

Synapse

The newsletter designed to connect with you

N° 31 - November 2022

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Generosity

Paris Brain Institute and Richard Mille : join forces and make a difference



After two years of uncertainty, 2022 has seen a return to "normality" in the health sector. With the energy boost it has brought, Paris Brain Institute teams were rewarded with countless exciting discoveries.

Just take the original study combining clinical and artificial intelligence to identify risk factors for Alzheimer's disease. This year's noteworthy results include the 3D mapping of the meningeal lymphatic network and decoding a direct dialogue between the gut microbiota and the brain.

Another core subject at Paris Brain Institute: strokes. Affecting 110 million people worldwide, these conditions impair motor functions, speech and vision. This issue's feature explores the subject and introduces you to how the Institute's teams are working on exciting projects to improve and tailor rehabilitation.

Thanks to your loyal support, Paris Brain Institute is working tirelessly to help patients and their families.

On behalf of the Institute's researchers and founding members, I would once again like to thank you for your generosity and hope that the world will get back on an even and more peaceful keel.

Jean Todt
Paris Brain Institute
Co-Founder and Vice-President



Involvement in World Alzheimer's Day

A live radio broadcast with Vivre FM took place at Paris Brain Institute on Wednesday September 21st to spread the word about Alzheimer's disease to the general public. The morning's line-up included several talks by our specialists to present the condition, discuss symptoms, screening, progress and ongoing research projects at the Institute. A Q&A session with the public underlined the importance of carers and specific support. Listen back to the broadcast on Paris Brain Institute website.



Women and pregnancy

What happens in a woman's brain when she gets pregnant? Using the latest findings in neuroscience, psychiatrists Lucie Joly and Hugo Bottemanne (Paris Brain Institute researcher) tell us how changes in the brain occur during pregnancy, explain the highs and lows of motherhood and unravel mysteries such as pregnancy denial, false pregnancy and post natal depression. An essential book for any mums and dads to be.

Dans le cerveau des mamans - La maternité, l'amour et le baby-blues expliqués par les neurosciences, by Hugo Bottemanne and Lucie Joly, éditions du Rocher, 312 pages, 20.90€



Interglitches, round 2!

After a thrilling first outing, Le French Restream association is back with its speedrun event raising money for Paris Brain Institute on November 11th, 12th and 13th: Interglitches. Come and support incredible young players as they complete a video game in record time. Let's put the "fun" into "fundraising"! On the agenda: 24-hour individual and team game sessions for 3 days raising funds to support our researchers, workshops for children and adults (speedrun introduction, banana DNA extraction etc.). Good times at the Institute! Information on Paris Brain Institute website.

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Breega takes a stand for Lou Gehrig's disease: a 105,544€ donation!

Breega is a venture capital fund created by entrepreneurs, for entrepreneurs, to finance technology start-ups worldwide. Following its first seed fund in 2015, it now has over 500 million Euros in assets under management and over 70 start-ups.

The first year saw the fund get its community involved in a never-before-seen gift matching operation to raise funds for the Institute's teams. *"Commitment and impact have always been in Breega's DNA and combatting ALS has always been dear to our hearts. This is just the beginning of our work with Paris Brain Institute."* Ben Marrel, Breega Founder and CEO.



2 minutes to understand

A clear and simple way to describe a condition or research project is vital to sending the right message. Paris Brain Institute's digital team tackled the challenge with a series of short videos: "2 minutes to understand". Parkinson's disease, Lou Gehrig's disease and MS are online on our YouTube channel. Watch them now!

Key figures

ON 30/06/2022, INTERNATIONAL RESEARCHERS AT PARIS BRAIN INSTITUTE ACCOUNTED FOR 22%

WITH 44 NATIONALITIES REPRESENTED!

Follow us



Ben Marrel, Breega Founder and CEO, with Séverine Boillée, ALS team leader at Paris Brain Institute

seen on the web

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



- The 3D mapping of the meningeal lymphatic network unlocks new mysteries
- Prolonged epileptic seizure: new biomarkers to improve outcomes for patients admitted to intensive care
- Modelling brain function and complexity to improve research

videos



- ▶ 21/09/22 Alzheimer's disease conference for donors
- ▶ Braincast #10 in partnership with Cerveau & Psycho: "Alzheimer's: artificial intelligence to aid diagnosis" with Ninon Burgos and Braincast #11: "The brain on the brink of death" with Pr Stéphane Charpier
- ▶ 20/10/22 Science Art and Culture conference: "I walk therefore I am" with Roger Pol Droit, philosopher and author, and Pr Yves Agid, neurologist

agenda

11, 12 and 13 November

Interglitches - Cogito Ergo Run, charity video game marathon run by Le French Restream raising funds for Paris Brain Institute.

