



# Synapse

The newsletter designed to connect with you

N° 30 - August 2022

## Feature

### Rare neurological diseases:

The thousands of patients affected by them motivate our most ambitious research

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Hypnotic suggestion informed by neuroscience

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#### Generosity

Olivier Goy, entrepreneur and major donor



The trail-blazing Paris Brain Institute may only have been in existence for 12 years, but it's already made its mark as one of the world's leading neuroscience research centers with the ambitious goal of improving how we analyze and understand the brain to treat and even prevent diseases that affect it.

This year has seen the Paris Brain Institute make even more scientific breakthroughs and continue to provide researchers and patients with an ever-more efficient organization. An international call for new research teams attracted an incredible number of very high standard applicants from around the world, a reflection of the Institute's reputation. Three new groups of scientists will join the Institute to develop cutting-edge research alongside our 25 existing teams in the next few months.

This issue of *Synapse* explores some of the rare neurological diseases in which the Institute's researchers and doctors are involved. It also features highlights of the past year and an overview of the Foundation's accounts which, despite the pandemic, finished on a high with a clean bill of health. As you can see, the Institute puts the same care and professionalism into its management as it does its research. Good news aside, we mustn't lose sight of our existing commitments or any additional resources we need to achieve the high standards we set ourselves.

We would like to thank you for your support. We wouldn't be here without it, and we are delighted to report back on the scientific work our teams have accomplished. Their work and the opportunities it provides will surely inspire you to continue supporting the Paris Brain Institute on its journey.

**Jean-Pierre Martel**  
Founding member of the Paris Brain Institute



### I walk therefore I am

Is thinking a form of walking? That's the question this brand new book tries to unravel with the help of Roger-Pol Droit, philosopher and author, and Prof. Yves Agid, neurologist and Paris Brain Institute founding member. The two men spent four seasons in discussion to try to understand what happens in our brains at any given moment. Walk this way!

*Je marche donc je pense*, by Roger-Pol Droit and Yves Agid, Albin Michel, 224 pages, 19.90 €



### Startup support: the importance of unlocking patient needs

The Medtech Generator & Accelerator (MGA) program, sponsored by Bpifrance and coordinated by the Paris Brain Institute in partnership with the Imagine Institute and Vision Institute, held a Masterclass on May 12th about the patient journey for startups and researchers to grasp the importance of the patient experience when designing their projects. Further information: <https://www.mga-program.com/>



### New Braincast!

The Braincast podcasts in partnership with *Cerveau & Psycho* magazine are back with brand new interviews featuring Paris Brain Institute researchers. The next episode introduces you to Ninon Burgos's career and research in improving diagnostics through imaging. Fascinating for sure!



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## Keep Fighting Foundation: the fight goes on

Michael Schumacher is considered by many to be the best driver in the history of Formula One. His successes on the track may be outstanding but so is his charity work off the track.

Right from the start in 2002, when the Paris Brain Institute was just an idea, Michael embarked on the adventure and became one of its founding members. He has supported the Institute in various ways ever since.

Just as Michael inspired others over many years, his family was encouraged by the sympathy and positive energy shown to them after his serious accident and launched the Keep Fighting Foundation at the end of 2016. In Michael's name, the foundation continues the charitable work that was always so important to him.

**An inspiration for all of us at the Paris Brain Institute.**



Par le ministère de l'Enseignement supérieur, de la Recherche et de l'Innovation

## fête de la Science

### 2022 Science Festival

The French Ministry of Higher Education, Research and Innovation has been hosting the Science Festival since 1991 to raise awareness about science, encourage researchers and the general public to share knowledge and inspire young people to work in the field. The Paris Brain Institute will take part in this year's national event (October 7th-17th), proposing an open house on Saturday October 8th. View the full schedule at <https://www.fetedelascience.fr/>

### Key figures

# 9 NEW STARTUPS

**joined the iPEPS incubator in 2021, bringing the total number of startups developing unique and exciting technology in biotech, medtech and digital healthcare to 25.**

Follow us



### seen on the web

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



- A new mathematical model of brain connectivity after a stroke
- Our pupil reveals elements of our imagination
- Spinocerebellar ataxia: Prof. Alexandra Durr's work awarded the EGP Foundation prize with the support of the Fondation de France

### videos



- ▶ 29/06/22 donor conference: Amyotrophic Lateral Sclerosis (ALS) (in French) <https://institutducerveau-icm.org/fr/conferences/>
- ▶ Understand multiple sclerosis in 2 minutes
- ▶ Science Art and Culture Conference on 21/04/22: "From the origin of species to the notion of stem cells: a continuum of the 19<sup>th</sup> century" (in French) with Martin Catala, psychiatrist, histology, embryology and cytogenetics professor at Pitié-Salpêtrière Hospital and Pierre and Marie Curie University

### agenda

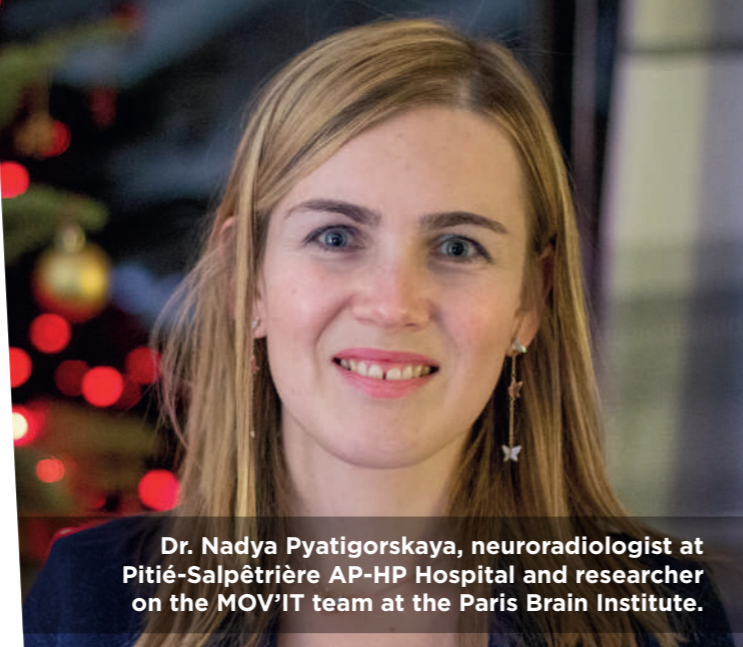
#### Thursday 15 September

1<sup>st</sup> *Monsieur* golf tournament raising funds for the Paris Brain Institute in Chantilly; information at <https://www.monsieur.fr/trophee-de-golf/>

#### Wednesday 21 September

Donor conference on Alzheimer's disease. Schedule and invitation coming soon.

