

Synapse

Paris Brain Institute
ICM

The newsletter designed to connect with you

No. 28 - March 2022

Special report

Neurodegenerative diseases: causes and consequences of the death of neurons

Microscopic imaging of meningeal lymphatic vessels (green), dural blood vessels (red) and meningeal immune cell populations (green and blue) at the confluence of sinuses in the brain performed by Paris Brain Institute.



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ALS: Interview with Séverine Boillée and Prof. François Salachas



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Is falling asleep a creativity booster?



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Generosity
Big Brain Theory: philanthropic investment for the future



For almost 50 years now, hundreds of laboratories around the globe have been striving to stop the progression and to prevent diseases that we refer to as neurodegenerative. These disorders are characterized by the death of neurons, which is slow but, at the same time, faster than in a normal aging process, and selective, as it only targets a fraction of nerve cells. The entire nervous system may be affected by the pathological process, from the cerebral cortex (Alzheimer's disease) to peripheral nerves (Charcot-Marie-Tooth disease), via the basal ganglia (Parkinson's, Huntington's), the spinal cord (amyotrophic lateral sclerosis) and the cerebellum (ataxia).

Although scientific research has made substantial progress, why are we still not able today to stop the progression of these diseases? Simply because, compared to other organs in the body, the nervous system is considerably more complex. This is why the Paris Brain Institute teams' research is so important for identifying the mechanisms at work in these disorders.

Thanks to our multidisciplinary approach centered on therapeutics for patients, we have good reasons to hope that we will, at long last, find treatment for a first neurodegenerative disease. With this in mind, our watchwords are: intelligence, perseverance, recruiting the best and involvement of those who can help us.

Prof. Yves Agid
Founding member of Paris Brain Institute



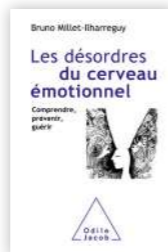
24th edition of the Brain Week

The 2022 edition of the Brain Week, in which the Institute and its teams will take part, will be held from March 14 to 20. This international event, initiated in 1999, aims to raise awareness among the general public of the importance of brain research. For this occasion, the Institute proposes a 100% online program, comprising exclusive videos, conferences and podcasts. Visit our social media too and discover exclusive neuroscience content every day from March 14 to 20. Program available on <https://www.semaineducerveau.fr> (in French)

Repairing neurons

Discover our latest Braincast podcast, in partnership with Cerveau & Psycho magazine, with Prof. Catherine Lubetzki, neurologist, Medical Director and co-team leader at Paris Brain Institute. Around 45 minutes of fascinating exchange addressing the ultimate multiple sclerosis challenge: repairing neurons. A listening must without hesitation! Discover Braincast on <https://www.cerveauetpsycho.fr/sr/braincast/> (in French)

Fighting mental suffering



In his most recent work, Prof. Bruno Millet-Ilharreguy, psychiatrist at the Pitié-Salpêtrière Hospital and researcher at Paris Brain Institute explains how the ever-accelerating progress in neuroscience has shaken up our knowledge of the psychological workings of the brain and its emotional functions. He also presents promising leads for treating mental and emotional disorders such as using virtual reality, neurofeedback or electrical and magnetic brain stimulation. A real message of hope! *Les troubles du cerveau émotionnel - Comprendre, prévenir, guérir* (Disorders of the emotional brain - Understanding, preventing, curing), book in French by Bruno Millet-Ilharreguy, Odile Jacob, 272 pages, 23.90 euros.

SYNAPSE, Paris Brain Institute's newsletter addressed to its donors. No. 28 - 2022. Editorial board: Jean-Louis Da Costa, Astrid Crabouillet, Nicolas Brard, Isabelle Rebeix, Claire Pennelle, Lauriane Gallier, Carole Clément and Aurélie Grosse. Design: Adfinitas. Printer: Imprimerie Jean Bernard. Print run: 115,000 copies. © Institut du Cerveau / JP PARIENTE / Adobestock : Kittiphan - ktsdesign - Robert Kneschke - pathdoc - BillionPhotos.com - fizkes - romaset - insta_photos - Syda Productions.



Sucres et Denrées Foundation renews its support to the Institute!

Sucden, a family-run French company, little known to the public at large, is a leading player in the international trade of sugar, cocoa and coffee that transports and supplies over 10 million tons of soft commodities every year. The Group, which has existed for almost 70 years now and boasts 6,000 employees across 25 countries, seeks to double its economic performance, by boosting it with a strong positive, sustainable impact throughout the regions where it operates.

