Feature

The Paris Brain Institute confronts pediatric brain diseases

Portrait
Alexandra Durr:
“To understand the origin of diseases and treat them before they appear”

Research
The Cohort project Covid - Neurosciences

Generosity
Sponsor the brains behind our Institute
The voice of neurons carries on!

The first two issues in our series of podcasts Braincast, in partnership with the monthly magazine Cerveau & Psycho is now online. Listen to Prof. Yves Agid, renowned neurologist and founding member of the Institute, who explains how the brain creates our thoughts, desires and emotions, and then Prof. Laurent Cohen who recounts three extraordinary facts about the brain.

Check it out at www.cerveauetpsycho.fr/fr/braincast

The next podcast will be produced with Prof. Lionel Naccache, team leader at the Paris Brain Institute and consciousness specialist.

Covid-19: a digital interface-based research project to measure and assist in mental health issues

To better understand the effects of confinement on physical and psychological well-being, incubated at the Institute, the start-up Ad Scientiam with the support of AP-HP and Sorbonne University has designed the platform VieCovid2020. This platform enables real-time self-assessment, but also to recreate a link between patient and caregiver, to ensure monitoring, and, if necessary, to give doctors the opportunity to assist people in difficulty. VieCovid2020 is available free of charge on the Apple and Android download platforms.

COVID 19: The Paris Brain Institute is mobilized

In the exceptional health context of the Covid-19 pandemic, doctors and all health care personnel have been working together from day one to fight the coronavirus. The Paris Brain Institute also took part in the nationwide effort to fight this pandemic through mobilization actions: the donation of 4 pallets of equipment (gloves, masks, gowns...) to the AP-HP, the manufacture of hand sanitizer gel, the provision of large equipment to help the Pitié-Salpêtrière hospital cope with the influx of patients and institute staff have volunteered for local initiatives.

A Covid-19 real-time diagnostic test laboratory has also been set up, in addition to a study - initiated by the medical-university neuroscience department of the Pitié-Salpêtrière hospital - involving 2 000 to 10 000 patients, to improve understanding of the possible neurological and psychiatric consequences of the infection. Finally, the Institute's LivingLab and Fablab were involved in the design and manufacture of essential tools validated by the caregivers. An essential mobilization.

Parkinson’s: the dual support of the IRCEM

Created by IRCEM, the French Institute for social protection of employees in the home employment sector, the IRCEM Foundation has decided to support two of our projects dealing with this debilitating and progressive pathology: the development of digital and interactive innovations by the Living Lab and a thesis by the Brain e-Novation laboratory on the effects of motor rehabilitation through video games. Since 2014, the IRCEM Foundation strives to support patients suffering from Parkinson's disease and their caregivers.

https://www.ircem.eu


13 RESEARCH TEAMS OUT OF 25 ARE CO-DIRECTED BY DOCTORS

In your bookshops

When the Institute’s neurologists and researchers take up the pen, the result is captivating. In his latest work, “Le Parfum du rouge et la couleur du Z”, Prof. Laurent Cohen presents twenty surprising encounters with patients, revealing the complex mechanics of our brain. Another literary release, “Penser droit”, by Paolino Bartolomeo, will immerse you in the mysteries of the right brain thanks to the contribution of neurosciences. A must read!

The figures

Jean Glavany

Founding member of the Paris Brain Institute

Our world is currently undergoing a considerable upheaval. Doctors, researchers and health care workers throughout the world are mobilized in the combat against Covid-19. The Paris Brain Institute, located in the heart of the Pitié-Salpêtrière Hospital, which receives many Coronavirus patients, is actively involved both in screening, one of our laboratories has been mobilized to process tests, and in research, because we are involved in a major study on the neurological and psychiatric impact of Covid-19, and even in care, several of the Institute’s nursing staff have volunteered to support the hospital’s teams.

This pandemic reminds us how important it is to invest in our health through advanced scientific and medical research.