## Imaging and neuromodulation hopes for rare diseases



Dr. Nadya Pyatigorskaya, neuroradiologist at Pitié-Salpêtrière AP-HP Hospital and researcher on the MOV'IT team at the Paris Brain Institute.

Dr. Nadya Pyatigorskaya, neuroradiologist at Pitié-Salpêtrière AP-HP Hospital and researcher on the MOV'IT team at the Paris Brain Institute.

### Nadya, what brought you to the Institute?

**N.P.** I studied medicine then joined the hospital's neuroradiology department as a senior registrar. I started my thesis with Prof. Stéphane Lehéricy at the same time. He's a team manager at the Paris Brain Institute and I ended up joining his and Prof. Marie Vidailhet's team on a permanent basis to continue my research.

“An industrial collaboration provides us with access to a very specific marker for Tau protein which accumulates and causes the brain to degenerate. „

### What are you currently working on?

**N.P.** I'm working on two major projects at the moment. The first is exploring further research into PET-MRI\* to improve the diagnosis, prognosis and knowledge of neurodegenerative disorders and brain tumors. I'm also researching progressive supranuclear palsy (PSP). An industrial collaboration provides us with access to a very specific marker for Tau protein which accumulates and causes the brain to degenerate. Our aim is to better diagnose it and understand the

pathological mechanisms in different forms of PSP. More regular forms of PSP, i.e. Richardson syndrome, are currently fairly easy to diagnose at an advanced stage but 60-70% of the time, we're dealing with rare forms that are harder to detect. It's very important. Patients with rare forms of it are not currently included in clinical studies because we don't have a clear understanding of their disease. It's also hard to make the right diagnosis in its early stages so that needs improving.

My second project involves focused ultrasound. We're using this technology to conduct the first essential tremor clinical trial in France at the Institute. That means we can treat patients without having to open the skull. The second exciting aspect of the technique is neuromodulation using low intensity ultrasound. It's a first for mankind. The idea is to create a transitory effect at first then make it last longer.

### What are your hopes for your research?

**N.P.** In terms of abnormal movements, **my hope is to be able to use our technological developments to benefit clinical trials.** I also think neuromodulation is a very promising non-invasive solution to modulate deep brain activity with several potential prescriptions including epilepsy, some psychiatric disorders, pain and brain tumors.



Rare neurological diseases: The thousands of patients affected by them are at the forefront of our minds and the focus of our most ambitious research

There are currently over 7000 diseases and 75% begin in childhood. They include rare neurological diseases on which the Institute's research teams focus their efforts. Despite major progress in research over the last few years, some patients are still being diagnosed too late, which makes treatment less effective.

\*Cutting-edge medical tool combining positron emission tomography and magnetic resonance imaging.

# Whether rare or common, all brain diseases pose the same challenge for research to support patients

Doctors and researchers at the Paris Brain Institute work together on a daily basis to diagnose diseases as soon as possible and provide effective targeted treatment for central nervous system disorders. By considering diseases in general and using a better understanding of normal brain function, we can learn from knowledge and breakthroughs in one disease to make strides in another.



There exist 500 rare central nervous system disorders

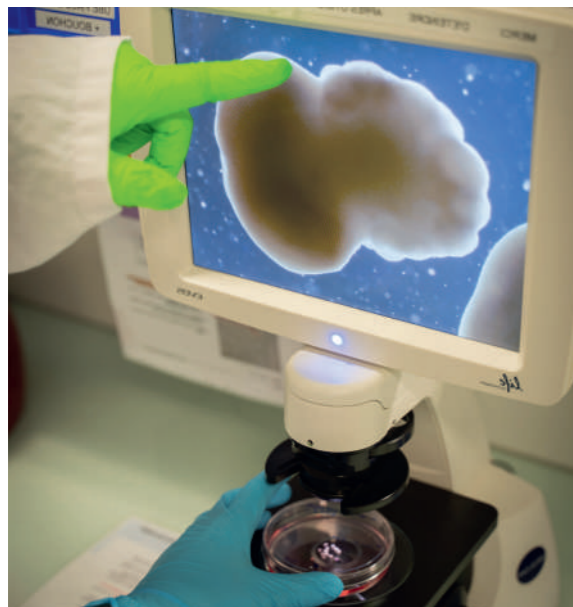
One of the difficulties in studying these disorders is the very limited number of patients. Another

is the broad spectrum of symptoms that not only differ between diseases but also between patients with the same disorder.

This clinical variation makes patients difficult to diagnose, with 25% being diagnosed at least 5 years after the onset of the first symptoms. This is the case in particular for non-hereditary diseases.

Several Paris Brain Institute research teams are focusing their work in this area to identify new reliable markers for diagnosis and efficient new treatments.

Their work is strengthened by the Paris Brain Institute's location on the campus of Pitié-Salpêtrière Hospital, several international partnerships and close collaboration between researchers and doctors, particularly those working at a rare disease reference center.

