuals (donations and bequests) and private businesses and foundations (corresponding to patronage and sponsorship actions), as well as communication campaigns. This represents a total of €3.2M, i.e. **8%** of the overall total of ISNF allocations.

Operating costs comprise the costs of the support teams (general administration, finance, human resources, legal, information technology, and logistics), which account for **6%** of the overall total of ISNF allocations, i.e. 2.9 M€.

ALLOCATION OF RESOURCES RECEIVED FROM THE GENERAL PUBLIC

The resources received from the general public that were spent in 2022 amounted to €12M. In a nutshell, for every €100 of resources received from the general public, €71 was used to fund social outreach programs and investments, €27 was used to cover the costs of fundraising and communication, and €2 was used to cover the operating costs of Paris Brain Institute. As indicated in the preamble, we draw your attention to the fact that these figures are only established over the first nine months of the financial year and not over an entire year.

2022 BALANCE SHEET

Assets (M€)	**2021**	**2022**
Net fixed assets	60	60
Current and available assets	93	86
Total	**153**	**146**

Liabilities (M€)	**2021**	**2022**
Associative funds	53	53
Profit and loss for the fiscal year	1.7	- 2.8
Dedicated funds	22	25
Debts	42	42
Deferred revenue	34	29
Total	**153**	**146**

The total amount of investments made by Paris Brain Institute since its creation amounts to €54M mainly dedicated to technology platforms that support research.

Investments during the 2022 fiscal year came to €2.8M (including change in assets in progress) and include:

- investments in scientific materials and equipment (€1.4M, including €0.7M for two microscopes);
- expansion of the Rue du Chevaleret site (basement acquisition, €0.7M).

Net fixed assets totaled €60.3 M. As of September 30, 2022, the amount of cash is €43.9M, including €19.2M dedicated to restricted funding. Paris Brain Institute's own funds amounted to €50.5M (including the impact of the result for the financial year of -€2.8M). They include a net position for €30.9M supplemented by investment grants of €19.6M. Non-expendable endowment of Paris Brain Institute totaled €1.2M. At the end of the fiscal year, dedicated funds (funds still to be committed to multi-year programs) totaled €22M.

Monetary reserve policy

The purpose of building up reserves is to ensure the sustainability of the ICM Foundation's activities and to provide it with the capacity to initiate and support its ambitious multi-year research programs. Thanks to rigorous budget management, the ICM Foundation has balanced its expenses and revenue for the last six years prior to 2022, thus avoiding drawing on its reserves. The 2022 fiscal year is in deficit due to an exceptional fiscal year of nine months, reduced by the last quarter of the calendar year, a quarter traditionally representing 50% of the annual collection from the public. Besides, not outside the availability intended to fund current expenses, Paris Brain Institute's treasury is invested in investment securities (capitalization contracts signed with leading banking institutions, guaranteed in capital and 100% in euro funds and term accounts guaranteed in capital).

IN-KIND CONTRIBUTIONS

Volunteering: Paris Brain Institute benefited from volunteer hours during the 2022 fiscal year, in particular for communication campaigns. The volume is estimated at 0.8 FTEs, i.e. on the basis of French hourly minimum wage, totaling an amount of €24K.

In-Kind Donations: In 2022, Paris Brain Institute benefited from in-kind donations as part of its communication initiatives and namely:

- media spaces with: France TV, Altice Média publicité, Radio France, 366, Canal+ Groupe, Amaury Média, Bein Sport, Bayard Média, RTL, NRJ Global, Orange, Groupe Barrière, JC Decaux, Klesia, Richard Mille.
- products and services provided free of charge: IDEC, Orrick Rambaud Martel, Publicis Groupe, Orange.

As Paris Brain Institute is committed to pursuing its level of excellence, it has rolled out internal and external control procedures to ensure it is managed rigorously and efficiently: it is a member of the "Comité de la Charte du don en Confiance" (Donating with Trust Charter Committee) and calls on the services of an independent statutory auditor.

DON EN CONFIANCE (DONATING WITH TRUST)

On November 3, 2010, Paris Brain Institute received the approval of the "Comité de la Charte du don en Confiance" (Donating with Trust Charter Committee), which was renewed in October 2022. For over 20 years, this Committee has been responsible for the professional regulation of the appeal to the public's generosity. This initiative is based on three commitments: accredited bodies must comply with the rules of ethics, they must observe a collective policy towards donors, and they must accept ongoing monitoring of the commitments made.

Interview with **Corinne Fortin**, General Secretary of Paris Brain Institute: ***"Without the generosity of donors, Paris Brain Institute could not exist! "***

Paris Brain Institute receives nearly 25 million euros per year. We thank you very much because through your donations, in 12 years the Institute has become one of the leading neuroscience research centers in the world. Researchers have more and more means and powerful tools to take risks, find solutions, and cure patients: this is our reason for existing.

What proportion of Paris Brain Institute's resources over a year is represented by donor generosity?

C.F. 40%, which is a lot! Donations are crucial to be able to do excellent research. Paris Brain Institute would not exist without our donors.

How are the donated funds used?

C.F. They fund original research projects and the scientific environment essential to these high-level research projects: technological platforms and equipment, research engineers, laboratory consumables, etc.

How is the arbitration on the allocation of donations carried out?

C.F. During the budget year, we assess the expenses and needs for the coming year and define the sources of funding for each item. We may also have to make a dedicated call for donations, for example, if we plan to acquire innovative equipment.

What are the processes to ensure the rigor of your accounts and transparency in the use of donations from the public?

C.F. It starts at the grassroots, internally, with staff trained in exemplary resource management. Then, independent auditors ensure the robustness of the processes and their application. Lastly, we scrupulously follow the ethics charter of Donating with Trust, and we report all this to our donors through the annual publication of our accounts.