Sucden Group's corporate foundation, created in 2009, oversees the lion's share of the 2 million dollars allocated every year to development projects and public interest causes

(nutrition, education, health, living standards, environment) from its Parisian head office. As a pragmatic Foundation, Sucres and Denrées seeks to identify and support the quest for holistic solutions without limiting itself to only resolving one-off issues.

The Institute has enjoyed a patronage partnership with the Foundation since 2018, which has recently been renewed for 3 years, until 2023.



Outstanding women!

The end of 2021 rhymed with women's awards! **Prof. Marie Vidailhet** (Sorbonne

University/AP-HP), team leader at Paris Brain Institute was honored with the **Mémain-Pelletier Award for her work on the physiopathology of abnormal movements** (dystonia, tremors); and **Prof. Catherine Lubetzki** (Sorbonne University/AP-HP), neurologist, Medical Director and co-team leader at Paris Brain Institute, received the **Pasteur-Weizmann / Servier 2021 Prize for her research on the regeneration of myelin in the treatment of multiple sclerosis.**

Figures

In 2020, 64.77% of those who answered our Nationwide Survey on neurological diseases* stated they are hopeful that, **one day, thanks to research, treatment will be found to cure nervous system diseases but not just over the short term.**

64.77%

*data collected in 2020 from our nationwide survey answered by 6,994 people.

Research on brain diseases is a pressing concern and your support is vital for researchers to be able to cure nervous system diseases.

Follow us



seen on the web

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



- Detecting the occurrence of auditory hallucinations from brain activity in schizophrenia
- Is falling asleep a creativity booster?

videos



- ▶ Replay of the donors' conference on Parkinson's disease from december 2021. www.institutducerveau-icm.org/fr/conferences/ (in French)
- ▶ Replay of the donors' conference on Alzheimer's disease from September 2021 (Introduction videos and subtitles in English)

agenda

From Monday, March 14 to Sunday, March 20

Brain Week (digital edition) - Program available on <https://www.semaineducerveau.fr/> (in French) and on parisbraininstitute-icm.org

Wednesday, March 15

Donors' conference LIVE & DIRECT about "Behind the scenes at Paris Brain Institute". Live at 5pm on: institutducerveau-icm.org/fr/conferencedonateurs/ (in French)

Joining forces in the fight against Lou Gehrig's disease



Séverine BOILLÉE, Inserm researcher and "ALS Causes and mechanisms of motor neuron degeneration" team leader at Paris Brain Institute

Prof. François SALACHAS (AP-HP, Sorbonne University), neurologist, Head of the ALS and Motor Neuron Diseases Unit, coordinator of the ALS-IDF remedy and skill center (centre de Recours et de Compétence) and clinician-researcher in the team led by Séverine BOILLÉE.

A disease one or more causes, involves one or more biological mechanisms and generates a range of symptoms, making it sometimes difficult to distinguish between causes and consequences. That is precisely what Séverine BOILLÉE's team is working on. A team in which scientists and clinicians specialized in amyotrophic lateral sclerosis (ALS), also known as Charcot disease or Lou Gehrig's disease, interact on a daily basis.

Séverine, what is the greatest asset of the team you lead?

S. B. The diversity of expertise that it brings together. Our research work focuses on genetics, studying motor neurons and immune cells, analyzing brain and spinal cord tissue that we correlate with a detailed description of patients' symptoms.

For each field, we benefit from the in-depth knowledge of a geneticist, three cell biologists, an anatomical pathologist and two neurologists who are experts in caring for patients suffering from ALS.

François, you are a neurologist specializing in ALS at the Pitié-Salpêtrière Hospital, how relevant is it for you to be a member of a Paris Brain Institute research team?

F. S. Contrary to popular belief, ALS is a very heterogeneous disease in terms of the progression and severity that causes motor neuron death, most likely, by different mechanisms.

For years, specialized neurologists have been monitoring patients from the moment they are diagnosed. It is more vital than ever before to work hand-in-hand with scientists to optimize the analysis of clinical and biological information to drive the next therapeutic discoveries.

What are the key challenges of your joint research and what perspectives does it open for patients?

F. S. **S. B.** A great deal of research today focuses on discovering early biological markers specific to the degeneration of motor neurons in ALS: the aim is to treat patients as early on as possible, i.e. before they reach the irreversible developmental stage.