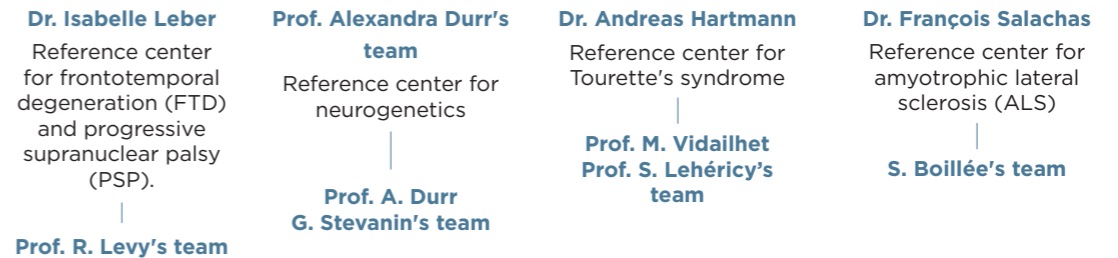


## A major asset: rare disease reference centers

To overcome the challenge of limited patient numbers, the Paris Brain Institute works closely with rare disease reference centers including 4 at Pitié-Salpêtrière itself for nervous system diseases (see box ①). These centers are built around highly specialized teams to promote patient care and provide a range of treatments in partnership with all the affected

healthcare professionals. They represent patient organizations and families and play a key role in the development of clinical trials. These centers have national approval and are recognized for their standard of scientific and clinical excellence. Their aim is to improve diagnosis, care and treatment. For the Paris Brain Institute, being at a reference center hospital fast-tracks progress by pooling knowledge between researchers and doctors and having patients available for clinical trials (see box ②).

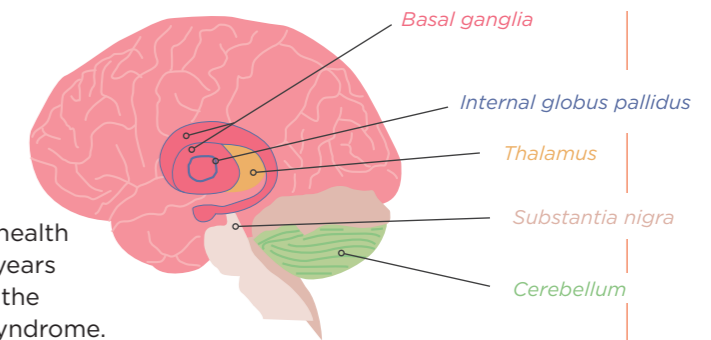
### ① Reference centers for rare neurological disorders in collaboration with the Paris Brain Institute.



### ② There are 10 ongoing clinical trials in 2022 at the Paris Brain Institute including 1 for Tourette's syndrome, 2 for frontotemporal degeneration (FTD), 2 for Huntington's disease, 4 for dystonia and 1 for ataxia.

A clinical trial example: pre and post-surgery evaluation of patients with Tourette's syndrome treated with bilateral high frequency stimulation of the front of the internal globus pallidus.

Evaluation of the success of treatment and health condition of 20 patients over a course of 5 years after bilateral high frequency stimulation of the internal globus pallidus to treat Tourette's syndrome.



## Better understand the origins of disorders to provide better and earlier diagnosis

12 research teams at the Paris Brain Institute are studying the causes of rare disorders, identifying biomarkers to aid diagnosis and predict progression and developing new treatments (medication and devices). The results of their research are already being explored, i.e. deep brain stimulation in Tourette's syndrome and gene therapy for Huntington's disease.

- Down syndrome
- Tourette's syndrome
- X Fragile
- Cerebellar ataxia
- Leukodystrophy
- Dystonia
- Spastic paraplegia
- Mirror movement disorder
- Huntington's disease
- Frontotemporal dementia
- Prion/Creutzfeldt-Jakob diseases
- Amyotrophic lateral sclerosis
- Progressive supranuclear palsy





## Rare neurological diseases: research breakthroughs at the Paris Brain Institute

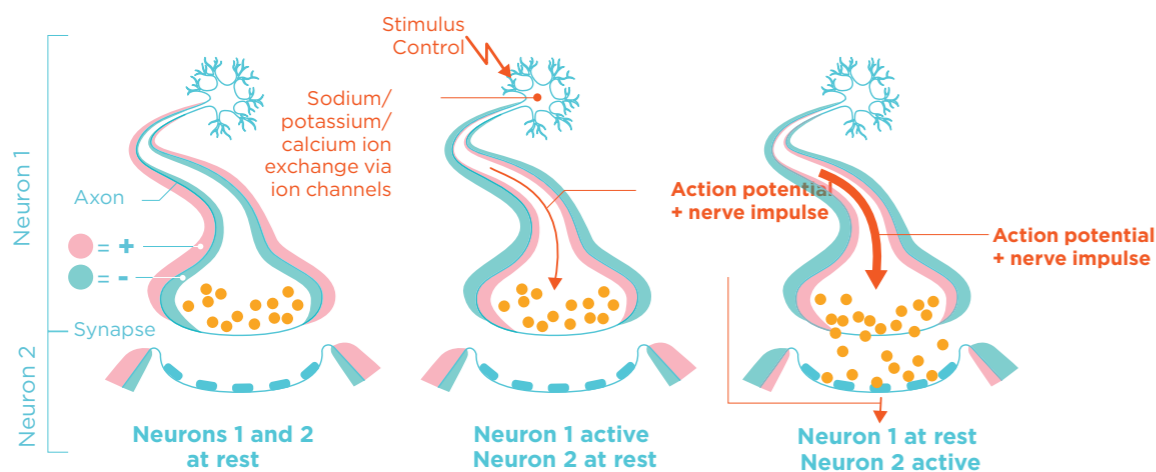
### The discovery of the cause of a brain disease leading to both intellectual disability and abnormal movements

When information passes between neurons, the pores on the neuron membrane open and close. These pores are called ion channels and let different ions (i.e. sodium, potassium and calcium) in or out. A malfunction in the ion channels affects how information is passed between neurons and between neurons and muscles.