Would you have any examples of projects or acquired equipment made possible thanks to donors?

C.F. One example is the recent leaps forward in multiple sclerosis research with state-of-the-art imaging equipment that we would not have been able to fund without donors' support. There is also brain vascularization project, a world first carried out by Nicolas Renier's team, which paves the way for major advances against all brain diseases.

Lastly, what are the major goals ahead that depend on generosity?

C.F. In our development plan, we want to increase the internal funding envelope to:

> Enhance our support for exciting new projects, the true DNA of the Institute;

> Continue to develop technological platforms and recruit the most experienced engineers to process and analyze data;

> Accelerate clinical research, in particular by funding cohorts.

These three areas will serve our ultimate mission to "research, find solutions to, and cure" brain diseases, and in the short term "prevent, relieve, and repair" for the direct benefit of patients who are at the heart of all our concerns.

Many thanks to all our donors: you are essential!

Transatlantic partnership with the Lycée Français de New York

Paris Brain Institute and the Lycée Français de New York, a French-American bilingual school with 1200 students from around the world, recently launched an innovative five-year partnership focused on the contribution of neuroscience to primary and secondary education. The resources, workshops, projects, and conferences offered by Paris Brain Institute to the high school community will allow students to better understand the functioning of the brain and to further their knowledge of metacognition and their socio-emotional skills. This will not only improve their learning and creativity, but also their self-awareness and understanding of their social interactions.

Students will have the opportunity to explore careers in the field of neuroscience by meeting or interning with researchers. This collaboration between the two institutions also aims to develop the expertise of the teaching staff in the integration of recent advances in neuroscience in the educational field. Teachers will be able to integrate the recommendations resulting from the Institute's research into their teaching methods by implementing pedagogical strategies that optimize the learning conditions, motivation, and well-being of their students. This transatlantic partnership fits perfectly into the mission of the Lycée Français de New York, which *"prepares students from many backgrounds to become thinkers, innovators, and leaders in their own countries and around the world."*

Professor Alexis Brice, Director General of Paris Brain Institute, responded to the fifth-grade students on "the brain machine" during a visit to the high school in early June.

Credit: Sitara Herur-Halbert/Lycée Français de New York

F.A.Q.

As we are very concerned about the impact of our philanthropy, my wife and I would like to fund a specific research project over the next three years. Is this possible at Paris Brain Institute?

Of course you can. You can allocate your donation to the scientific project, disease, or team of your choice. For example, you may decide to fund a student's thesis, help acquire equipment, or even sponsor a team. It is the role of the team dedicated to philanthropy and major donors to listen to you, and work in partnership to accommodate your wishes within the overall scientific strategy of Paris Brain Institute. Once your philanthropic project is defined, it ensures the proper allocation of the donation. Please contact the Circle of Friends Office.

Can I make a donation by bank transfer to Paris Brain Institute?

Yes. Bank transfer is the preferred method of payment of our major donors. Please ask for Paris Brain Institute's bank details at **cercle@icm-institute.org** or by calling **+33 (0)1 57 27 40 32**.

At Paris Brain Institute,
it's not just researchers who are driving research forward.

Like Jeanne and François, make a bequest to support our 800 researchers in their search for new discoveries.

© Vincent Desailly.

ALZHEIMER'S - PARKINSON'S - BRAIN TUMORS - DEPRESSION - STROKE

Paris Brain Institute

To find out more about bequests, donations, and life insurance policies, contact Carole Clément at **+33 (0)1 57 27 41 41** or visit **legs.institutducerveau.fr**

Institut du Cerveau - Hôpital Pitié-Salpêtrière - 47 boulevard de l'Hôpital 75013 Paris, France

DONATION FORM

Please make your check payable to the Institut du Cerveau and send it along with this form to the Institut du Cerveau - Hôpital Pitié-Salpêtrière – CS 21414 75646 Paris Cedex 13 – France

Paris Brain Institute

☑ **Yes, I'd like to help Paris Brain Institute researchers advance their research into brain and spinal cord diseases.**

I'd like to donate: ..... **€**
(amount at my discretion)

66% TAX REDUCTION IN FRANCE
A donation of €5000 only costs you €1700

☐ **Ms.** ☐ **Mr.** ☐ **Mr. and Mrs.**

Surname name: ..... **First name:** .....

Address: .....

Postcode: City: .....

Email: ..... @ .....

☐ **I would like to receive free information on bequests and donations.**

Would you like to donate on behalf of your company?

Please specify company name and company registration number (SIREN in France): .....

DON en CONFIANCE

Paris Brain Institute Foundation complies with the rules of ethics of the "Comité de la Charte du don en Confiance" (Donating with Trust Charter Committee).

The information collected in this form is recorded in a computer file managed by Paris Brain Institute for the purposes of transmitting your tax receipt, reporting on the use of your donation, inviting you to conferences and events, appealing to your generosity, and occasionally for study purposes to get to know you better, elicit your opinion and improve our practices. These data, intended for Paris Brain Institute, may be passed on to third parties mandated for printing and mailing your receipts, and managing our donation appeal campaigns and studies. You have the right to access, rectify, delete, oppose and limit the processing and request the portability of your personal data by contacting the Bureau du Cercle des Amis de l'Institut du Cerveau - Hôpital Pitié-Salpêtrière - CS 21414 - 75646 Paris Cedex 13 - France. You can also a complaint to a supervisory authority. Paris Brain Institute attaches the greatest importance to protecting your personal data and respecting your wishes. Paris Brain Institute does not transmit or exchange the contact information of major donors.

GDO63