Clinical gene therapy trials, currently carried out on asymptomatic people with a mutation, boost us and motivate us to **identify together the early markers that will enable us to include the right patient in the right trial and to treat earlier and more effectively.**

“ A great deal of research today focuses on discovering early biological markers specific to the degeneration of motor neurons in ALS. „

NEURODEGENERATIVE DISEASES: causes and consequences of the death of neurons

Neurons only make up 5% of the cells in the brain and yet they are indispensable to vital functions-such as breathing, heartbeat, and higher functions-such as the ability to think, attention and memory. But, what happens when they degenerate?



Neuronal degeneration : why, where, how and with what effects?

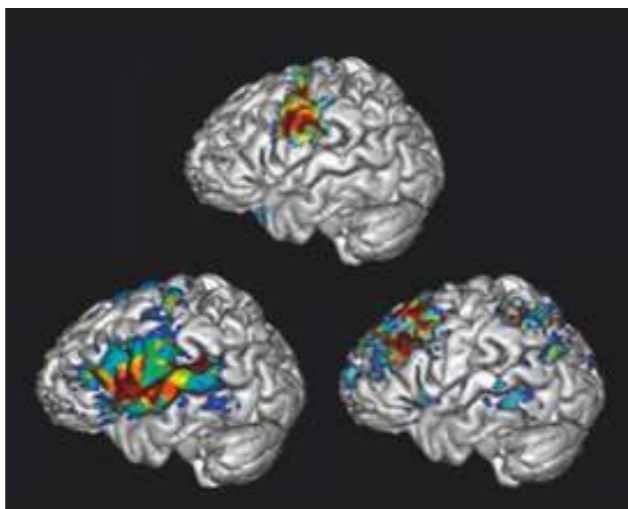
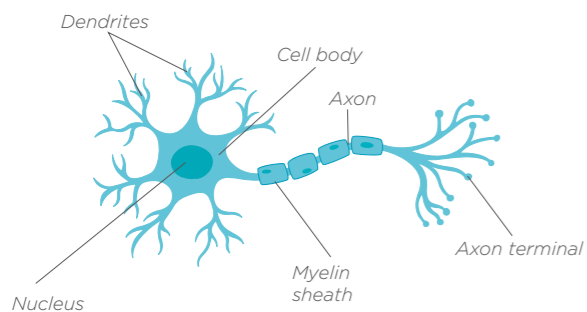
The human central nervous system (brain and spinal cord) comprises around 2,000 billion cells including 100 billion neurons (i.e. 5%).

Although we are used to representing the brain in terms of different areas (motor, visual, emotional, etc.), it is now known that many brain regions play a role in the performance of a motor task or of an emotional reaction, making it even more complex to assign a precise role to a specific region of our brain and thus to understand the consequences of a dysfunction of this region.

The brain cells that enable the brain to accomplish all this are neurons.

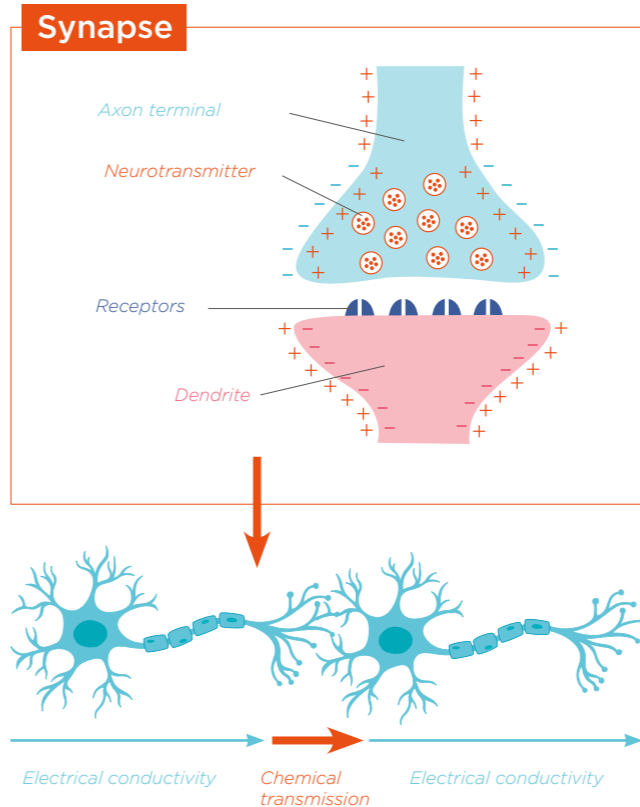
A neuron comprises three separate parts and each play a specific role.

