Giving startups a powerful boost

The Medtech Generator & Accelerator (MGA) support program, developed conjointly by Paris Brain Institute, the Imagine Institute, the Pasteur Institute and the Vision Institute, and winner of the French Future Investment Program’s 2nd call for SIA projects run by Bpifrance, aims to accelerate the growth and development of medtech startups in the fields of neuroscience and rare diseases. This support began with participation in the Brain to Market Summer School which took place at the Institute from September 6 to 10 this year.

Accelerating the teaching of neuroscience

Great news! ARTE Education - a subsidiary of ARTE responsible for developing the European cultural channel’s educational projects - and Paris Brain Institute (via the Open Brain School, its training body) concluded a partnership designed to raise high school pupils’ awareness to neuroscience. Consequently, throughout 2021-2022, dedicated content will be made available to teachers and pupils of the 2,200 establishments registered on the platform. This alliance will also promote the international neuroscience competition, Brain Bee, to middle-school pupils and high-school pupils across France and will encourage them to take part in it.

Great honor

Last July, Mr Philippe Meignan, Immediate Past District Governor of the Lions Club East Ile-de-France District, honored Prof. Gérard Saillant, President of Paris Brain Institute, with the prestigious “Melvin Jones Fellowship” award. This award, named in tribute and in memory of the founder of the philanthropic organization, rewards the dedication of its members and its supporters.

Crédit Mutuel Nord Europe, generosity that knows no limits!

As fall 2021 comes around, Crédit Mutuel Nord Europe - CMNE will make its mark yet again as one of the Paris Brain Institute’s major patrons during the 20th-anniversary celebrations of the Concert d’Astrée, an exceptional event where proceeds will be donated to our researchers. CMNE, involved hand-in-hand with the 90 high-profile artists who will donate their fee, supports the event that will take place on November 12 at the Théâtre des Champs-Élysées. Further to the generosity of Crédit Mutuel Nord Europe, it was perfectly natural to sponsor this initiative that brings together two of its most valued partners and unites the greatness of baroque music and the excellence of neuroscience research.

CMNE’s generosity, however, goes far beyond this. Crédit Mutuel Nord Europe, one of Paris Brain Institute’s historic patrons since 2012, is also behind an innovative philanthropic initiative: Pierval Santé, which is the first-ever shared real-estate investment trust. The success of the 2014-launched Pierval Santé, boosted by the voluntary commitment of CMNE and its partners La Française AM and Euryale AM, ensures that medical research is supported substantially this year yet again. Thanks to the determination of the three partners (CMNE, Euryale AM and La Française AM), the associates of this first-ever shared real-estate investment trust are making a tangible contribution through their subscription to supporting medical research at Paris Brain Institute.

PSP France grant

A great reward for the researchers, Nadya Pyatigorskaya and Stéphane Lehericy from the “Normal and abnor- mal motor control: movement disorders and experimental therapeutics” team whose research project on pro- gressive supranuclear palsy (PSP) was awarded a €30,000 grant by the PSP France patients association. PSP is a rare neurodegenerative disease that results in the progressive para- lysis of eye movement. It affects between 5,000 and 10,000 people in France.

7,300 works are held by the Charcot Library, specialized in neuroscience and hosted at the very heart of Paris Brain Institute’s premises.

This space hosts a historical collection mainly comprising Jean-Martin Charcot’s personal library. Exceptional archives to discover right now!

The library is open to the public from Monday through Friday from 13:30pm to 5:30pm.
Vanessa Batista Brochard is CRA coordinator at the Neuroscience Clinical Investigation Center (Neuroscience CIC) at the Pitié-Salpêtrière Hospital headed by Dr Céline LOUAPRE and located within Paris Brain Institute.

CICs were created on the French National Institute of Health and Medical Research’s (Inserm) initiative for the purpose of coordinating studies focusing on Humankind.

The Neuroscience CIC at Paris Brain Institute has staff trained in clinical research for studying neurological and psychiatric diseases under optimal quality, ethics and safety conditions.

It can be called on by doctors from the neuroscience Medical-University Department (DMU), by Paris Brain Institute research teams as well as by drug manufacturers.

The Neuroscience CIC operates as a hospital department and currently totals 53 people (doctors, nurses, caregivers, neuropsychologists, laboratory technicians, clinical research associates and administrative staff). It also offers expertise in pharmacology and biostatistics.

Vanessa, what is a CRA’s key role?