Dr. Fanny Mochel, geneticist at the Pitié-Salpêtrière AP-HP Hospital genetics department and researcher at the Paris Brain Institute (M. Vidailhet/S. Lehéricy's team) and Prof. Christel Depienne, geneticist and researcher at the Paris Brain Institute (S. Baulac/E. Leguern's team) have identified a new syndrome associated

with mutations in the SK2 ion channel. The study was conducted on 10 patients, 6 men and 4 women aged 2-60 with more or less severe intellectual disability, some of whom also have autism spectrum disorders or psychotic episodes. Tremors, cerebellar ataxia symptoms or abnormal movements presented in all cases of these cognitive disorders.

**This new disorder, of which we now know the cause, is very diverse in terms of symptoms and requires cross-disciplinary care incorporating genetics, for research into mutations of the KCNN2 gene, neuropediatrics and neurology for treating cognitive and motor manifestations in patients.**



### Brain abnormalities detectable before birth in Huntington's disease

Huntington's disease is a rare, hereditary genetic disease of the central nervous system. It usually manifests between the ages of 30 and 50 through psychiatric, cognitive and motor disorders which gradually worsen. It is caused by the mutation of a coding gene for a protein called huntingtin. A person needs only one copy of the non-typical gene to develop the disorder. Approximately 18,000 people in France are affected by it: 6000 already present symptoms and almost 12,000 present the gene carrying the mutation but are asymptomatic.

Prof. Alexandra Durr's team at the Paris Brain Institute works with Sandrine Humbert's team

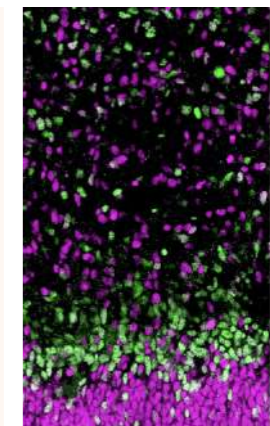
at the Grenoble Institute of Neuroscience to research the early stages of Huntington's disease and the long period before symptoms appear.

In embryos carrying the mutation, the huntingtin protein is abnormally located in cells which become cortex neurons. These anomalies disturb the balance of the progenitor cells that differentiate into neurons faster, depriving the brain of a reservoir of undifferentiated cells prematurely.

The research now needs to explore how these early defects affect the adult disease and how the compensation observed between the embryo stage and advanced age of the appearance of symptoms can be adjusted to delay or even stop the disease.

*" At this stage, our hypothesis is that the brain puts compensation mechanisms in place early on to enable it to function normally. The same may go for carriers of mutations associated with other forms of degeneration (i.e. Alzheimer's disease or amyotrophic lateral sclerosis). This discovery also has significant consequences on how and when treatment to alter the development of the disease should be considered. "*

Prof. Alexandra Durr



Human brain cross-section (cortex). The pink progenitor cells are less involved in neuron differentiation than the green ones.

## Share your experience



### How do you tell the difference between progressive supranuclear palsy (PSP) and Parkinson's disease during diagnosis?

Early symptoms can be similar to Parkinson's disease in the first few years, but there are key markers to help make the right diagnosis. Specific criteria include oculomotor dysfunction and loss of balance in a backwards direction due to early postural instability (retropulsion).

The most characteristic oculomotor symptom is difficulty looking up or down. There are also muscle contractures on both sides of the body, especially around the neck with difficulty bending the neck and abnormal postures in which the head tilts backwards (retrocolis).

The absence or cessation of tremors at rest are another difference between PSP and Parkinson's disease.



### Let's talk about strokes

Email us your question for our next issue with a special report about strokes. Your question may be published in the November 2022 issue of *Synapse*.

▶ [contact@icm-institute.org](mailto:contact@icm-institute.org)

## Can we use genetic markers to predict the risk of developing Alzheimer's disease?

**Dr. Marie-Claude Potier's (CNRS) team at the Paris Brain Institute has found a connection between the presence of amyloid plaques, the characteristic lesions of Alzheimer's disease, and a combination of 17 genetic variants.**

Although only 1% of Alzheimer's cases are hereditary, there are predisposing genetic factors that increase the risk of developing the disease. Early studies have found that people with a specific allele of the APOE (APOE $\epsilon$ 4) gene were 3-15 times more likely to deve-

The "Alzheimer's disease, prion diseases" team, co-managed by Dr. Marie-Claude Potier (CNRS) at the Paris Brain Institute, has presented the hypothesis that there could be a link between a polygenic score and amyloid plaques appearing in the brain, meaning people more at risk of developing the disease could be identified earlier.

Based on data from the INSIGHT cohort at the Paris Brain Institute and French

Institut de la Mémoire et de la Maladie d'Alzheimer (IM2A), made up of 291 asymptomatic elderly people, including 83 presenting with amyloid plaques on the brain, the team found a link between a polygenic score including 17 variants in predisposition genes for Alzheimer's disease other than the APOE and the presence of amyloid plaques. The score was

confirmed by an independent cohort.



Assessing the genetic charge of these 17 variants before amyloid plaques in the brain or plasma can be detected would enable very early identification among patients most at risk of developing amyloid plaques and could also prevent the disease from appearing with more intervention and support.

**“Assessing the genetic charge (...) would enable very early identification among patients most at risk.”**

lop the disease than non-carriers. They have also found that some Alzheimer patients do not carry this variant of the APOE gene. Since then, over 40 variants in predisposition genes for the disease have been discovered. None of them suffice alone but a combination of several of them (polygenic risk) means someone is more at risk of developing the disease.

## Hypnotic suggestion informed by neuroscience

**Prof. Lionel Naccache's team (Sorbonne University - AP-HP) at the Paris Brain Institute has reported a unique observation that sheds light on the cerebral and psychological mechanisms of hypnotic suggestion.**

Hypnotic suggestion introduces a person to diverse states of consciousness and can be used in research in the biology of consciousness or in therapy (i.e. to ease the memory of a painful surgical experience in a conscious and awake person).