- The cell body, which is the "control room" and which integrates information.
- The axon, which is the part that transmits messages and through which the nerve impulse travels to other neurons or to other cells such as muscle cells, for example. It is surrounded by a protective sheath, myelin, that enables the nerve impulse to move faster.
- Dendrites, extensions that receive nerve messages transmitted by other neurons.



Brain regions activated in a subject moving their hand (top), repeating a sentence (bottom left) and performing a more complex task such as a calculation (bottom right). The more active the region, the redder it appears.

On average, a neuron is able to communicate with 10,000 others with the same function, as such creating networks that can be enabled or disabled depending on our brain's activity.



The death of neurons entails very heterogeneous consequences even though the brain is able to compensate for the loss of some neurons via mechanisms such as redundancy (the fact that it has more neurons than it needs), the ability to form new connections as well as to produce new neurons, especially in the hippocampus.

But, why and how do neurons die?

Irrespective of the type of neuron, of its location of the neurotransmitter that it uses to communicate or its role, a common mechanism of degeneration exists which is the toxic aggregation of proteins.

Proteins are encoded by our genetic heritage, DNA, and provide a host of vital functions to cells and organs. They are used in cell structure, they enable muscle cells to be mobile for example, and they are vital for energy metabolism as well as for transmitting information between cells, like the nerve impulse.

Proteins have a three-dimensional structure that is based on their composition and ensures that they carry out their biological function.

Occasionally, some proteins may develop an abnormal shape but these are then corrected or eliminated by "monitoring" systems.

Nonetheless, under certain conditions that are not yet well defined, abnormal proteins accumulate and aggregate to form oligomers, which in turn aggregate to form fibrils inside the neurons or around their periphery.

The brain cannot destroy these abnormal protein aggregates and, as such, they become toxic for the neurons through mechanisms that have not yet been identified but for which three hypotheses are being studied:

- the death of neurons would be caused by the loss of the activity of these proteins essential for neurons to survive
- protein aggregates would introduce a new toxic function for the neuron
- the presence of abnormally-aggregated proteins would trigger an inflammatory reaction resulting in the death of neurons.

Consequences of the death of neurons, neurodegenerative diseases

70 million people across the world are currently affected by neurodegenerative diseases and the number of new cases increases every year as the population ages.

Although neurodegenerative diseases all have neuronal death as a common cause, they affect different types of neurons in different parts of the brain and spinal cord and cause a variety of symptoms ranging from motor impairment to loss of cognitive abilities such as memory, language and mental integrity.

These diseases are genetic, i.e. stemming from a hereditary mutation in less than 5% of cases. The origin of the 95% of non-family-based cases is still unknown but probably results from an interaction between a genetic predisposition and environmental factors. With the exception of Alzheimer's and Parkinson's diseases, where it is clearly established that age is a risk factor, there is no other environmental factor that has been proven to be involved in the onset of these diseases.

Although around a hundred diseases are considered neurodegenerative, the most common are Alzheimer's and Parkinson's diseases, Charcot disease or Lou Gehrig's disease aka amyotrophic lateral sclerosis (ALS), frontotemporal degeneration or dementia (FTD), progressive supranuclear palsy (PSP), Huntington's disease and ataxias.

Locating brain functions and their dysfunctions

1 Alzheimer's disease

35 million people worldwide are affected; 1 person in 20 from the age of 65 and more than 1 person in 4 over the age of 85.

Its symptoms: memory impairment, altered thinking and language, behavioral changes.



2 Frontotemporal degeneration (FTD)

2 million people worldwide between the ages of 50 and 60 are affected.

Its symptoms: behavioral disorders, personality changes such as apathy and/or disinhibition, language impairment, muscle rigidity.

3 Progressive supranuclear palsy (PSP)

Approximately 420,000 people worldwide from the age of 60 are affected. It represents 3 to 6% of **atypical Parkinson's syndromes**.

Its symptoms: intellectual slowdown, apathy, language, visual and swallowing impairment, loss of balance, eye disorders.