The CRA is pivotal in setting up and running a clinical trial. They provide logistical expertise before, during and after participants are taken in charge. They are the key contact person for the people included in the trial. They contact them, organize the examination schedule and sequencing, explain the purpose of the study to them, make sure they have signed the consent form and that there are no grounds for excluding them from the trial.

They accompany the participant throughout the day to the different platforms where the examinations take place and compile and check the clinical and biological data collected during the day.

So, what’s your role as the coordinator?

I’m involved in optimizing research activities as part of the best clinical practices framework. I also sit on the various in-house committees which study the feasibility of the studies in terms of financial, human and technical resources.

On a daily basis, I look after the schedule for a team of 12 clinical research associates. The CRA acts as the interface between the researcher or the industrial, the doctor and the patients.

The CRA acts as the interface between the researcher or the industrial, the doctor and the patients. ”

Clinical trials are, firstly, a crucial, must-do step for better understanding human pathologies and, secondly, for assessing "non-harmfulness" and for proving the effectiveness of novel drugs stemming from research.
Clinical trials, when, who, why and how?

Clinical trials are always initiated by an investigator, based on a hypothesis in the case of physiopathological trials intended to better understand diseases, or in order to test the effect of a new drug in a therapeutic trial. The role of the investigator is to ensure the trial is conducted smoothly and to recruit and inform patients.

The investigator can be a pharmaceutical laboratory or a researcher who drafts the trial protocol and defines participant inclusion criteria. A physiopathological or therapeutic trial can only be carried out under the responsibility of a public or private promoter. The promoter deals with the trial’s legal and ethical aspects to ensure being issued with the authorizations required from the Agence Nationale de Sécurité du Médicament et des Produits de Santé (ANSM - French Agency for Drug and Health Product Safety) and from an Institutional Review Board (IRB) or Independent Ethics Committee. The IRBs are made up of patients, scientists and experts in the field of ethics and their purpose is to ensure that participants’ integrity and health are respected.

Trials may be financed by a private body such as a pharmaceutical laboratory or a public one such as a research center or associative funds. We use the term clinical trials because they are based on the study of patients and healthy individuals and follow on from fundamental studies carried out in laboratories on isolated cells and from analyses of experimental models.

Physiopathological trials

They are intended for gaining better understanding of biological mechanisms involved in a disease and for correlating them with the clinical symptoms observed in patients. They result in scientific publications that present the results obtained to other researchers and contribute to furthering research and/or, in certain cases, lead directly to therapeutic trials.

They have two key goals:

- To identify therapeutic targets at the heart of the cellular and molecular mechanisms that cause the disease. As the principle of a drug (therapeutic molecule) is to activate or inhibit the production of molecules by cells in order to reduce deleterious effects.

- To identify disease “biomarkers”.

Biomarkers, or biological markers are molecules or brain imaging criteria in the case of neurological and psychiatric diseases that make it possible to diagnose or even prognosticate or monitor the evolution or severity of the diseases or to tailor the therapeutic dose.

Therapeutic trials

Their ultimate goal is to market a new drug or to reposition an existing drug, i.e. use it in a disease other than the one treated to date.

Once the therapeutic molecule has been validated “in vitro”, i.e. in the laboratory on isolated human cells, or using experimental models, they go through 4 phases.

- **Phase I** to assess tolerance, i.e. side effects on a few dozen healthy participants.
- **Phase II** to assess the effectiveness of the drug on a hundred or so patients.
- **Phase III** to assess if the drug has a more powerful effect than the ones already used on several hundred patients.
- **Phase IV** which takes place after the marketing authorization has been granted by national or international health authorities and consists in monitoring patients in order to compile side effects and determine the clinical profiles of patients who respond best to treatment.

The blue oval shapes represent Paris Brain Institute’s state-of-the-art technological platforms used for collecting all patients’ imaging and biological data.

Physiopathological trial results published in a scientific journal

New leads on the causes and biological mechanisms of diseases

New research hypotheses

Phase 1
Assessing tolerance and optimal dose

Phase 2
Assessing effectiveness

Phase 3
Assessing if the effect is more powerful than treatments already on the market

Phase 4
Long-term monitoring of side effects

Market authorization granted by independent boards

Data analyzed by research teams via 10 technological platforms
Clinical trials at Paris Brain Institute

Today, Paris Brain Institute’s Clinical Investigation Center (CIC) coordinates some 115 clinical trials, including 68 (59%) initiated by public investigators and 47 (41%) by industrials. 57% of these trials are for therapeutic purposes, 22% are physiopathological and 21% are for developing clinically and biologically characterized cohorts.

