Paris Brain Institute
ICM

Synapse

The newsletter designed to connect with you

No. 36 - March 2024

Special Report

The quest for new therapies for multiple sclerosis

Generosity and altruism are the founding values of Paris Brain Institute. This is reflected in the support provided by sponsors, donors and volunteers, and in the mobilization of research teams. These teams work on a daily basis to advance knowledge about the nervous system and related diseases and to find therapeutic solutions.

These values are also evident when people decide to take part in a clinical trial, whether or not they themselves are living with a disease. Their involvement is critical in advancing research: clinical trials are necessary to assess the non-toxicity, safety and efficacy of any new treatment, procedure, or strategy.

The Institute carries out outstanding clinical research thanks to the collaborative efforts of researchers and clinicians within its teams and with the support of a dedicated neuroscience clinical investigation center.

In the central feature of this issue on multiple sclerosis, a disease that affects young people, you will discover some inspiring real-life examples of trials conducted by the Institute.

Trials involving human subjects are highly regulated and taking part in them is an act of solidarity in support of research and all current and future patients. Without you and your generosity, there would be no scientific progress.

Jean Glavany
Founding member of Paris Brain Institute

The Saint-Michel Fund: long-term support for the Iceberg project

Fonds Saint-Michel

For the 5th year in a row, the Saint-Michel Fund, a partner of Paris Brain Institute since 2017, has renewed its support for the Iceberg project, carried out by Prof Marie Vidailhet. The aim of this project is to better understand the mechanisms involved in Parkinson's disease, in order to develop new, more effective treatments.

The Saint-Michel Fund is dedicated to supporting high-potential research projects that are likely to bring about positive change for everyone's health.

The Iceberg project is an innovative initiative that uses cutting-edge techniques, such as MRI, to study the brains of patients living with Parkinson's disease. The project's researchers hope to identify biomarkers of the disease, in order to diagnose it at an earlier stage, monitor its progression, and develop more targeted treatments.

The Saint-Michel Fund's support for the Iceberg project will enable Prof Vidailhet's team of researchers to continue carrying out their work and move forward the quest for new, more effective treatments.

Discover the Institute

LA SEMAINE DU CERVEAU
Société des Neurosciences

Brain Week is an international scientific event coordinated by the French Neuroscience Society in which Paris Brain Institute has been taking part for several years. It aims to raise public awareness of the importance of brain research. In 2023, almost 30,000 adults and young people participated in this event all across France.

For the next edition, the Institute will once again be opening its doors, on Saturday March 16 from 11 am to 6 pm non-stop. The program for the day includes tours of the building, workshops, and two captivating conferences, one of which will focus on the process of learning to read. Don't miss out on this opportunity!

Visit our website for more information or to register.

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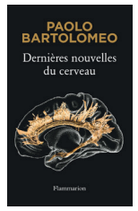
2024 'MATINALES' CONFERENCES: SAVE THE DATE

Every year, Paris Brain Institute organizes four face-to-face and/or remote conferences on the progress achieved and the research carried out by its researchers on a daily basis. The Institute is committed to sharing these quarterly events with you as part of its mission, which is to share knowledge with as many people as possible.

We are pleased to give you a preview of the program for the 2024 season, which is sure to be fascinating. The themes chosen for this year's conferences include **ataxia** (March 27), **multiple sclerosis** (date to be confirmed), **dementia** (October 3) and **the use of artificial intelligence** to benefit patients (December 3).

For more information, go to our dedicated page (in French): **https://institutducerveau-icm.org/fr/les-matinales/**



Mysteries of the brain

In his most recent book, neurologist Paolo Bartolomeo, research director at INSERM and co-head of the "PICNIC - Neuropsychology and functional neuroimaging" team at Paris Brain Institute, takes stock of current knowledge on the brain, from the period of Paul Broca's discoveries in the late 19th century to recent advances in imaging and behavioral analysis. This fascinating book delves into the mysteries of this complex organ that neuroscientists are still endeavouring to understand in a holistic manner.

Bartolomeo, P. (2023). *Dernières nouvelles du cerveau* (192 pages). Flammarion.

At Paris Brain Institute, Key figure

826 experts

work day in and day out to understand how the brain works and enable treatments to be rapidly developed for central nervous system disorders.