Nervous system disorders affect all of us and can occur at any age. While Alzheimer’s and Parkinson’s diseases affect the elderly, many brain conditions such as epilepsy and dystonia develop at an early age. You can imagine the difficulties encountered by these young people, but also the anguish felt by their parents or grandparents at seeing them affected in this way. Research at the Paris Brain Institute tackles these pathologies with multidisciplinary approaches which are its strength.

I hope that this issue will teach you a little more about the outstanding work of the Paris Brain Institute’s researchers in the fight against pediatric brain diseases, and that you will carry on supporting them so that they can continue to find solutions to better diagnose and treat these diseases.
Understand the origin of diseases and treat them before they appear

Alexandra Durr, University professor, consultant neurogeneticist and co-leader of a research team at the Paris Brain Institute, has been caring for patients with rare neurological diseases for more than twenty years. She is driven by the hope that one day these diseases can be treated before they appear.

**Professor, as a geneticist, can you explain why you research the genes that cause disease?**

“Once the causative gene and/or mutation has been identified, the family can access genetic testing and specialist counselling to find out how the disease is transmitted within their family. Twenty-eight years ago, with Josué Feingold and Marcela Gargiulo, we set up a clinic at the Pitié-Salpêtrière Hospital for people at risk of developing a disease that they are familiar with. Their parents or grandparents have been affected, and they know that one day they may develop it too. When the genetic variation responsible for the disease is detected, a choice becomes available: to know or not before the disease begins.”

**This is a persistent question, what is the point of knowing the genetic cause of a disease if there is no treatment?**

“It is not entirely true to say that no treatment exists. The referral centre treats patients, and even if the cause of their disease is not always known, some symptoms are treatable, such as spasticity, a muscular stiffness observed in various diseases. Participating in clinical research studies is crucial in understanding the individual pathways of the disease to enable therapeutic trials adapted to rare diseases.”

**What are your hopes for the future?**

“I hope to treat these diseases before irreversible damage occurs. Current research has never been more dynamic. Clinical trials based on antisense oligonucleotides - short segments of genetic material that block not the mutated gene itself but its RNA, the messenger that enables synthesis of the toxic protein causing diseases such as Huntington’s disease or certain ataxias. They offer high hopes to patients.”

Alexandra Durr, University Professor - Consultant neurogeneticist at Pitié-Salpêtrière Hospital, AP-HP Sorbonne University and co-head of a research team at the Paris Brain Institute

Pediatric brain diseases

The Paris Brain Institute confronts neurological and psychiatric pathologies that appear in childhood and adolescence.

1 out of 120 young people under the age of 20 are affected by a neurological or psychiatric disorder that can disrupt their daily lives.

For example, did you know that:

- Over 300 000 young people under the age of 20 suffer from epilepsy
- Over 800 000 from obsessive compulsive disorders
- Over 170 000 from depressive syndromes
Neurological diseases that begin in childhood or adolescence range from epilepsy to movement disorders such as dystonia, to neuropsychiatric and neurodevelopmental disorders such as Tourette syndrome. The onset of the first symptoms - often impressive - in children, is a source of concern for the family and raises questions about development and therapeutic management.

Eighty percent of pediatric neurological diseases have a genetic origin. Diagnosis is a critical factor in disease management, but presents a major challenge for physicians due to the heterogeneity in symptoms observed from one patient to another.

At the Paris Brain Institute, 14 research teams are committed to discovering the causes of these pathologies, to identifying biomarkers to aid diagnosis and develop treatments. The identification of genes, specific neural networks, brain imaging studies or the identification of early pathology markers are all promising results for the development of therapies.

Therapeutic avenues resulting from this research are already being explored, such as deep brain stimulation in Tourette syndrome, for example.

Once the diagnosis has been established, appropriate care is implemented, considering not only the specificities of the child’s disease, but also their development, their schooling, correct treatment monitoring and the child’s perception of their illness. A whole team of experts, doctors, psychologists, physiotherapists, occupational therapists and speech therapists are assembled.