Moreover, around 60 clinical trials are carried out within the University Hospital Institute (IHU) framework, which groups together Paris Brain Institute and a dozen of the Pitié-Salpêtrière Hospital’s clinical departments. Most of these trials are conducted within the scope of 13 new Clinical Research Infrastructures, known as iCRINs.

Furthermore, in 2018, Paris Brain Institute created a new early clinical development unit, NEUROTRIALS. NEUROTRIALS, a pioneering player in Europe, brings operational excellence in designing, conducting and delivering proof-of-concept studies in the central nervous system field. In addition to its academic, scientific and medical excellence, this unit is committed to delivering clinical studies on schedule, on budget and in keeping with quality (industrial standards).

"Since Paris Brain Institute was created in 2010, major efforts have been made to structure clinical research and we can now say that the Institute drives clinical research at the Pitié-Salpêtrière Hospital, which is one of the world’s most reputed neurology and psychiatry centers."

Prof. Catherine LUBETZKI, neurologist (AP-HP, Sorbonne University), Director of the Neuroscience Medical-University Department of the Pitié-Salpêtrière Hospital, Medical Director of Paris Brain Institute and “Repair in Multiple Sclerosis: from biology to clinical translation” team leader.

RESIST: a national multicentric therapeutic trial

Coordinated by Prof. Philippe FOSSATI, psychiatrist, Head of the Adult Psychiatry Department at the Pitié-Salpêtrière Hospital and "Control-Interoception - Attention" team leader at Paris Brain Institute.

This is a Phase II, double-blind, randomized controlled trial assessing the effectiveness, safety, pharmacokinetics* and pharmacodynamics** of daily oral administration of MAP4343 for 6 weeks in patients suffering from an antidepressant-resistant major depressive episode.

Depression is the most common psychiatric disorder affecting around 10% of the French population. It is determined by two factors: characteristic symptoms lasting at least 15 days with an impact on patients’ personal, professional and social life. 38% of patients, however, do not respond to drug treatments, which means continued research to identify and test new therapeutic avenues.

MS-BIOPROGRESS: a collaborative, multidisciplinary physiopathological trial

Coordinated by Dr Céline LOUAPRE, neurologist, head of the CIC Medical Unit, and researcher in the “Repair in Multiple Sclerosis: from biology to clinical translation” team at Paris Brain Institute.

This is a collaboration between several researchers and clinicians from 3 of Paris Brain Institute’s teams.

The aim of this trial is to identify the biological markers or predictive imaging markers in severe progression of multiple sclerosis. 50 pairs of brothers and/or sisters suffering from the disease (i.e. 100 patients) are included in the trial and are compared with each other in order to identify differences that would determine divergent progression of severity.

Multiple sclerosis is an inflammatory disease of the central nervous system (brain, spinal cord, and optic nerves), characterized by lesions (plaques) where a degeneration of neurons leading to progressive motor disability is observed.

"I recently learned that I have Parkinson’s disease and I’d like to know if I could join in a clinical trial for this pathology? Thank you for your answer."

Patients and healthy individuals who may take part in clinical trials must meet a list 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.

MS-BIOPROGRESS: a trial exploring all multiple sclerosis mechanisms

Clinical symptoms

Coordinated by Dr Céline LOUAPRE, neurologist, head of the CIC Medical Unit, and researcher in the “Repair in Multiple Sclerosis: from biology to clinical translation” team at Paris Brain Institute.

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MS-BIOPROGRESS: a trial exploring all multiple sclerosis mechanisms

Clinical symptoms

Let’s talk about neurodegenerative diseases!

Many thanks for the questions and experiences we have received. In this issue, we are going to answer the question asked by Michel, 61, who suffers from Parkinson’s disease:

“I recently learned that I have Parkinson’s disease and I’d like to know if I could join in a clinical trial for this pathology? Thank you for your answer."

Patients and healthy individuals who may take part in clinical trials must meet a list 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.

Contact@ICM-Institute.org
Attention and sleep slow waves

The onset of slow waves similar to those observed during sleep can be used to predict loss of attention.

Attention enables us to allocate our cognitive resources to signals from the outside world. We are actually constantly bombarded by information and it is thanks to our attention that we are able to focus on the most relevant signals.