Event open to the general public. Further information on <https://institutducerveau-icm.org/fr/actualite>

Saturday, November 19

10th Music Passion Parkinson event in Caissargues raising funds for Paris Brain Institute. Information on <https://zicpassionparkinson.jimdofree.com>

Saturday, 26 November

Release of the Braincast #12 podcast in partnership with Cerveau & Psycho featuring Mathias Pessiglione

Wednesday, 7 December

Donors' conference about brain lesions Booking required. Please email cercle@icm-institute.org or call +33 (0)1 57 27 40 32

Tuesday, 6 December

National Huntington's Disease Day

Elsa DEGAND

Occupational therapist physical medicine and rehabilitation department at Pitié-Salpêtrière

Cécile DESSAGNE

Occupational therapist physical medicine and rehabilitation department at Pitié-Salpêtrière

Sarah BENESSIONO

Care Lab designer and operations manager



The story designing a support tool to help brain injury survivors be independent

How did this collaboration come about and what are your respective roles?

S.B. Paris Brain Institute's Care Lab designs and makes medical devices based on feedback from patients and healthcare providers. These devices are intended to launch on the market through partnerships such as the one with Humans Matter.

C.D. When the Institute's Care Lab asked to work with us, we soon brought up the idea of improving knowledge transfer from the hospital to home, specifically in cookery which is essential to independence. Cooking is a complex activity that most people used to do before their stroke or brain damage but struggle to do alone when they come back from the hospital.

What type of device have you designed? What is its objective?

S.B. It's an app called "BRO" which provides help making recipes. Bro is now developed by our partner Humans Matter.

E.D. We realized that even if patients were able to make a recipe on their own in class at hospital, it was far harder or impossible for them to replicate it at home. The idea behind the app is to offset the cognitive impairment affecting people with brain damage to get them back into the habit of doing an activity and regaining some of their independence.

How does the tool work?

C.D. Patients are taken through a recipe step by step. Every step is detailed by a voice, images or videos i.e. weighing out ingredients or breaking eggs. A single recipe can contain 40-80 instructions depending on the set-up by occupational therapists and based on the patient's cognitive ability following their hospital assessment. Additional information is provided to the patient at each step to answer questions such as "how do you balance the scale before weighing?" The app also has reminders such as "make a shopping list" or "cook" and has text alerts to safeguard every potentially dangerous cookery stage.

“It's very rewarding for us to see a patient getting back into their habits ,,”

Cécile DESSAGNE Occupational therapist physical medicine and rehabilitation department at Pitié-Salpêtrière



15 million people worldwide suffer a stroke every year:

5 million die from it and 5 million suffer a permanent impairment which can affect their family and community. How can research help these patients regain their autonomy?



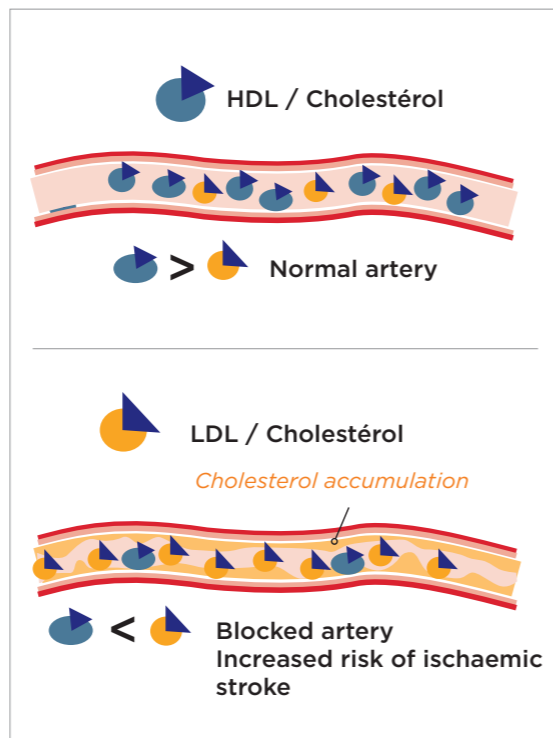
How to spot stroke causes and symptoms to act fast and save lives

60% of strokes occur in people under 70 years old and 16% in people under 50 years old. Significant progress has been made in recent years in treating acute strokes but the affliction is still a major cause of disability worldwide.

Paris Brain Institute's research in this field focuses on our brain's ability to recover after a stroke to help improve understanding, prediction and patient care.