Follow us

seen on the web

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

- Multiple sclerosis: a new study highlights five warning signs of the disease
- Probing the unimaginable: new data help to understand the nature of aphantasia

videos

- 09/21/23 Alzheimer's disease conference for donors (in French)
- 10/19/23 Science, Art and Culture conference: "The brain of an orchestra director!" (in French) with Cyril Diederich, orchestra director
- Just Published: "The numerical discrimination capacities of fruit flies" (in French)
- 2 minutes to understand: "Care Lab" (in French)

agenda

March 11 to 17: 26th edition of Brain Week; view the complete program for 2024 at https://www.semaineducerveau.fr/

March 17: National Sleep Day

March 18: World Schizophrenia Day

March 20: World Bipolar Day

April 11: World Parkinson's Day

at the Institute

March 16

Open Day at the Institute in honor of Brain Week 2024 Information and registration at https://institutducerveau-icm.org

March 27

'Matinale' conference on ataxia. Registration required. Send an email to invitationcercle@icm-institute.org or call +33 (0)1 57 27 42 51

Artificial intelligence and clinical applications: a successful partnership

Prof Bruno Stankoff and Olivier Colliot

Portraits of a neurologist, Prof Bruno Stankoff (Sorbonne University, AP-HP), and a mathematical modeling researcher, Olivier Colliot (CNRS).

How did you start working together?

B. S. For the first time ever, thanks to positron emission tomography-magnetic resonance imaging (PET-MRI), the research team that I co-lead at the Institute was able to quantify two mechanisms of disease progression: inflammation and loss of myelin in lesions. And yet this highly innovative molecular imaging technology is uncommon and expensive and therefore difficult to use in routine clinical practice.

What is the role of a computer science research team in this type of project?

O. C. The team that I jointly lead is developing an artificial intelligence algorithm that, by comparing PET-MRI and MRI scans from the same patients, will be capable of learning and then autonomously recognizing characteristics of inflammation and myelin loss on MRI images.

> **“This project would not have been possible anywhere other than Paris Brain Institute, which boasts a wide range of multidisciplinary skills, in this case in imaging, clinical assessment, the pathophysiology of multiple sclerosis, computing, and artificial intelligence.”**
>
> Prof Bruno Stankoff

What are this project’s expected clinical impacts?

Multiple sclerosis is an autoimmune disease characterized by inflammatory flare-ups directed at myelin, the sheath that protects the part of neurons that conducts nerve impulses. One of the aims of research is to better understand the mechanisms responsible for disease progression in order to develop effective treatments that will halt the development of disability.

This major innovation will enable any neurologist with access to an MRI scan to:

- visualize inflammatory and demyelination characteristics predictive of disease and disability progression,
- provide patients with an early, personalized management approach,
- select patients based on objective imaging criteria in order to provide the right treatment for the right patient,
- more accurately assess the efficacy of new therapies.

The research teams involved

- **ARAMIS team**
  Numerical models of brain diseases
- **Remyelination in multiple sclerosis team**

The quest for new therapies
for multiple sclerosis

At present, several treatments are available that can slow down or even stabilize the course of the disease; however, they are not yet able to cure it. Further research will therefore be necessary, in order to identify new therapeutic options capable of regenerating myelin and preventing disability and axonal degeneration.

Individual PET-MRI map of innate immune cell activation in an MS patient, with extensive activation of innate immune cells.

Towards new effective therapies for everyone living with multiple sclerosis

Multiple sclerosis (MS) remains one of the most common causes of neurological disability in young adults. It is estimated that over 2 million people have MS worldwide. In the United States, 200 new cases are diagnosed every week.

This disease is a major public health challenge, as it affects an active population in the prime of life with an average age at onset of 30 years.

MS is an inflammatory disease of the central nervous system (brain, spinal cord). It is known as an "autoimmune" disease because the immune system, whose role is to protect the body from pathogenic agents (viruses, bacteria), attacks a "self" compound in the body called myelin.

Myelin is the protective sheath that forms around nerve cell extensions (axons). It also speeds up nerve impulse conduction. Multiple sclerosis is characterized by lesions in the brain or spinal cord ("plaques"), in which myelin is destroyed. Within these lesions, acute or chronic inflammation leads to neurodegeneration with loss of communication between the brain and peripheral organs.