Notwithstanding, although attention is an extremely flexible magnifying lens, its stability is limited and we often fail to keep our attention focused on a specific activity, and all the more so if the activity in question is of little interest to us.

Recent studies have shown that we spend half of our time awake thinking about something other than the task at hand. This is known as “mind-wandering”.

Occasionally, loss of attention may lead to a “mental void” and partial suspension of the flow of conscious thoughts. This loss of attention may result in instantaneous, dramatic consequences (accidents at work or on the road) as well as long-term ones (reduced productivity, drop in performances, etc.).

Loss is even more frequent whenever we are tired, which suggests there may be a link between loss of attention and sleep.

These slow waves similar to sleep ones exist in the different loss of attention cases, but in separate regions of the brain mind-wandering or mental void.

To understand these neuronal mechanisms underlying loss of attention, Thomas Andrillon (Inserm) studies the behavior, feelings and neuronal activity of healthy control participants carrying out a specific task.

The measurement of electrical signals in participants’ brains using high-density electroencephalography showed that, during loss of attention, it was possible to record neuronal activity characteristic of the transition from wakefulness to sleep.

PET 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 particles, the positrons. These particles then collide with electrons generating an emission of photons (light particles). The tracer is chosen to attach itself to a specific organ or tissue to reproduce an image of the organ studied, such as the brain.

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

This technique is used to real-time directly view in vivo the kinetics and distribution of the injected radiotracers and, as such, those of the molecules to which they attach themselves.

Swings in attention would therefore have a common physiological origin related to the emergence of a local activity similar to sleep in an awake but tired brain, and open up avenues for studying pathological attention disorders.

Recent studies have shown that we spend half of our time awake thinking about something other than the task at hand.

PET-MRI: an innovation that brings hope

Prof. Bruno Stankoff’s (AP-HP/Sorbonne University) team is developing new imaging tools based on the combination of MRI and positron emission tomography (PET) to better understand the biological mechanisms that lead to neuronal degeneration and disability in Multiple Sclerosis (MS).

PET-MRI brain profile of a MS patient

Individual profile of the mechanisms of brain damage in an MS patient assessed using PET MRI

In MS, the death of neurons leads to the progression of the disability during the progressive stages of the disease. This neurodegeneration begins even before the symptoms appear. It is therefore crucial to understand its causes and to identify reliable, accessible biological markers so as to develop new therapies capable of stopping this process before the onset of irreversible disability.

Thanks to this technique, Bruno Stankoff’s team recently confirmed the existence of a correlation between the activation of specific immune cells around the ventricles, areas favored by MS lesions, in contact with cerebrospinal fluid (CSF), and worsening disability in patients.

The molecules contained in the CSF could, as such, worsen inflammation in patients and favor a deleterious progression of the disease, making these molecules candidates for future treatment research.

On the right, the colored regions correspond to the inflammation areas detected in the normal-appearing white matter (light blue), in the lesions (red) and in the peri-lesions (violet).
As he has not been able to participate in a dedicated research program, Michael Craig Gradwell chose to fight for the future in another way. Even though the disease now prevents him from speaking, he can still ride a bike.

So, on September 1st this year, Michael Craig Gradwell, a round-the-city cyclist, set off from Donaueschingen (Germany) en route for Constanta (Romania), located on the western shores of the Black Sea, along the Danube; i.e. over 2,800 km! His goal: to raise public awareness to the disease and to raise money for ALS research at Paris Brain Institute.

This charity project is also a means for real-time collecting Michael Craig Gradwell's physiological data that will be analyzed with the aim of furthering science, and for sharing experiences with other patients suffering from Lou Gehrig's disease.

Paris Brain Institute and all its teams thank Michael Craig Gradwell warmly for his commitment and assure him of their unfailing moral support in this meaningful and courageous fight against this disease.

To discover Neurobike 2021: https://www.facebook.com/Michaelcraiggradwell
Reduce your taxes and help tackle nervous system diseases with Paris Brain Institute before December 31!

Generosity knows no borders Launch of the «Friends of Paris Brain Institute» in the US

Since Paris Brain Institute was created, it has established close scientific collaborations with leading American institutions such as Yale and Stanford as well as the University of San Francisco, California and MIT. And the Institute’s researchers are regularly honored for the quality of their work by prestigious US foundations or federal agencies.