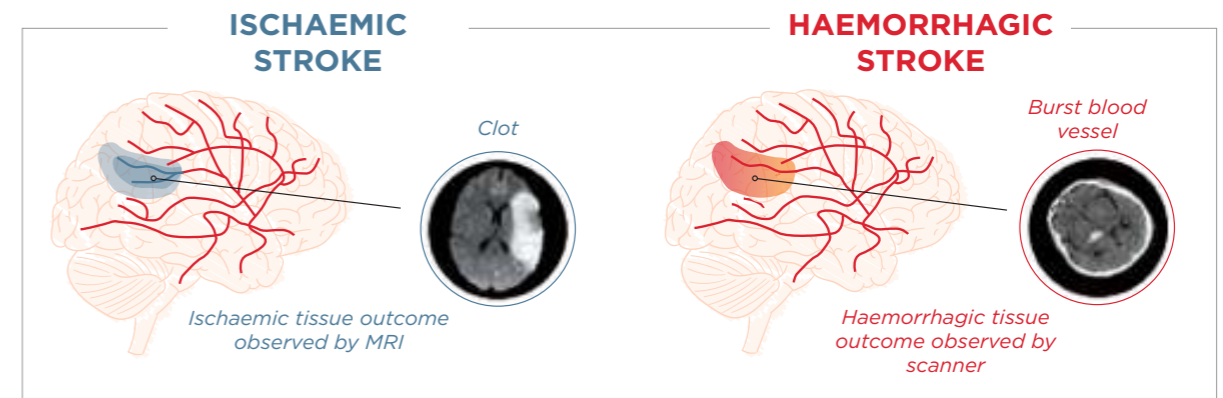
Stroke risk factors

- High blood pressure is the biggest risk for strokes so you should check your blood pressure on a regular basis and consult your GP if the maximum exceeds 140 or often exceeds 90 mmHg at rest.
- Cholesterol level which should be checked every 5 years. The two molecules in charge of carrying cholesterol are LDL and HDL. LDLs carry cholesterol to cells whilst HDLs collect excess cholesterol and take it to the liver. If LDLs carry more cholesterol than the cells needs, unused LDLs collect in artery walls and form plaques that block blood vessels. On the other hand, HDLs "clean" blood vessels.



What is a stroke?

- 85% of strokes are the result of a blockage (usually a blood clot) cutting off the blood supply to the brain. This is an ischaemic stroke or cerebral infarction. The main cause is plaque build-up in the arteries which restricts blood vessels and can cause blood clots. Plaque build-up or atherosclerosis sometimes occurs in the brain but cholesterol deposit fragments away from the brain can break off and form a clot that travels through the blood stream.
- 15% of strokes are haemorrhagic and caused by a burst blood vessel which causes bleeding in the brain. A burst blood vessel can be caused by weakness due to high blood pressure (main cause), a deformity or treatment.



In both cases, brain cells are affected by hypoxia so they are starved of the oxygen and sugar they need to survive and that are normally carried in blood. This kills 1.9 million neurons per minute (total number of neurons: approximately 86 billion) in a specific area.

You have to act FAST (face, arm, speech, time) when it comes to strokes so what are the signs?

Stroke symptoms can appear suddenly and be very wide-ranging: motor impairment, drooping mouth, weakness in one arm, slurred or garbled speech. If the stroke occurs in the left side of the brain, the right side of the body will be affected and vice versa. If someone suddenly presents any of these symptoms, you must call the emergency services as soon as possible.

Early diagnosis and immediate treatment in a neurovascular emergency unit help reduce fatality by 30% and decrease the severity of brain damage and complications.

The main objective in the first 6 hours is to minimize irreversible brain damage by restoring blood flow in the event of an ischaemic stroke or reducing inflammation of the blood vessels in the event of a haemorrhagic stroke. Complex and all-encompassing care is established in the weeks that follow with doctors, physiotherapists, speech therapists and occupational therapists.

SUDDEN SYMPTOMS?

» Every minute counts
Act FAST

- FACE**
The mouth is drooping, a sign of facial paralysis. The person cannot smile.
- ARM**
An arm or leg stops moving. The person cannot lift both arms.
- SPEECH**
The person's speech is slurred. The person cannot repeat a simple sentence.
- TIME**
The person cannot complete 1 of these 3 tasks.
CALL EMERGENCY SERVICES IMMEDIATELY



Boosting neuroplasticity, a focal point at Paris Brain Institute

Paris Brain Institute researchers are trying to understand the neurological process of brain plasticity occurring in the brain in response to a stroke with a focus on post-stroke recovery to outline criteria for the best rehabilitation.