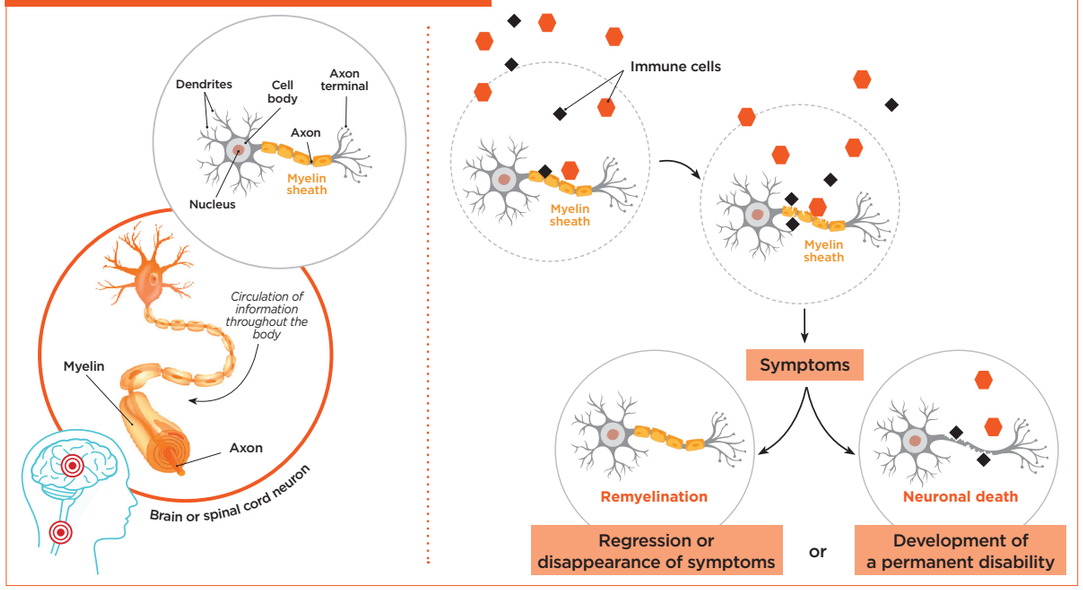
There are several progressive forms of the disease:

- **Relapsing-remitting form**: this is the most common form at the start of the disease (accounting for 80 to 85% of cases). This form is characterized by acute inflammatory phases, or flare-ups, during which patients present with a wide variety of severe symptoms; these phases alternate with periods of complete remission, without any symptoms.

- **Secondary progressive form**: after five to 20 years of the relapsing-remitting form, less than half of patients transition to this phase. It is characterized by the development of a permanent and progressive disability.

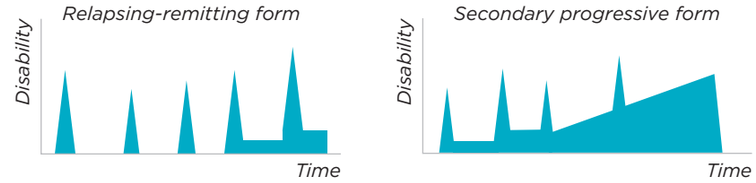
- **Progressive form from the time of onset**: this form affects 10 to 15% of patients from disease onset and progresses very quickly. Disability progresses continuously, without any remission phase. In general, the onset of this form of MS is more common in older people, with an average age at onset of 50.

Molecular and cellular mechanisms in MS

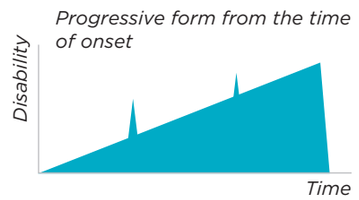


Progressive forms of MS

85% of MS cases



15% of MS cases



Over the past 15 years, advances in research have enabled several effective therapeutic molecules to be developed for the relapsing-remitting form of the disease. These immunosuppressive or immunomodulatory molecules work by controlling the inflammatory reaction, i.e. by reducing the immune cells' attack on the myelin sheath. Today, these therapies are able to:

- reduce inflammation and the development of new plaques by 80%,
- significantly reduce the frequency of flare-ups, and therefore the periods when the most disabling symptoms occur,
- reduce the number of patients progressing to a secondary progressive form of the disease (50% 20 years ago versus 15% today).