Dr. Esteban Munoz-Musat, Prof. Lionel Naccache and their colleagues made a healthy female volunteer temporarily deaf whilst "dissecting" the cerebral stages of her auditory

perception using high density electroencephalography (EEG) to track brain function on a fine-scale to the thousandth of a second.

The auditory perception of an external stimulus begins in the inner ear where variations in air pressure caused by sound are converted into electric impulses before continuing to relay neurons to the auditory cortex. Auditory perception continues in three main stages that enable the subjective

awareness of the sound: "I can hear X".

Analyzing the volunteer's brain activity produced a precise cerebral scenario of hypnotic induction, which specifically affects the awareness stages without affecting the initial subconscious perception stages.

This unique project has provided a major proof of concept and will be explored further with a larger group of people. These results provide therapeutic prospects not only in terms of medical hypnosis but also in the related field of frequent functional neurological disorders (almost 20% of neurological emergencies) which present debilitating symptoms in patients.





## Paris Brain Institute: a pioneering model to accelerate the fight against brain diseases

The Paris Brain Institute is a leading international scientific and medical research center in Paris at the Pitié-Salpêtrière Hospital. Its innovative model brings together patients, doctors, researchers and entrepreneurs in one place with a common goal: to understand the brain and discover new treatments for diseases of the nervous system faster.

The Institute has 760 employees across 25 research teams, 10 cutting-edge technology platforms, a clinical investigation center, a training center and a start-up incubator covering over 2000m<sup>2</sup>. The Paris Brain Institute's unique model is based on a partnership between a mixed research unit (Inserm, CNRS, Sorbonne Université, AP-HP) and a private foundation of public interest.

### THE NEXT LEVEL OF SCIENTIFIC AMBITION

Technological innovation in biology has radically changed over the last five years to provide a clearer view of almost every level of brain function and disease.

The Paris Brain Institute's strategy encourages teams to work independently as well as share their different areas of expertise.

Find out more in our comprehensive 2021 Annual Report on our website: [institutducerveau-icm.org/en](http://institutducerveau-icm.org/en)



### GOVERNANCE

The governance of the Institute, through its Board of Directors, comprising four colleges (founders, qualified individuals, ex-officio members and Friends of the Foundation), reflects the deep partnership between the public and private sectors.

It ensures that its scientific objectives and resources are aligned. The management implements measures to ensure effectiveness and regularly assesses the work and performance of the teams, thus constantly pursuing excellence.

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

## 2021 Highlights

### A NEW INCUBATOR SITE FOR STARTUPS

The Institute has opened a new 1500m<sup>2</sup> medical technology and artificial intelligence incubator campus on Rue du Chevaleret in the 13<sup>th</sup> arrondissement in Paris. The goal of the incubator is to develop health technology that is socially responsible, affordable and available for the purposes of prevention. The projects will enable the Institute to provide new diagnostic and imaging tools, therapy solutions for patients suffering from neurodegenerative or psychiatric disorders and new tools to improve patient quality of life and independence. Funding from the City of Paris and the Île-de-France Region and a loan from the Caisse des Dépôts have brought this project to fruition.

### THREE NEW TEAMS TO JOIN THE INSTITUTE

In June 2021, the Paris Brain Institute launched the recruitment of three new research teams for 2023. They will receive a competitive starter package, annual funding and access to the Institute's entire ecosystem.

### A NEW FIELD OF RESEARCH

A fifth field of research exploring computational modelling in neuroscience launched at the Institute in 2021. The cross-disciplinary subject using data science is used in other fields so the aim is to bring it into the medical arena and create new relationships between teams.

The teams will research the following areas: mathematical modelling of brain mechanisms from molecular to behavioral processes, development of data exploration methods for neurological and psychiatric disorder diagnosis and prognosis, development of scientific software and engineering tools for neuroscience.

### THE PARIS BRAIN INSTITUTE SIGNS THE ALBA DECLARATION ON EQUITY AND INCLUSIVITY

The Paris Brain Institute is one of over 150 neuroscience bodies involved in building equitable and inclusive scientific communities.

## 2021 KEY FIGURES



**762** employees  
**25** research teams  
**10** technology platforms  
**5** fields of research



**Over 600** publications in international scientific journals  
**155** clinical trials  
**25** startups incubated  
**7** patents filed  
**12** training programs in the Open Brain School



**277,242** donors  
**20.4 M€** thanks to public generosity  
**18.6 M€** revenue from external competitive grants

## INNOVATIVE APPROACHES TO ADDRESS THE CHALLENGES OF NERVOUS SYSTEM DISEASES

### INCUBATING INNOVATIVE COMPANIES AND EXCITING COLLABORATIONS

The Paris Brain Institute has opened its third business incubator site. The new site on Rue du Chevaleret is an accelerator for medical technology and artificial intelligence in healthcare.

It has three new laboratories for research and business teams to work together. They are studying digital therapy for people with brain damage, building a national tele-expertise center to improve epilepsy care pathways and exploring new digital biomarkers for Parkinson's disease stratification.

10 new startups have joined the Paris Brain Institute incubator. They are all designing unique and exciting technology in biotechnology, medtech and digital health.

Another highlight of the year was a transatlantic collaboration with Pfizer on frontotemporal dementia markers and a European partnership with Askbio on a gene therapy program for Parkinson's disease.

### NEW CANDIDATE DRUGS

One of the seven patents filed in 2021 was for a new and unexpected drug target for multiple sclerosis, with positive results and several compounds. Two other repositioned compounds have proved promising for Creutzfeldt-Jakob disease and have been patented, alongside a neurosurgery device that makes it easier to implant electrodes for deep brain stimulation i.e. for Parkinson's disease.