After a stroke, plasticity enables the brain to change certain connections to recover all or some of its capacities. In many cases, it is currently difficult to predict how a patient will recover. It is therefore essential that we better understand the mechanisms behind connectivity and how different regions interact with each other straight after a stroke to implement new therapy strategies.

A new mathematical model of brain connectivity after a stroke

Researchers in the "ARAMIS: Algorithms, Models and Methods for Images and Signals of the Human Brain" team have been working with doctors at Padua University (Italy) on a project involving a group of stroke patients who do a functional MRI 2 weeks, 3 months and 1 year after their stroke.

The researchers modelled the rise in connection intensity in the side of the brain affected, between both sides and the affected region and its equivalent on the other side in each patient over time. The results of the neural network dynamics were compared with clinical scores assessing

"The first thing that happens after an acute stroke is the brain's plasticity enables it to make a spontaneous recovery. The neurons are capable of intrinsic recovery within the first 10 days. The most important time for active recovery is 2 weeks after a stroke."

Pr Pascale Pradat-Diehl, head of the physical medicine and rehabilitation department at Pitié-Salpêtrière

each patient's motor skills, vision, speech, concentration and memory.

The study found that you can reliably predict speech recovery after a stroke and the findings are an innovative tool for identifying patient profiles who may respond to rehabilitation best.



An exciting avenue for combined rehabilitation

Researchers and doctors on the "Mov'It: Movement, Investigations, Therapeutics" team conducted a clinical study of 27 stroke patients presenting a loss of fine motor skills in their hands (dexterity). The patients were treated with a series of transcranial magnetic stimulations simultaneously between the cerebellum and motor cortex for 5 days and completed a course of physiotherapy focusing on the upper limbs.

The trial found that the combination of different types of rehabilitation results in increased activation (assessed by functional MRI) in the main motor cortex (the area of the brain that is involved in the planning, control, and execution of voluntary movements) in the affected side of the brain as well as a significant improvement in dexterity which continues one month after rehabilitation sessions. Recordings of neural connections during and after stimulation sessions also provided a better understanding of recovery which will help update these therapies to deliver the best possible rehabilitation.

Dextrain, a start-up incubated at Paris Brain Institute since December 2021

Dextrain designs new digital tools used in hospitals and at home for manual dexterity testing and rehabilitation. The courses can be adapted to suit patients based on their needs and level of performance to provide them with consistent, tailored, enjoyable and motivational rehabilitation.

The visual-motor and audio-motor training exercises are based on neurological rehabilitation expertise and aim to promote the recovery of key dexterity components, help patients be independent in day-to-day activities and improve their quality of life.



Stroke research at Paris Brain Institute

A continuum of scientific, medical and technological expertise



4 research teams

1 clinical research network (iCRIN)

with collaboration between Paris Brain Institute and Pitié-Salpêtrière Hospital - AP-HP research teams



2 start-ups incubated

1 living lab (Care Lab)



Pitié-Salpêtrière Hospital - APHP with:

- a cerebral vascular emergency care department
- an aftercare and rehabilitation department
- a physical medicine and rehabilitation department
- a neuroscience medical university department (DMU)

Share your experience



How do you spot when someone is having a stroke and what should you do?