However, at present, immunomodulatory and immunosuppressive treatments are still relatively ineffective for the progressive form from the time of onset and for the secondary progressive phase of the relapsing-remitting form of the disease. Research is therefore focusing on the possibility of preventing neuronal damage and the development of irreversible disability, thanks to new therapies capable of stimulating myelin sheath regeneration (remyelination).

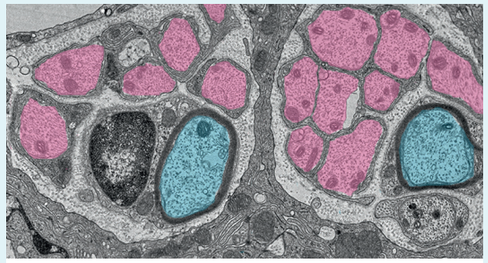
At Paris Brain Institute, researchers and clinicians coordinate clinical trials aimed at better understanding the molecular and cellular mechanisms associated with the disease (pathophysiological trials) and assessing the beneficial effects of new treatments (therapeutic trials).

Clinical trials to limit neurodegeneration in multiple sclerosis

Researchers are currently facing a new challenge: that of setting up and developing specific therapeutic trials for assessing the degree of myelin repair in the brains of patients.

Thanks to new cerebral imaging techniques [specific MRI sequences, positron emission tomography (PET)], some of which are developed and tested at Paris Brain Institute, it is now possible to "quantify" and locate repaired (remyelinated) lesions in patients.

Using these techniques, researchers have observed that some patients have intrinsic remyelination capacity, whereas the repair capacity of other patients is lower. This repair capacity is very significantly inversely correlated with the patient's disability measured clinically, making remyelination strategies even more relevant.



Murine model spinal cord seen with electron microscopy: remyelinated axons (blue) and demyelinated axons (pink).

"For the first time, in MS patients, we showed that remyelination protects not only the lesion, but also the surrounding tissue. This result underlines the importance of combining current anti-inflammatory strategies with a remyelinating strategy to protect all tissues, even those with a normal appearance."

Prof Bruno Stankoff
Neurologist, team leader at Paris Brain Institute

Better understanding the effects of inflammation on remyelination capacity with the SMART-IN-MS pathophysiological trial

This clinical trial is based on collaborative work between clinicians and researchers from two Paris Brain Institute research teams dedicated to the study of multiple sclerosis:

- **"Myelin Plasticity and Regeneration" team**
- **"Repair in Multiple Sclerosis" team**

The high level of variability in the proportion and effectiveness of remyelination observed in multiple sclerosis patients determines the progression of the disability.

But while inflammation is responsible for myelin destruction and axonal degeneration, causing the most severe symptoms of MS, it is also essential for remyelination. It is therefore crucial to determine which inflammatory contexts are conducive to repair and which ones lead to a chronic lesion.

The trial is being conducted with 40 MS patients (20 with the relapsing-remitting form and 20 with the progressive form) and has several objectives:

- **define individual** inflammation and remyelination capacity profiles for the 40 patients using PET-MRI,
- **precisely characterize** these patients' immune cells, in particular their lymphocytes,
- **conduct** *in vitro* and *in vivo* tests to determine the effects of these lymphocytes on remyelination mechanisms.

Preliminary results show that the lymphocytes of certain patients prevent remyelination and lead to chronic inflammation in the lesions of experimental models. The PET profiles of these patients are currently being analyzed.

The results obtained could lead to new generations of therapies aimed at better managing MS.

Assessing the neuroprotective and promyelinating effects of testosterone with the TOTEM therapeutic trial