4 Huntington's disease

Approximately 350,000 people worldwide are affected by this genetic disease. Symptoms appear between the ages of 35 and 50 in before the age of 20 in less than 10% of cases.

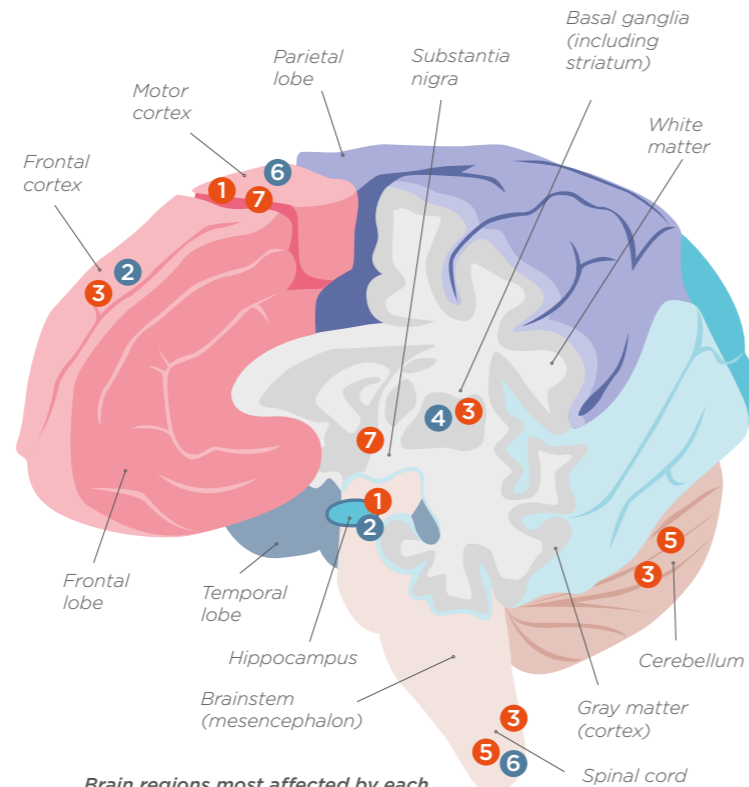
Its symptoms: motor disorders with involuntary and uncontrollable muscle contractions (chorea), breathing difficulties, speech and swallowing disorders.



5 Hereditary ataxias

400,000 people worldwide are affected and the disease appears between the ages of 2 and 60.

Its symptoms: poor muscle tone, loss of coordination of movements and balance.



Brain regions most affected by each of these 7 cited neurodegenerative diseases

6 Charcot disease aka Lou Gehrig's disease or amyotrophic lateral sclerosis (ALS)

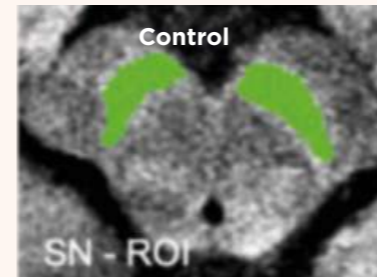
380,000 patients worldwide, with an average age of the onset of the disease at 60 years old.

Its symptoms: progressive paralysis of the muscles which become atrophied, involuntary and persistent muscular contractions, breathing and swallowing disorders.

7 Parkinson's disease

6.3 million people worldwide affected of which 80% after the age of 60.

Its symptoms: tremors in the limbs at rest, slowdown in carrying out gestures, decrease in spontaneous mobility, muscular stiffness.



MRI view of the disappearance of neuromelanin (white area surrounded by green) correlated with the duration of Parkinson's disease progression

Identification of a genetic variation delaying the onset of FTD

Around 50% of patients suffering from frontotemporal degeneration (FTD) have a mutation in the C9orf72 gene which codes for a protein present in the brain but whose role is still unknown.

At Paris Brain Institute, Dr Isabelle LEBER (AP-HP) and her team (Basic to Translational Neurogenetics) identified a genetic variation on the X chromosome which, when it exists,

delays the onset of the disease which, in turn, explains the variation in the age of onset of symptoms in patients with the same mutation on chromosome 9.

This genetic marker could eventually be used to predict the age of onset of the disease in patients with C9orf72 gene mutations and, as such, better target their therapeutic management.



To find out more

Neuromelanin, a MRI marker for the progression of Parkinson's disease

Parkinson's disease results mainly in the degeneration of neurons that use dopamine as a neurotransmitter and that are located in the substantia nigra.