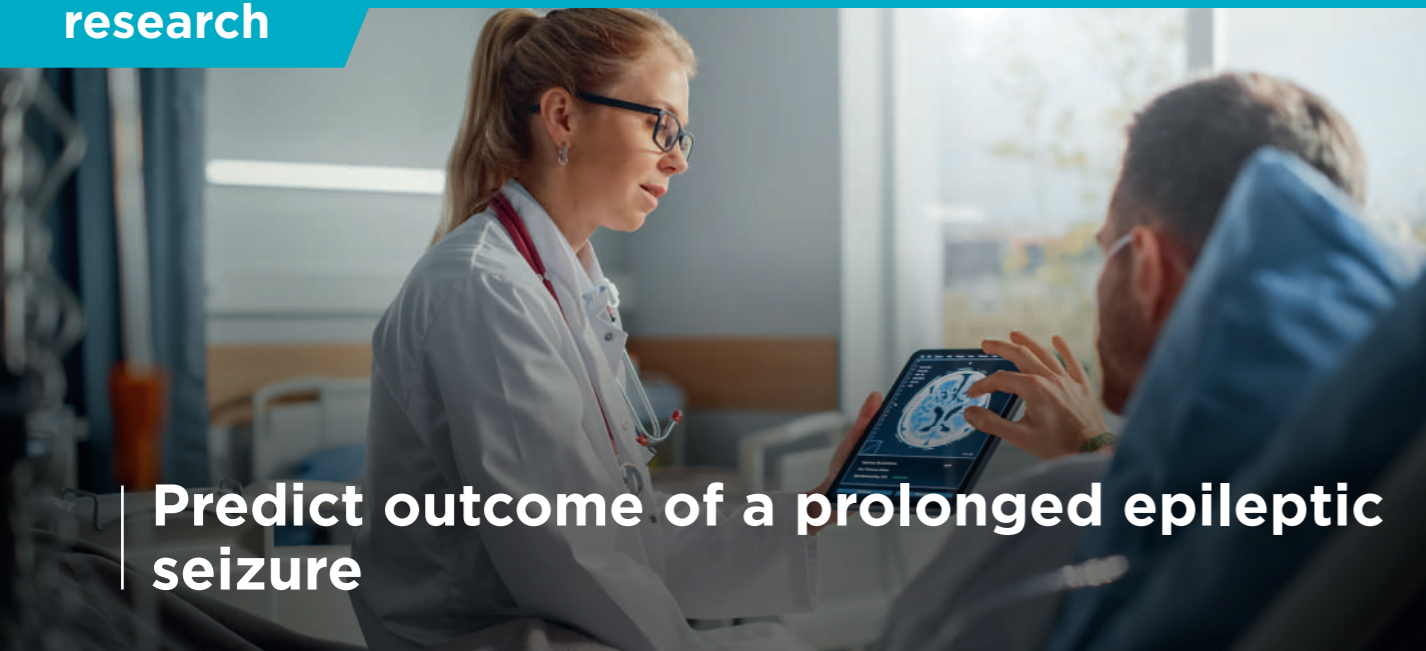
This is a vital question as the faster you act, the more of the person you save. i.e. the more likely the person is to stay alive and avoid significant, long-term disabilities. Strokes should be treated within three hours of the first symptoms appearing.

If in doubt, call emergency services.

Which topics or conditions would you like to read about in future issues of Synapse?

Email us your suggestions for subjects for our next issue's feature. Your subject may be covered in the March 2022 issue of Synapse.

▶ contact@icm-institute.org



Predict outcome of a prolonged epileptic seizure

A status epilepticus is a major neurological emergency. It is an epileptic fit that may cause irreversible brain damage and serious complications.

Researchers and doctors at Paris Brain Institute (Inserm/CNRS/Sorbonne University) and Pitié-Salpêtrière Hospital - AP-HP have recently identified new clinical biomarkers to help assess a patient's recovery

France every year. Almost 25% of status epilepticus are resistant to medical treatment and require critical care.

Assessing the future condition of the patient leaving critical care is essential to help the medical team and family provide appropriate care.

Dr Aurélie Hanin, from the "Cellular Excitability and Neural Network Dynamics" team at

Paris Brain Institute, conducted a study on a group of 81 patients in critical care at Pitié-Salpêtrière Hospital - AP-HP. Their condition was assessed before their prolonged epileptic seizure, when they left critical care and 6-12 months after leaving hospital.

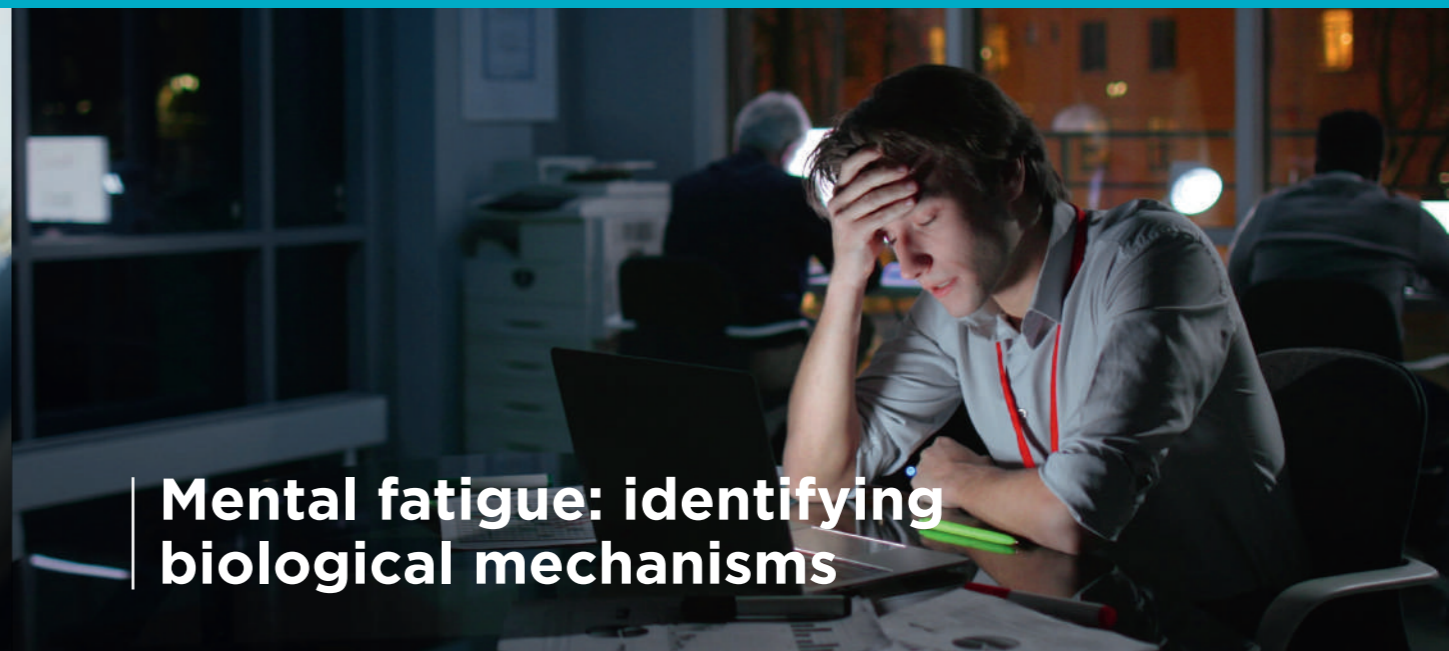
The findings resulted in the first time a simple biological score