To enable donors residing in the US to support Paris Brain Institute’s research, the Institute created the “Friends of Paris Brain Institute” fund in 2021. This fund, hosted by our partner foundation the King Baudouin Foundation United States, supports the Institute’s activities and, at the same time, enables donors to benefit from tax advantages specific to American legislation.

If, as Louis Pasteur said, “Science knows no country because knowledge belongs to humanity”, then generosity has no borders.

In Europe, one in eight people will be affected by a nervous system disease during their lifetime. The Institute’s 700 researchers and experts rally on a daily basis to tackle this public health issue. Your support for them is vital to help them further their understanding of the brain and to better treat and even heal diseases that affect it. As this year draws to a close, why not grasp the opportunity to make your taxes a real incentive for progress that will benefit thousands of patients and, at the same time, enjoy significant tax advantages.

If your tax residence is in France, make your donation before December 31 and deduct 66% of the amount from your 2021 income tax!

There are several ways to do this: you can make a donation by check, online, by bank transfer, etc.

Three fiscal devices to support your generosity:

Do you pay income tax?
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
€6,000
You benefit from a tax deduction of:
€3,400
And your donation costs you:
€6,600

Do you pay solidarity tax on wealth?
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:
€20,000
€15,000
You benefit from a tax deduction of:
€5,000
And your donation costs you:
€15,000

Do you pay corporate tax?
60% of the amount of your donation to Paris Brain Institute is deductible from corporate tax within the limit of €20,000 or 0.5% of the turnover if it is conducted as patronage. For amounts above this, the reduction is 40%.

If you wish to support us with a donation by check, please make your check payable to the Institut du Cerveau.

To make an online donation and receive your tax receipt within 24 hours, please visit our secure site www.institutducerveau-icm.org/en/

If you wish to support us via bank transfer, our Donor Department is on hand to send you our bank details.

Make a donation to the "Friends of Paris Brain Institute"

You may make your donation to the “Friends of Paris Brain Institute” by check, bank transfer or directly online by credit card on our dedicated page. Our fund also accepts donations of securities and real estate.

To find out more, contact Marielle Lethrosne marielle.lethrosne@icm-institute.org
+33 (0)1 57 27 45 72

F.A.Q.

I’m a taxpayer in Luxembourg, can I deduct my donation to Paris Brain Institute?

Of course. As an income tax-payer in Luxembourg, and irrespective of whether you live there or not, your donation to Paris Brain Institute is tax-deductible. In Luxembourg, donations are deductible for up to 20% of your taxable income up to a limit of 1 million euros and as long as the total amount of donations made exceeds €120 over the year. To check all the requirements, you can contact the Grand Duchy governmental departments.

My bank is asking me to authenticate my donation made by credit card, how do I do this?

There are several ways to do this but the most common is that your bank sends you a text message to your phone with a one-time code that you should enter on the donation screen. Once authentication is confirmed by your bank, the payment is authorized and the transaction finalized. Some banks may also ask you to authenticate the transaction by logging on to your bank app.

your dedicated contact at the Circle of Friends Office
Ms Marielle Lethrosne +33 (0)1 57 27 45 72 cercle@icm-institute.org
Cercle des Amis de l’Institut du Cerveau

Together, let’s push back the limits of neuroscience and invent tomorrow’s medicine.

Paris Brain Institute’s Circle of Friends groups together exceptional women and men who wish to help research push back the limits of neuroscience through their financial and human commitment and around shared values, including generosity, efficiency and innovation for the benefit of Humankind.

Our Circle intends to grow. This is why we invite you to join our Circle, YOUR Circle, where we create a privileged link with doctors-researchers, startups created in the Institute and its dedicated, committed members. Tomorrow’s medicine is being created today, for you and through you. Thank you!

Martine ASSOULINE and Maurice LÉVY
Co-Chairs of the Friends of Paris Brain Institute Committee

Invest intelligently in the future against nervous system diseases.

75% of your donation is deductible from solidarity tax on wealth.
66% of your donation is deductible from income tax.

More details on +33 (O)1 57 27 40 32 or cercle@icm-institute.org

Yes, I want to help the researchers at Paris Brain Institute make progress in research against diseases of the brain and spinal cord.

I’d like to donate: ................................................ €

☐ Mrs ☐ Mr ☐ Mr and Mrs

First name:

Last name:

Address

Postcode:City:

Email: ____________________________ @ ________________

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

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