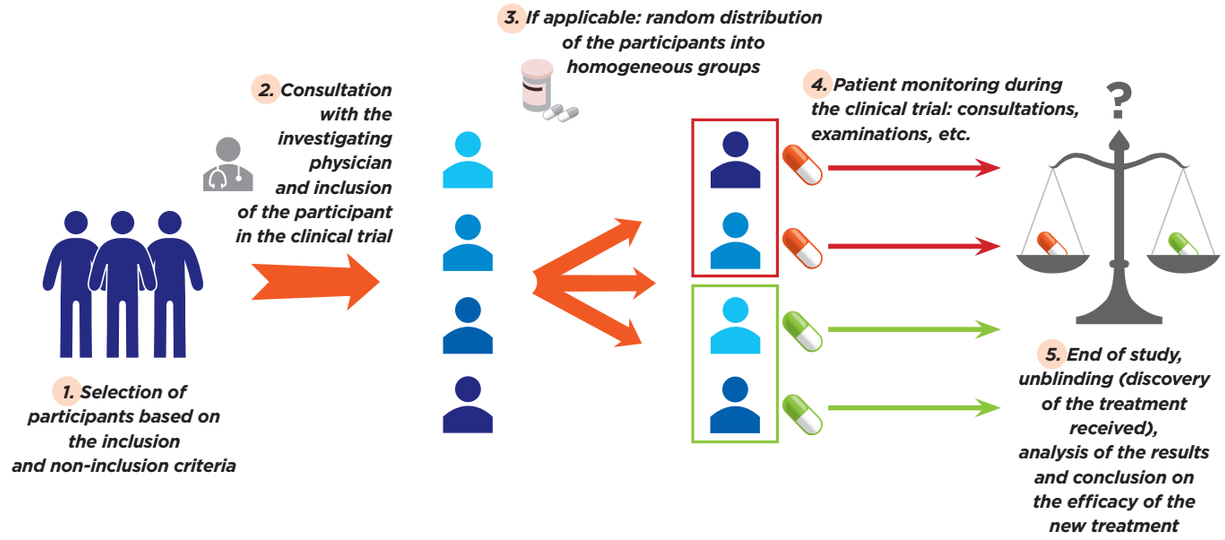
An experimental model was used to show that testosterone can modulate the proliferation and differentiation of oligodendrocytes, i.e. the brain cells that synthesize myelin.

TOTEM is a randomized, double-blind, placebo-controlled *(see diagram)*, multi-site (with five French university hospitals participating) phase II trial.

The primary objective is to assess the effects of testosterone on remyelination and neurodegeneration using MRI techniques.

The secondary objective is to study the impact of testosterone supplementation on clinical symptoms such as cognition, fatigue, anxiety and depression, in order to improve the quality of life of patients. Indeed, no treatments are currently available for fatigue, for example.

The results of this trial, expected in 2027, could pave the way for a new therapy aimed at slowing down, or even stopping, the development of irreversible disability.



Share your experience

Many thanks for the questions and experiences we have received. In this issue, we are going to answer the question asked by Claude, 64, who suffers from Parkinson's disease:

"I was recently diagnosed with Parkinson's disease. I was wondering if I could take part in a clinical trial on this disease. I look forward to hearing from you."

Patients and healthy individuals who may take part in clinical trials must meet a lot of specific criteria established prior to the trial by the investigator and the promoter, such as age, gender, disease duration and progression, type of symptoms, drug treatment, etc. Your neurologist knows the list of trials currently underway across the country and is the only person who can decide whether or not you may join one of these trials. We suggest you contact your neurologist to find out more.

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

Potential benefits of psychedelics for obsessive compulsive disorder

In a new study, Anne Buot, a post-doctoral fellow in cognitive neurosciences, Prof Luc Mallet (AP-HP) and their colleagues from the "Neurophysiology of Repetitive Behaviors" team have shown that LSD and psilocybin have high potential for providing lasting relief for the symptoms of OCD patients.

Obsessive-compulsive disorder (OCD) affects around 2% of the population and takes the form of intrusive thoughts and the involuntary repetition of movements and undesirable behaviors together with a high level of anxiety. Highly disabling, it often results in isolation, as patients are disproportionately focused on their obsessions, to the detriment of social relations, work, and leisure activities.

The gold-standard treatment for OCD is cognitive behavioral therapy (CBT), which teaches patients to better control their thoughts, combined with the use of antidepressants. Unfortunately, it takes a long time for treatment to take effect, and 30 to 40% of patients do not respond to it at all.

In this context, one clinical research option proposed in the 1970s is currently resurfacing: it involves the use of psychedelics, a class of psychoactive substances. Assessing their efficacy is a difficult task, because these substances are banned in a number of countries. However, to organize robust clinical trials, encouraging preliminary data is needed.

This work was undertaken by Anne Buot and Prof Luc Mallet at Paris Brain Institute, where researchers retrospectively analyzed the experiences of 174 people with OCD who had consumed psilocybin – derived from hallucinogenic mushrooms – or LSD to relieve their symptoms.