has been established covering the patient's original cholesterol and creatinine levels. This helps predict how much independence 80% of patients will lose post-critical care.



"In the long term, we hope these prediction scores will provide a broader overview of the patient's condition to hospital teams which will improve their care".

Pr Vincent NAVARRO



Mental fatigue: identifying biological mechanisms

Mental fatigue can be described as the condition we sometimes find ourselves in after hours of demanding and complex cognitive exercises, with a sense of depletion and an inability to think harder or make decisions.

A Paris Brain Institute study has found a link between the onset of mental fatigue and the accumulation of a neurotransmitter called glutamate in a specific part of the brain (lateral prefrontal cortex) for the first time. The brain is unable to remove the molecule which begins to poison it and stops the brain from working harder. This finding explains why we make more impulsive decisions while being tired and may open up new doors to better understand conditions affected by mental fatigue i.e. burnout.

An initial study published in 2016 saw researchers in Paris Brain Institute's "Motivation, Brain and Behaviour" team find that cognitive or mental fatigue can make us choose instant rewards i.e. the satisfaction of eating a chocolate over deferred long-term rewards i.e. weight loss. Scientists found that this form of exhaustion resulted

in a drop in activity over the course of the day in a specific part of the brain: the lateral prefrontal cortex.

New collaborative projects have seen researchers prove that the accumulation of glutamate, the most abundant excitatory neurotransmitter released by nerve cells, increases in the lateral prefrontal cortex throughout the day.

The underlying biological mechanism therefore probably isn't specific to "intellectual" tasks but may come into play during any complex and lengthy task such as elite sports training which requires intense and sustained concentration. So any "non-automatic" activity.





Paris Brain Institute on the cutting edge of neuroimaging technology

Paris Brain Institute received a new transcranial magnetic stimulation system (TMS) in April 2022 to empower research and care technology. The Institute's CENIR platform, specializing in neuroimaging, has helped the Institute fuel basic and clinical research into several conditions.



Pragmatic healthcare emPowering People

CLINICAL ASSESSMENT IN A FLASH

Among the latest start-ups at the iPEPS incubator - The Healthtech Hub at Paris Brain Institute, P3Lab is working on a diagnosis tool for neurological disorders using eye tracking. This pioneering technology aims to provide an all-round solution that is scientifically sound and easy to use. Specific focus has been given to making it part of the patient journey, a key part of the NeuroClues TM experience. The portable laboratory conducts measurements and analyses to provide neurologists with a means to increase their diagnostic certainty in just minutes and better treat the patient.



Transcranial magnetic stimulation is a non-invasive procedure that uses a magnetic pulse to stimulate nerve cells in the brain. The procedure focuses on a specific part of the cortex to achieve long-lasting therapeutic results in conditions such as depression and neurogenic pain.

Institute researchers got exciting results with this technology in treating strokes and understanding inhibitory control in Tourette's syndrome and abnormal movement such as dystonia and autism.