The Sleeping Beauties project has now reached the stage of generating the first new patents for small molecules with therapeutic potential. Interaction with investors has begun and reporting has shown persuasive data about its benefits.

### TEACHING THE KNOWLEDGE GAINED THROUGH RESEARCH

2021 stood out at the Open Brain School for a gradual return to the classroom and the continuation of digital development to maintain and provide the Paris Brain Institute's discoveries to the masses, including virtual reality video, hybrid and e-learning events, etc.

The Institute presented the creation of a new international PhD course as part of its endless drive to boost its reputation abroad and attract high potential talent.

### MULTIPLE SCIENCE OUTREACH INITIATIVES FOR THE PUBLIC:

- A 100% digital Brain Week providing a series of films to introduce the public to research work
- The continuation of the Braincast podcast in partnership with *Cerveau & Psycho* to raise awareness about brain research
- The return of the Open Brain Bar, social get-togethers for anyone who wants to understand how science applies to their everyday lives
- Interglitches, a charity video game marathon to raise funds for the Institute

## LOYAL SUPPORT

The Institute is grateful for multi-year agreements with Bolloré SE, the Sucres et Denrées Foundation and UNIM. Air France, Boston Scientific SA, Crédit Mutuel Nord Europe, the Saint-Michel Fund and Philippe Foundation also renewed their annual support in 2021. Countless other fundraising campaigns by the Institute's long-standing partners have continued to provide vital stability. They include the watch brand F.P.Journe, whose Centigraphe Souverain sales were donated to the Institute, and the Pierval Santé shared real estate investment fund, supported by Crédit Mutuel Nord Europe, La Française and Euryale AM. The Fondation de France also funded a research project exploring the neurological and psychiatric effects of the SARS-CoV-2 virus, namely in pa-

tients with a neurodegenerative disease. More and more donors from overseas are supporting the Institute's research. Two agreements have been signed to allow fundraising through Transnational Giving Europe, which already enables donors from 18 European countries to donate to the Institute.

The Richard Mille brand is a loyal supporter of the Paris Brain Institute and, in 2019, Richard Mille himself became a generous member of the Institute's Campaign Committee. The brand took its commitment to new heights with the launch of the Richard Mille Donors' Club in 2021 to support the Institute and brain research.

## A YEAR MARKED BY SCIENTIFIC BREAKTHROUGHS

The Institute's teams made major scientific breakthroughs in 2021, with the vital support of reorganized technology platforms.

### Amongst these breakthroughs:

- Discovery of a new form of communication between neurons and immune cells in the brain
- Identification of a key gene in human sporadic cavernoma
- Completion of a new model in prion diseases
- France's first implantation of a neurostimulator capable of recording intracerebral activity in patients with Parkinson's disease
- Trajectory mapping of the evolution of Alzheimer's disease
- Mathematical mapping of an inflammatory mechanism in multiple sclerosis
- A genetic modifier for the age of onset of frontotemporal degeneration
- New data about inflammation in multiple sclerosis
- Promising results for a new non-invasive therapy for primary orthostatic tremor treatment
- Two-way communication between sleepers and research workers during dreams
- Showing that the first sleep phase after falling asleep is a creativity booster
- A link between weight loss, the connectivity of the reward and regulation system in the brain for satiety
- A new control mechanism for posture and locomotion
- A specific brain disorder identified by electroencephalography in COVID-19

### EXCELLENT RESULTS IN CALLS FOR SCIENTIFIC PROJECTS IN FRANCE AND EUROPE

The Institute broke a new record for the ANR's (French National Research Agency funding research for all figures in the scientific community) generic call for projects in 2021: the Institute's success rate rose to 38%, double the national rate. Two of the Institute's researchers have also been awarded the highly competitive ERC Starting Grants by the European Research Councils. The Institute's researchers have received 17 ERC grants since its foundation.

### CUTTING-EDGE TECHNOLOGY PLATFORMS

- The Paris Brain Institute's ten platforms continued developing to fulfil the research teams' needs in 2021.
- Continuation of the Ultrabrain project, a trial attempting to treat essential tremor patients for the first time in France using focused ultrasound and funded by the Bettencourt Schueller Foundation
  - Development of a brain-machine interface platform
  - Development of a new ex vivo ultra high-resolution imaging technique
  - Participation in the Deep Time study, concerning the experiment of spending 40 days in isolation without natural sunlight or clocks

### COLLABORATIONS WITH LEADING INTERNATIONAL NEUROSCIENCE RESEARCH FIGURES

The Institute was able to continue and increase its international cooperation efforts throughout the year. Even though international travel was impossible, and the usual exchanges were suspended (MIT, Stanford, Yale, St. John's University in the US), the teams were able to adapt and digitalize many of their initiatives. The CURE-ND consortium (Catalysing a United Response in Europe to Neurodegenerative Diseases) launched in 2021 by lobbying the European Commission as well as improving collaborations and events among its members.



## 2021 Financial Situation

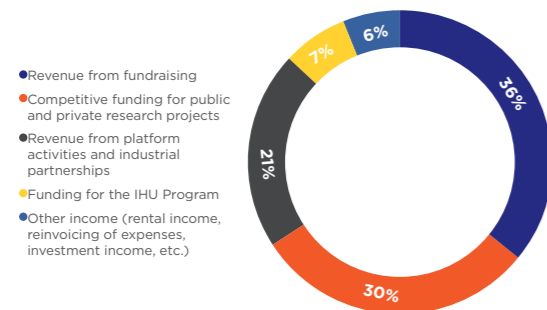
### INCOME STATEMENT BY NATURE AND FUNCTION (ISNF) AND EXPENDITURE STATEMENT - ALLOCATION OF RESOURCES (ES)

#### 2021 REVENUE BY ORIGIN

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.