The effects reported by the participants included the disappearance of obsessive thoughts, a decrease in anxiety and avoidance behaviors, and better acceptance of the disease. Thirty percent of the people interviewed indicated that these positive effects had lasted longer than three months.

However, these results should be interpreted with caution. Indeed, the subjective assessment of the therapeutic effects of psychedelics is likely to be affected by a number of biases – relating to the participants' beliefs, personal history, culture, and imagination.

These biases are reinforced by the transformative symbolism of the psychedelic experience itself, during which some individuals feel a sense of euphoria, ecstasy or connection with the universe that encourages them to see the world with a fresh perspective.

To make the most of potential new treatments, it will be necessary to undertake many rigorous clinical trials and also to determine what biological mechanisms are responsible for the long-term effects of psychedelics. Researchers believe that they might increase neuroplasticity by promoting the remodeling of synaptic connections. But in this area, a great deal still remains to be discovered.

We are capable of responding to external demands while we sleep

Researchers from Paris Brain Institute and the Sleep Pathology Department of the Pitié-Salpêtrière Hospital have made a surprising discovery: sleep is not a state that perfectly isolates us from our environment. We are capable of hearing and understanding words while we sleep.

Even though it seems familiar to us since we give into it every night, sleep is a highly complex phenomenon. Recent research has shown that it is made up of a vast mosaic of moments – in some of these, we are conscious, while in others, we do not seem to be. Similarly, in the middle of the day, we experience times when we are very unaware of our environment.

It is essential to better understand the cerebral mechanisms that underlie these intermediate states between wakefulness and sleep: when deregulated, they can be associated with disorders such as sleep-walking, sleep paralysis and hallucinations.

And yet to distinguish between wakefulness and the various stages of sleep, simple physiological indicators have been used up to now, including specific brain waves made visible with electroencephalography. But these indicators do not provide a detailed understanding of what goes on in the minds of sleepers and, indeed, they sometimes conflict with their testimonies.

To get to the bottom of how sleep works, Delphine Oudiette (INSERM), Prof Isabelle Arnulf (Sorbonne University, AP-HP), Prof Lionel Naccache (Sorbonne University, AP-HP) and their colleagues tested a new approach. Researchers recruited 22 people without sleep disorders and 27 patients with narcolepsy, characterized by an irrepressible need to sleep during the day. People with narcolepsy are unique in that they experience many lucid dreams, i.e. dreams in which they are aware they have fallen asleep. In addition, they easily and rapidly enter REM sleep (the stage in which lucid dreaming occurs), making them good candidates for studying consciousness during sleep under experimental conditions.

The study participants were invited to take a nap. The researchers had them take a "lexical decision" test during which a human voice read out a series of real words and invented words. The participants were expected to respond to them by smiling or frowning, so they could be classified into either of these categories. All throughout the experiment, they were monitored via a comprehensive polysomnography test where their cerebral and cardiac activity, eye movements and muscle tone were recorded.

Lastly, upon waking, they were asked to report whether or not they had experienced a lucid dream while they were napping, and whether they remembered interacting with anyone. Most of the participants, whether they had narcolepsy or not, had managed to understand the words and respond to them appropriately while remaining asleep, during almost every phase of sleep – as if windows to the outside world had temporarily opened on this occasion.

These new fascinating data could help revise the definition of sleep, which it turns out is a very active state where we might be more conscious than we thought and may be quite open to the world and to other people.

PET-MRI: a cutting-edge technology for exploring the brain

Positron emission tomography (PET) is used in real-time to directly view the *in vivo* kinetics and distribution of injected radiotracers and therefore those of the molecules to which they attach themselves. When combined with MRI, it is able to achieve more precise images of the organs being studied.

This technology is based on the intravenous injection of a substance (the "tracer") labeled with a radioactive atom – fluorine 18 or carbon 11 – which, by attaching itself to target cells, emits specific particles called positrons.

These particles then collide with electrons generating the emission of photons (light particles). The tracer is chosen to attach itself to a specific organ, tissue, cells or molecules to reproduce an image of the organ studied, such as the brain for neurological and psychiatric diseases.

The radioactive substances used in PET are risk-free for humans and the very low radioactivity disappears completely within a day.