April 2022's acquisition of the robotic TMS-COBOT system opened up countless opportunities for Paris Brain Institute's research ecosystem. There are 40 examples of this technology worldwide with 3 in the Île-de-France region. It provides solutions to classic TMS issues with three main functions:

- › increased spatial resolution for more accurate targeting;
- › cortical mapping for improved temporal resolution, key to studying muscle activity;
- › improved probe orientation in cortical sulci for more accurate stimulated neuron targeting.

“Brain to Market” Summer School: 2022 devoted to epilepsy



Paris Brain Institute's Open Brain School hosted the 8th edition of its neuroscience entrepreneurship training programme between September 12th and 16th.

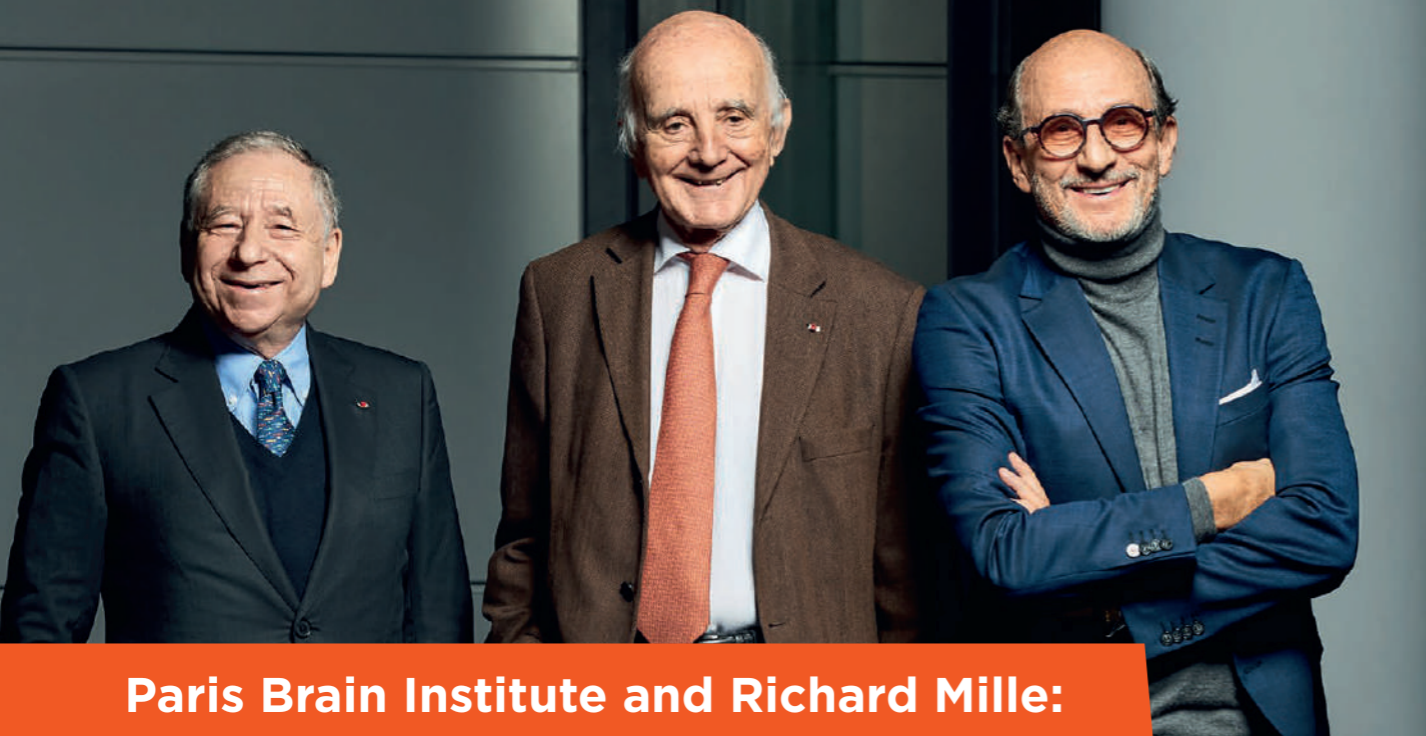
The “Brain to Market” Summer School is an intensive 5-day training course to get to grips with key skills in health entrepreneurship. It brings together fifty international attendees: students, researchers, private figures, engineers, designers and doctors who team up to create innovative solutions to benefit patients, their families and people in the medical and research sectors.

Attendees took part in presentations by Paris Brain Institute researchers, AP-HP doctors, Collège des Ingénieurs entrepreneurship consultants and clinical innovation and development specialists. The Epilepsie France patients association, start-ups and industry manufacturers also took part in the event. The sheer variety of figures enabled attendees to experience the key stages of a pioneering health project: understanding the issues of the disease, providing relevant solutions for beneficiaries which are viable from a scientific and business point of view.