2021 revenue totaled 75.1 M€, including 56.5 M€ revenue for the year and 18.6 M€ in carry-over of resources allocated and not used in previous years. 36% of revenue for the financial year consisted in fundraising revenue (i.e. 20.4 M€), which includes donations (13.1 M€, i.e. 64%), private grants (4.6 M€, i.e. 23%), and planned giving (2.7 M€, i.e. 13%).

#### 2021 revenue breakdown



It also includes:

- Revenue from technology platform activities (8.4 M€) and research collaborations with industrial partners (3.2 M€).
- Competitive funding for public and private research projects (17.1 M€).
- Funding for the University Hospital Institute (IHU) Program (4.1 M€).
- Miscellaneous revenue (rental revenue, re invoicing of expenses, investment revenue) (3.3 M€).

#### 2021 EXPENSES BY FUNCTION

Overall 2021 expenses totaled 73.4 M€: 52.7 M€ used in 2021 and 20.7 M€ to be used subsequently from the allocated resources. Of the 2021 allocations, 44.3 M€ was allocated directly to **implementing the Institute's programs**, representing **85%** of total ISNF allocations.

The Paris Brain Institute's programs include:

- Research programs ;
- Technology platforms ;
- Scientific activities and the development of international partnerships ;
- Incubation of innovative businesses.

#### Allocation breakdown 2021



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 fundraise from individuals (donations and bequests) and private businesses and foundations (grants), as well as communication campaigns. This represents a total of 4.7 M€, i.e. 9% 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 2021 amounted to 2.4 M€. For every 100€ of resources received from the general public, 74.3€ was used to finance programs and investments, 23.1€ was used to cover the costs of fundraising and communication, and 2.6€ was used to cover the operating costs of the Paris Brain Institute.

#### 2021 BALANCE SHEET

Assets (M€)	2020	2021
Net fixed assets	63	60
Current and available assets	86	93
<b>Total</b>	<b>149</b>	<b>153</b>

Liabilities (M€)	2020	2021
Associative funds	55	53
Profit and loss for the fiscal year	0.95	1.7
Dedicated funds	20	22
Debts	41	42
Deferred revenue	32	34
<b>Total</b>	<b>149</b>	<b>153</b>

The total sum of investments made by the Paris Brain Institute since its foundation totals 52 M€, mainly dedicated to the technology platforms that support research.

Investments during the 2021 fiscal year came to 2.8 M€ (including change in assets in progress) and include:

- Investments in scientific material and equipment (0.9 M€ including 0.2 M€ for a scanner).
- Continued construction at the Rue du Chevaleret site (1 M€).

Net fixed assets totaled 60.3 M€. On December 31 2021, cash and cash equivalents totaled 47.3 M€ including 19.2 M€ for earmarked funding. The Paris Brain Institute's associative funds totaled 55 M€. They included shareholders' equity of 34.5 M€, complemented by investment grants of 20.5 M€. Non-expendable endowment totaled 1.2 M€. At the end of the fiscal year, dedicated funds (funds still to be committed to multi-year programs) totaled 22 M€.

#### Monetary reserve policy

When it was created in 2006, the Paris Brain Institute Foundation received an endowment of 11.7 M€, of which 1.2 M€ was a non-expendable endowment. Through careful budget management, the Paris Brain Institute Foundation has been able to balance its expenses and revenues for the past 6 years, as such avoiding having to draw on its reserves. Furthermore, the investment policy of the members of the Board of Directors is extremely conservative. The Paris Brain Institute's cash flow is invested in marketable securities (capitalization contract taken out with leading banking institutions, capital-guaranteed and 100% in euro funds).

#### IN KIND CONTRIBUTIONS

**Volunteering:** The Paris Brain Institute benefited from volunteer hours during the 2021 fiscal year, in particular for communication campaigns. The volume is estimated at 0.4 FTEs, i.e. on the basis of French hourly minimum wage, totaling an amount of 11 k€.

**In kind donations:** In 2021, the Paris Brain Institute Foundation benefited from in kind donations within the frame of its communication initiatives and from an appeal to the public's generosity, namely:

- Media space: France TV, TF1 Publicité, Altice Média Publicité, Next Régie, Canal+ Group, M6, Amaury Média, Bein Sport, Radio Classique, Lagardère Active, Radio France, Teads, Seedtag, Bayard Média, Premium Média, NRJ Group, FIA-Fédération Internationale Automobile, Groupe Barrière, JCDecaux, Klesia, Richard Mille.
- Free products or services: Air France, ANACOFI, HN6 ACTIVE (Hôtel des Académies des Arts et Hôtel Monsieur Aristide), Holiday Inn, Hôtel Barrière Le Fouquet's Paris, IDEC, Hôtel Indigo Paris Opéra, InterContinental Hotels Group, Le Bristol Paris, Kimpton Saint Honoré Paris, Orrick Rambaud Martel, Publicis Groupe, Tribe Paris Batignolles.

**As the Paris Brain Institute is particularly committed to upholding its high standards, it has rolled out internal and external control procedures to ensure it is managed with diligence and efficiency: it is a member of the "Comité de la Charte du don en Confiance" (Donating with Trust Charter Committee) and uses an independent auditor.**

#### DON EN CONFIANCE (DONATING WITH TRUST)

On November 3, 2010, the 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 2019. For over 20 years, this Committee has been responsible for the professional regulation of fundraising in France. Its initiative is based on 3 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 Olivier Goy: entrepreneur and major donor

**Olivier Goy was diagnosed with Amyotrophic Lateral Sclerosis (ALS) or Lou Gehrig's disease in December 2020 at the age of 46. It is a serious and debilitating neurodegenerative disease that causes death within 3-5 years of diagnosis. Deciding to take a stand and shed light on his fight, Olivier joined the Paris Brain Institute Circle of Friends as a major donor and has become an ambassador for the Institute in order to raise awareness and fuel research.**

### Why did you come forward?

**O.G.** I decided to publically discuss this disease because so little is still known about it. There's a simple reason why it's not talked about much: most people die within 3-5 years. We don't know what causes it and, worse still, we don't know how to treat it.