These neurons have the particularity of containing a pigment, neuromelanin, which is the source of the dark color of this region of the brain and, as such, its name.

At Paris Brain Institute, the MOV'IT team led by Prof. VIDAILHET and Prof. LEHERICY demonstrated that the level of neuromelanin observed on a MRI in the substantia nigra was correlated with patients' clinical symptoms.

This protein could therefore be considered a reliable biomarker for assessing the effectiveness of treatments intended to slow down the progression and reduce the severity of the disease.

Share your experience



Many thanks for the questions and experiences we have received.

"My name's Catherine and I'm 67 years old. My mother suffers from Alzheimer's disease and I'm afraid that one day I'll be affected too. How can I know if I'm also at risk of developing the disease?"

First of all, hereditary forms, referred to as "family-based", of Alzheimer's disease represent less than 1% of cases. Moreover, thanks to the monitoring of 400 healthy subjects over the age of 70 complaining of memory impairment, the Insight study carried out by teams of the French Institut de la Mémoire et de la Maladie d'Alzheimer (IM2A) and the Paris Brain Institute, at the Pitié-Salpêtrière AP-HP Hospital, aims to understand why and how this disease develops in some people and not in others, and to identify its triggering factors.

Let's talk about innovation

Email us your question on the special report theme for our next issue, which will deal with innovation dedicated to research. Your question may be published in the June 2022 issue of Synapse.

► contact@icm-institute.org



Is falling asleep a creativity booster?

What if a few minutes of sleep could act as a trigger for creativity? This is what a study conducted by Célia Lacaux, Delphine Oudiette (Inserm) and their associates at Paris Brain Institute and the Sleep Pathology Department at the Pitié-Salpêtrière AP-HP Hospital suggests.

A legend about the inventor Thomas Edison says that he used to take short naps to stimulate his creativity. During these naps, he held a metal ball in his hand. The ball would fall noisily when he fell asleep and wake him up just in time to record his creative flashes.

“There is therefore a phase conducive to creativity at the time of falling asleep.”

Célia Lacaux and Delphine Oudiette (Inserm), researchers at Paris Brain Institute and at the Pitié-Salpêtrière AP-HP Hospital, were inspired by this story and wished to explore this very particular phase of sleep and determine whether this phase did indeed have an effect on creativity. To do this, the team proposed mathematical problems to 103 participants, all of which were

long and tedious to solve. But there was a hidden twist inside each of these problems that made it possible to solve them almost instantly, of course unknown to the participants at the beginning of the test. The subjects tried to solve the problems a first time. All those

who had not found the hidden rule were invited to take a twenty-minute nap under the same conditions as Edison, with an object in their hand, before taking the mathematical tests again.

Spending at least 15 seconds in this very first phase of sleep after falling asleep tripled the chances of finding this hidden rule, through the famous

“Eureka!” effect. This effect disappeared if the subjects went deeper into sleep.

There is therefore a phase conducive to creativity at the time of falling asleep. To activate it, we need to find the right balance between falling asleep quickly and not falling asleep too deeply.

These “creative naps” could be an easy and accessible way to stimulate our creativity in everyday life.



Spinocerebellar ataxia type 2: a therapeutic trial opens new avenues

A clinical trial conducted by the team of Professor Alexandra Durr (Sorbonne University, AP-HP) at Paris Brain Institute and at the Pitié-Salpêtrière AP-HP Hospital shows that despite the hopes raised in recent years, riluzole does not improve the clinical or radiological symptoms of patients suffering from spinocerebellar ataxia type 2.

Spinocerebellar ataxias (SCA) are a group of genetic neurodegenerative diseases, which are heterogeneous from a clinical and genetic point of view. To date, at least 50 genes are involved. The main symptoms are coordination and balance disorders, dysarthria and eye movement impairment.

“This information could provide new biomarkers for the disease, indispensable for assessing potential new treatments.”

Very few drug treatments exist for managing these pathologies.

In recent years, positive results of riluzole, a therapeutic molecule already used against amyotrophic lateral sclerosis, had been recorded for SCA. However, its effectiveness had not been proven and remained

variable. As ataxias are very different from one type to another, from one patient to another depending on the stage of the disease, specific studies by ataxia type were essential.