PET-MRI is able to quantify each biological component and thus identify any over- or underactivated mechanisms and the chronological order of dysfunctions in patients with a disease.

THE NEUROTRIALS EARLY CLINICAL DEVELOPMENT UNIT

Neurotrials and the Support Unit for Human Subjects Research constitute a medical-scientific and regulatory consulting platform for European and international multi-center early (phase Ib/IIa) clinical trials in neurology and psychiatry.

This Paris Brain Institute platform, coordinated by Dr Louise-Laure Mariani and Pierre Georges Francois, implements clinical trials sponsored by Paris Brain Institute, 13 of which are currently in progress.

> *"Neurotrials combines the scientific excellence of academia with the efficiency of industry to optimize the development of health products."*
>
> **Dr Louise-Laure Mariani**
> Neuropharmacologist (AP-HP, Sorbonne University)
> Neurotrials Lead Medical Director.

NEUROTRIALS
Institut du Cerveau

Interview with Marine Barnérias, who tells us about her experience living with "Rosy"

At the age of 21, Marine Barnérias*, TV producer and host, learned she had multiple sclerosis. After the shock of the news and a period of denial, she embarked on a journey to discover the world and above all, get in touch with herself. Below, she shares her love for life and her conviction that every donor has a major role to play!

"At first, I kept my disease a secret, because I didn't want to show I was vulnerable. But after I lost my vision the second time, something clicked, and I realized I had to go on a trip, all by myself.

I hiked around New Zealand and learned the power of words. That's where I gave "sclerosis" a new name: "Rosy." That experience gave me a new lease on life. In a monastery in Burma, I discovered that silence would give me answers. In Mongolia, I crossed the steppes on horseback and realized that no matter what choices we make in life, they still open up a multitude of possibilities. We shouldn't be afraid to say "no" and listen to ourselves.

This year-long journey connected with the uniqueness of my personality and gave me an opportunity to finally listen to myself.

The end of the adventure was truly a new start. I understood that my disease was going to be part of my life. I knew that I wasn't cured, and that I would have to live with "Rosy," whereas before, I hadn't wanted to let her in. We have to learn to live with what we hate and stop resisting what life throws at us. I wrote a book about my experience, and then I created my own audiovisual production company, even though I didn't know anything about the sector, to co-produce my documentary film *Rosy*.

Every morning, I wake up wondering how I'll get through the day, and whether I'll still be able to use my legs. So I try to live every day as if it were my last. Doing so lets me be creative, saving myself from paralysis. But my strength is fragile.

There's still so much scientific groundwork to be done because we have access to treatments, but they aren't curative! Researchers are working hard to understand why multiple sclerosis develops and we need to donors to provide them with means to find answers.

Paris Brain Institute is a technological marvel that's truly one of a kind! I'd like to do what I can to make it known to everyone and raise awareness of this essential fight.
I want people to know that the Institute needs their donations and that they have a role to play that goes far beyond the financial aspect. Donations not also facilitate advances in research; they also provide hope to patients and their families, so they can see life differently.

We are all concerned, and we can all take action through solidarity."

*Author of *"Seper Hero, Le voyage interdit qui a donné sens à ma vie"* (Ed. Flammarion, 2017), with preface by Frédéric Lopez.
Director of the documentary film entitled *"Rosy,"* released in 2022.

The multi-annual letter of commitment: inspiring courage in the long term

At present, the time lapse between an initial discovery and the benefit to society is around 30 years. Paris Brain Institute's ambition is to halve this time. Indeed, time is of the essence when it comes to research. It is critical for all patients and their families. By making a long-term commitment in the form of multi-annual support, you are ensuring that researchers have the strong financial foundation they need to make key discoveries for the future.

What is a multi-annual letter of commitment?

Easier to implement than a sponsorship agreement, the multi-annual commitment letter is a simple document that you sign that allows you to choose the annual amount of your contribution, the duration (between 3 and 5 years), and the due dates of your payments (with one or more yearly installments) to ensure that your contribution is in line with your habits, in particular in terms of taxes (year-end or IFI wealth tax period). It also allows you to express your wish to have your generous donation allocated to all of Paris Brain Institute's missions or to a particular disease or team.

What difference does it make for researchers and the Institute?