Talking about it is a way to break the taboo. It came as a total shock when I was diagnosed. Then in March 2021, I broke the news about my disease on Matthieu Stefani's *Génération Do It Yourself* podcast, saying I'm going to fight it and live life to the full. I received thousands of messages after the podcast and realized just how many people are suffering. I want to lift their spirits and show them how beautiful life is.

That's the idea behind the documentary I'm filming with 3<sup>e</sup> Œil Productions, directed by Stéphanie Pillonca. The film *Invincible été* - of which the title is based on a quote by Camus "*au milieu de l'hiver j'ai trouvé en moi un invincible été*" - will share my story and the story of three other people who have decided to live life to the full despite being personally impacted by a handicap.

Any profits from the film (due for release in early 2023) and from photos from the shoot will be

donated to the Paris Brain Institute. This is one of the multiple fundraising projects I'm currently conducting for this Institute conducting pioneering research into ALS.

### Why philanthropy?

**O.G.** Philanthropy is a breath of fresh air. It connects you to others and makes you feel useful. That's why me and my wife Virginie founded the Photo4food Foundation at the Institute of France in 2019.

I'm involved in the Paris Brain Institute because I want to support the teams researching ALS and identifying treatments to slow down the disease's progression. I probably won't personally benefit from the results of their work. But investing in research and its applications is the only way to give hope to future generations.

**Olivier Goy**, co-founder of October, a Next40 FinTech alumni.

**Support the Olivier  
Goy fundraising  
campaign**



## F.A.Q.?

**I noticed the Donor Wall in the lobby the last time I visited the Brain Institute. Who are the donors listed and who can have their name engraved?**

The Donor Wall is updated every year and pays tribute to major donors since the Institute was founded. Anyone (companies, foundations, associations, individuals) who donates over 10,000€ in any given year has their name engraved on the wall. The Circle of Friends takes particular care to recognize the involvement of major donors and also hosts regular events throughout the year.

**I run a business and one of my close colleagues has just informed us that he has brain disease. I would like to rally my staff and company to support the Paris Brain Institute's research work. What should I do?**

It's always hard when a disease is disclosed at work, whether it be for the employer or employee. The Institute has received lots of spontaneous donations from individuals or companies because of this. Some companies raise funds online or do sporting challenges on our Alvarum platform. Recently companies have been contacting us to provide *matching gifts* and create a community spirit: the company donates 1€ every time one of its employees donates 1€. These campaigns are motivating and vital to supporting our researchers' work. We would be delighted to support you and your project.

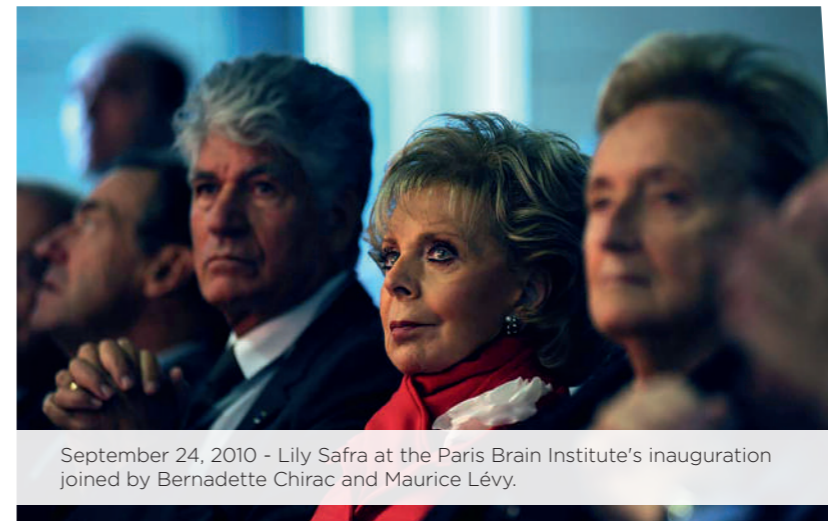
## Death of Ms. Lily Safra

**President of the Edmond J. Safra Foundation and President of Honor of the Paris Brain Institute Friends Association.**

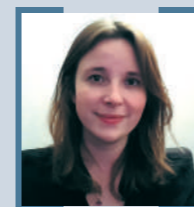
The founding members and the entire scientific, medical and administrative community at the Paris Brain Institute would like to pay tribute to the Institute's great patron and send their sincere condolences to Ms. Lily Safra's friends and family.

Ms. Safra's loyal trust, incredible generosity and commitment to the cause helped the Paris Brain Institute's dream become a reality in 2010 and come into its own to the benefit of many people.

Inspired by her husband's life and values, Ms. Safra put her passion into over 20 years of outstanding charity work for the Edmond J. Safra Foundation. Back when the Paris Brain Institute was just an idea in 2005, Ms. Safra made a major and vital donation to support work by the Institute's neuroscience researchers, doctors and consultants. She has ensured the Edmond J. Safra Foundation has continued providing regular donations essential to first class research projects, namely in Parkinson's disease, for the last ten years.



September 24, 2010 - Lily Safra at the Paris Brain Institute's inauguration joined by Bernadette Chirac and Maurice Lévy.



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in the Circle of Friends Department**

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At the Paris Brain Institute,  
the researchers aren't the only ones powering research.

Like Jeanne and François, make a bequest  
and help our 700 researchers reach new heights  
of discovery.



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



To find out more about bequests, donations and life insurance policies,  
contact Carole Clément at +33 (0)1 57 27 41 41 or [visitlegs.institutducerveau.fr](http://visitlegs.institutducerveau.fr)

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## 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



**Yes, I'd like to help Paris Brain Institute researchers go even further in their  
research in brain and spinal cord diseases.**

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

Mrs     Mr     Mr and Mrs

Last name: ..... First name: .....

Address: .....

Postcode: ..... City: .....

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

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



The 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).

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