Attendees designed their projects working together in multi-disciplinary groups put together to cover every aspect of entrepreneurship.

The action-packed week ended with a presentation of the projects to a panel of experts and the best being researched by Care Lab, Paris Brain Institute's living lab, to explore further.





Paris Brain Institute and Richard Mille: join forces and make a difference

The watch brand has been working with Paris Brain Institute since 2012 and took its commitment to new heights with the launch of the Richard Mille Donors' Club.

The Richard Mille Donors' Club brings its community together in the fight against brain diseases and in support of the institute. The idea is to provide long-term financial support to give Paris Brain Institute visibility and a secure future.

The Club founded by Richard Mille provides Paris Brain Institute with the strength, flexibility and reactivity it needs to fulfil its mission: search, find, cure. By creating a global philanthropic community with the same values, the Club is committed to the billion people affected by neurological and psychiatric disorders worldwide.

The generosity of the Club's donors has already seen over 450,000 Euros raised since it launched at the end of 2021. These funds from all over the world boost and encourage Paris Brain Institute's staff of 750 who work tirelessly to unlock the mysteries of our brain and its diseases.

«Supporting such a cutting-edge and exciting structure as the Institute is a worthwhile cause. Furthering this research helps save and improve many people's lives,» said Richard Mille.

"Support from the Richard Mille Donors' Club is a real asset. It gives us the opportunity to pursue our commitment to a vital public health cause in the long-term. We are extremely grateful to everyone at the Richard Mille group for their involvement and generosity."

**Pr Gérard Saillant,
Paris Brain Institute President**

Your question

“ I would like to name Paris Brain Institute as a beneficiary in my life insurance policy. What do I do? ”

Paul D.

Our answer

A life insurance policy is a well-known savings and contingency fund. It provides capital as additional revenue when you retire for example. It's an asset transfer tool too. Every policy contains a clause where you can assign the beneficiary/beneficiaries you want to receive the capital when you pass. Transferring your life insurance policy is an easy and efficient way to leave something for a loved one and/or support Paris Brain Institute. Just update the beneficiary clause in your life insurance policy as follows: "I appoint Paris Brain Institute at Hôpital Pitié-Salpêtrière - 47, boulevard de l'hôpital - 75013 Paris as beneficiary of my life insurance." You can update your life insurance beneficiary clause at any time simply by contacting your insurance provider, adding Paris Brain Institute to your current list of beneficiaries and stating how much each is entitled to.

As a public utility foundation, Paris Brain Institute is tax exempt no matter the life insurance entitlement. That way all the savings that you have chosen to leave us in a life insurance policy will contribute to research and the fight against brain disease.

To find out more about different ways to leave money to Paris Brain Institute in your will, donations or life insurance, please contact the Circle of Friends or visit legs.institutducerveau.fr

F.A.Q.?

I am a European citizen and wish to support Paris Brain Institute but with the tax relief provided by my home country's legislation. How should I proceed?

Paris Brain Institute is affiliated to TRANSNATIONAL GIVING EUROPE, a partnership of leading European foundations and associations facilitating tax-efficient cross border giving within Europe.

Through TGE, as an individual or a company, you can now make an online donation from Germany, Belgium, Italy and Switzerland while benefiting from the tax advantages and exemptions provided by the legislation of your country of residence.

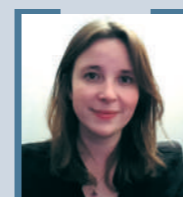
If you wish to make an online donation via the TGE, please scan the QR CODE below.



Online donations are not yet available for other countries, such as the United Kingdom, that only accept checks or wire transfers.

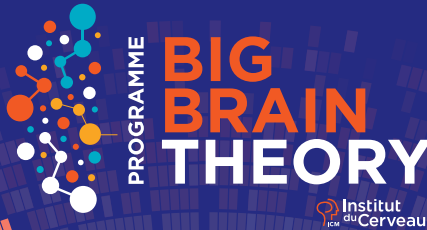
How much of my donation to Paris Brain Institute is deductible from income tax?

As a public utility foundation, up to 66% of your donation to Paris Brain Institute is deductible from French income tax based on 20% taxable income. For example, if your taxable income is 200,000 € then up to 40,000 € of the donation is tax-deductible. Donations made online, by bank transfer or check must be sent or processed by December 31st 2022 to be deducted from your 2022 tax.



**YOUR CONTACT
at the Circle of Friends Office**

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Please make your check payable to Institut du Cerveau and send it to us along with this form to the Institut du Cerveau
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Yes, I would like to help Paris Brain Institute researchers go forward in their research into 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.



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