Research project funding is typically diverse in terms of sources of funding, with a long-term perspective in order to produce knowledge and key neuroscientific breakthroughs. By knowing in advance what resources they have at their disposal, researchers can plan for the future, without worrying about a hold-up in their projects.

Because just 30% of Paris Brain Institute's budget comes from public funding, this private philanthropic support gives it the courage to initiate an ambitious international scientific strategy and to invest in technologies and innovation by acquiring cutting-edge equipment and expertise.

Make a commitment and take advantage of favorable tax provisions.

Are you subject to real estate wealth tax (IFI) in France?

75% of your donations to Paris Brain Institute are deductible from this tax, up to a limit of €50,000.

For example:

With your donation of: €10,000

You benefit from a tax deduction of: €7,500

And your donation costs you: €2,500

Do you pay income tax in France?

66% of your donations to Paris Brain Institute are deductible from this tax, up to a limit of 20% of your net taxable income.

For example:

With your donation of: €10,000

You benefit from a tax deduction of: €6,600

And your donation costs you: €3,400

Is your company liable for corporate tax or income tax?

60% of the amount of your donation to Paris Brain Institute is deductible from your corporate tax or income tax depending on the tax regime you are subject to, within the limit of €20,000 or 0.5% of company revenue. For more than €2 million in cumulative annual donations, the deduction is 40%.

Are you a tax resident of a country outside of France?

You may still be able to benefit from tax advantages on your donation in your country of residence. Visit our webpage here for more information: https://institutducerveau-icm.org/en/make-donation-outside-france/

Launch of our newsletter: a new information channel and forum for the Circle of Friends

You may have received the first newsletter of the Circle of Friends in September. Its aims are to share recent news about the Circle of Friends, showcase new members, look back at major accomplishments, and inform you of upcoming events. Three times a year, you will discover the portrait of an individual (for example, a researcher, a member of the Management Committee, the CEO of a start-up, or a major donor) involved in advancing research at the Institute. You will also find scientific news articles.

Are you not receiving *the newsletter of the Circle of Friends* in your inbox? You may have disabled some preferences in our previous email campaigns, causing your address to no longer be accepted. **To sign up again, please contact the Circle of Friends Office.**

YOUR DEDICATED CONTACT
at the Circle of Friends Office

Ms Emma Kavcic Mondoloni
+33 (0)1 57 27 40 32
cercle@icm-institute.org

F.A.Q.

If I'm subject to real estate wealth tax (IFI) in France, can I deduct my donation to Paris Brain Institute?

Absolutely. Paris Brain Institute is a public utility foundation. As such, 75% of the amount of your donation is deductible from your IFI tax (within the limit of €50,000).

I made my donation to Paris Brain Institute at the end of 2023. Can I deduct it from my 2024 real estate wealth tax (IFI)?

Of course you can. Donations taken into account for calculating the tax reduction are the ones made from the day following the deadline for filing your 2023 tax return (between May and June depending on where you live, if in France) and until the deadline for filing this year's return.

In addition to my one-off donations in spring and at the end of the year, I've just signed up for direct debit. When will I receive my tax receipt?

First of all, many thanks for your loyal support. At the start of next year, you will receive your tax receipt, which will show all of your deductions for the year 2024.

Paris Brain Institute

Because 1 in 8 people is affected by a brain disease, **give us the means to search, find, cure.**

Alzheimer's disease, Parkinson's, stroke, brain tumors, Charcot's disease (Lou Gehrig's disease), as well as multiple sclerosis, depression, epilepsy... Brain diseases, the medical challenge of our century, can affect us all, directly or indirectly, today or tomorrow. Paris Brain Institute's 800 researchers are deeply committed to making new discoveries, to developing groundbreaking treatments and to beating these diseases. By supporting them with a donation, you are giving them the means to protect what is most precious to all of us: our brain.

DONATE AT institutducerveau-icm.org/en

75% of the amount of your donation is deductible from the French tax on personal real estate assets (known as IFI in France).

66% of your donation is deductible from income tax.

DONATION FORM

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

Paris Brain Institute

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

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

75% DEDUCTION ON TAX ON PERSONAL REAL ESTATE ASSETS (IFI)
A donation of €5,000 only costs you €1,250

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☐ **I'd 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): .....

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. This 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 may also file a complaint with 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 disclose the contact information of major donors.

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