Alexandra Durr’s team took up the challenge for spinocerebellar ataxia type (SCA2). The ATRIL clinical trial was conduc-

ted with 45 patients at a moderate stage of the disease, in eight centers, gathered within the French Neurogene network, a national reference center for rare neurogenetic diseases. In conjunction with the treatment, researchers and clinicians collected MRI data and clinical scores of ataxic symptoms.

Study results did not show any improvement in clinical or radiological signs in patients suffering from SCA2, despite good tolerability and absence of side effects.

However, thanks to the monitoring of patients during this trial, valuable clinical and brain imaging data on the progression of the disease were acquired. This information could provide new biomarkers for the disease, indispensable for assessing potential new treatments. Even though this study did not demonstrate any benefit from riluzole, it shows that it is possible to perform a conclusive trial on a rare disease.

This result does not exclude a possible beneficial effect for other forms of ataxia, but highlights the importance of assessing treatments in homogeneous groups of patients, including for rare diseases.



Healthy Mind: Virtual therapies to tackle pain and anxiety

Healthy Mind is a startup that proposes virtual therapies to alleviate pain and anxiety in hospitalized patients. It is hosted in the iPEPS incubator — Paris Brain Institute's Healthtech Hub, at Station F.

7T MRI: A TECHNOLOGICAL BREAKTHROUGH

Every year, through the hundred or so studies conducted, 2,500 people have a MRI at Paris Brain Institute. The Institute, forever striving to be at the cutting-edge of technology, dedicated to research and to patients, intends to acquire new equipment, the 7T MRI.

What does 7T mean exactly? T for tesla, in honor of its discoverer, the Serbian physicist Nikola Tesla, is the unit that measures magnetic field intensity.

MRI scanners that we find in radiology practices have average power of 1.5T. Paris Brain Institute is now equipped with two 3T MRI scanners, which deliver even more detailed images of the brain and its activity.

By increasing magnetic field intensity from 3T to 7T, the Institute will obtain images of higher microscopic resolution, which will pave the way for studying regions of the brain that were inaccessible until now and, as such, will enable better understanding of the diseases that affect it, more detailed diagnosis and, ultimately, treatments that are more targeted and more effective.



During hospitalization, especially for surgery or palliative care, patients may be subject to severe anxiety or pain. Although drugs exist to treat these symptoms, they cannot be administered systematically and are not free from side effects. Seeking non-invasive solutions to treat these symptoms is as such a key challenge.

By combining neuroscience, psychology and virtual reality technologies, the company has developed and commercialized a medical device that can be easily used before, during or after an anxiogenic or painful procedure. The benefits are seen at various levels of anxiety and pain, either as an alternative or as a complement to sedation.

Its effectiveness means it can be used for a wide range of applications and is part of the therapeutic arsenal of many medical departments such as anesthesia-intensive care, surgery, pediatrics, oncology and palliative care.

Healthy Mind is currently working with teams at Paris Brain Institute, in particular with the Neurotrials Early Clinical Development Unit, to validate other therapeutic areas for its device and with the Magnetoencephalography-Electroencephalography Platform for a clinical study.



Committed together

Every year, sports club and societies organize events to support the Paris Brain Institute. These events, which are so special in terms of the values they promote, are essential for pursuing and accelerating research on nervous system diseases. Amongst the numerous initiatives that we welcome with open arms, we have chosen to present 3 fundraising events organized in 2021. They embody the commitment and going the extra mile that are vital in sports as well as in research!



The French association "La Tomate contre la dystonie" has been rallying for Paris Brain Institute for several years now by organizing an enjoyable cycling tour where the proceeds go to Prof. Marie Vidailhet's work on dystonia. For the 2021 edition, €6,000 was collected.



■ €23,100! This is the amount collected over a weekend by the French association Le French Restream during its Interglitches event. This charity video-game marathon brought together 66 high-level competitors, 200 visitors and dozens of thousands of Internet users logged onto the Twitch platform in a festive, family-style atmosphere, on November 12, 13 and 14 last year.



■ The wonderfully motivated French association Amour Amour (AAA) made a donation of €47,000 to the "Genetics and Development of Brain Tumors" team, led by Prof. Marc Sanson and Dr Emmanuelle Huillard, on November 16, 2021. This incredible fundraising is mainly thanks to the donations made on the Alvarum AAA page for a virtual race organized last June and a semi Ironman Triathlon won by Arthur Corbin.

Paris Brain Institute is deeply touched by all these generous sports initiatives that are full of meaning and wishes to thank all the participants and donors wholeheartedly.

Big Brain Theory.

Philanthropic for the future.



What if there was a different way to do research? An audacious and unconventional way based on interdisciplinarity. A way that could lead to major breakthroughs and revolutionize the approach and treatment of neurological diseases and psychiatric disorders. Paris Brain Institute is leading an unprecedented campaign to seed projects for the Big Bang Theory (BBT) Program.

> Funding remarkable projects with great potential for discoveries

The BBT Program projects are selected by an eminent International Scientific Advisory Board and embody Paris Brain Institute's vision: to pursue a groundbreaking research strategy that is not afraid to dare and take cross-disciplinary paths. Because these projects are «high risk» they require seed funding so that researchers can get the proof of concept they need to subsequently obtain public funding and carry them through. Our goal : to finance 10 projects in 2021 and 2022, corresponding to a 1.7 million euros investment.

> Philanthropic investors, your generosity increases our discoveries tenfold

Based on the proof of concept established over previous years, BBT scientific projects have great chance of taking off. On average, they are able to obtain 2.5 times the amount invested during their startup phase. This is a sure guarantee for donors that their donation will make an impact in the long run.

> A startup effort encouraged by tax measures in effect

Do you pay tax on personal real estate assets (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

€7,500

You benefit from a tax deduction of:

€2,500

And your donation costs you:

Are you a tax-resident in another country?

Paris Brain Institute may offer you tax-deductible options in Hong Kong, the United States and in 20 countries in Europe, including the United Kingdom and Switzerland. For more information, please contact Marielle Lethrosne.

Thank you for your support!

**your dedicated contact
at the Circle of Friends Office**

Ms Marielle Lethrosne

**+ 33 (0)1 57 27 45 72
cercle@icm-institute.org**

Your question

“Every spring, I usually make a large donation to Paris Brain Institute that lets me completely offset the tax amount payable for French tax on personal real estate assets, known as IFI in France. The current increase in real estate prices will of course have an impact on my IFI calculation. Is it correct that certain types of donation made to the Institute could enable me to reduce my tax base?”

Jean L.

Our answer

Given the increase in real estate prices in 2021, you may be concerned that your tax on personal real estate assets (IFI) in France will increase. It is worth mentioning that the IFI tax measures in effect enable donors to earmark their generosity to the Institute within a limit of €50,000 deduction. This corresponds to a cash donation of €66,667.

Above this amount and, in addition, your commitment to our researchers can be expressed through donations.

• Temporary Donation of Usufruct (DTU)

The DTU consists in giving, by notarial act, the usufruct of a property to Paris Brain Institute for a limited and pre-determined period of time (3 years minimum) at the end of which the full ownership is fully recovered by the donor. For example, by initiating a DTU for an investment property with a good yield, you remove the value of this property from your tax base, reduce the amount of your IFI, and no longer declare the rental income from the property for income tax purposes. You enable Paris Brain Institute as the beneficial owner to collect the income related to your property for the duration of the donation.

• Bare ownership Donation

You may also gift the bare ownership of a property (building, apartment, house) to Paris Brain Institute whilst keeping the usufruct which enables you to occupy the property or to collect the rent. Paris Brain Institute will not become the owner until your death. The value of the property is totally excluded from the IFI tax base, as such you pay less tax whilst sustainably supporting the research carried out by the Institute.

Donations are instruments for transmitting assets during your lifetime that depend on your age, your personal situation (single, in a couple; without or with children) and, above all, your philanthropic desires. Please feel free to tell us about your projects.

F.A.Q.?

I made my donation to Paris Brain Institute at the end of 2021. Can I deduct it from my tax on personal real estate assets (IFI) 2022?

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 2021 tax return (between May and June depending on where you live) and until the deadline for filing this year's return.

I would like to come along and discover the Institute with my family. Is it possible to do so given the current health situation?

The Institute complies strictly with French governmental measures in effect and organizes private visits regularly so that its donors can really discover science. Contact the Circle of Friends Office on +33 (0)1 57 27 40 32 or via cercle@icm-institute.org

INCUBATOR OF HOPE

Revealing the discovery potential of pioneering projects

**TO HELP CURE NERVOUS SYSTEM DISEASES,
SUPPORT PARIS BRAIN INSTITUTE.**

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 French income tax.

Institut du Cerveau - Hôpital Pitié-Salpêtrière - CS 21414 - 75646 Paris Cedex 13, France
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