Diagnosis: a major challenge to act as quickly as possible

When we talk about "diseases of the brain", the most frequently mentioned are Parkinson’s and Alzheimer’s disease. Yet, among the diseases studied at the Paris Brain Institute, the onset of eleven occurs mainly during childhood or adolescence.

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Breaking new ground in pediatric brain disease research at the Paris Brain Institute

**EPILEPSY**

In France, 600,000 people are affected by this chronic neurological disease, which can take different forms depending on its origin. The onset for approximately 50% of epilepsies is before the age of 10.

S. Charpier / V. Navarro and M. Chavez’s team study the electrical activity of neurons during epileptic seizures. These researchers have demonstrated for the first time, “in real time”, the neuronal mechanisms leading to the interruption of conscious perception during absence seizures occurring in particular in young children and adolescents. S. Baulac and E. Leguern’s team have identified “brain-specific” mosaic mutations in focal epilepsy associated with brain malformations, paving the way for new therapeutic approaches.

**TOURETTE SYNDROME**

Tourette syndrome is a highly heterogeneous neuropsychiatric and neurodevelopmental disorder characterised by tics and sudden and repetitive involuntary movements. The latter appear during childhood, at around 6-7 years of age, and are almost always associated with psychiatric symptoms.

Cyril Atkinson-Clément and Yulia Worbe in M. Vidailhet and S. Lehéricy’s team, at the Paris brain Institute, have recently demonstrated that the control of motor impulsivity, the ability to inhibit a movement or action that has already started, **is not correlated with tics** in patients with Tourette syndrome. Marie-Laure Welter, Carine Karachi and Luc Mallet also reported the positive effect of deep brain stimulation in this syndrome, with an improvement in symptoms one year after implantation.

**SPINOCEREBELLAR ATAXIA and SPASTIC PARAPLEGIA**

Ataxia and spastic paraplegia are at two ends of a range of neurological disorders and include a wide variety of diseases.

A. Durr and G. Stevanin’s team identifies the causative genes responsible for these pathologies and the factors modifying the age of disease onset but also its severity, thanks to a unique network SPATAX. This work aims to open up new diagnostic and therapeutic pathways.

**LEUKODYSTROPHIES**

Leukodystrophies are a group of genetic diseases affecting the white matter in the brain. The latter essentially consists of neuronal axons surrounded by myelin, essential for the transmission of nerve signals.

Nathalie Cartier’s team is working on developing gene therapies to fight this pathology, and B. Nait Oumesmar and V. Zujovic’s team is using induced pluripotent stem cells to develop remyelinating therapies.

**DYSTONIA**

Dystonia is a neurological disease that affects about 20,000 people in France. People with dystonia suffer from involuntary muscle contractions, such as spasmodic torticollis or writer’s cramp.

M. Vidailhet and S. Lehéricy’s team researches the restoration of motor control in these pathologies and participates in various clinical trials on new drug and deep brain stimulation therapies.

**ANXIETY DISORDERS**

Obsessive Compulsive Disorder (OCD) affects more than 800,000 children, adolescents and young adults and manifests itself as obsessions in the form of thoughts and images with unpleasant content that are involuntarily imposed on the subject. These obsessions generate anxiety and require the latter to perform repetitive actions and rituals to deal with these distressing thoughts. These “rituals” are exhausting, time-consuming and only provide relative and temporary relief, seriously hampering “normal” schooling.

Eric Burguière’s team is researching how the dysfunction of a neural circuit, the “cortico-basal ganglia circuit”, can lead to the automatization of motivated behaviour, with the aim of developing new therapeutic strategies.

To learn more about the other pediatric brain diseases studied at the Paris Brain Institute, please visit our website at www.institutducerveau-icm.org.

**RARE DISEASES**

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**TRISOMY 21**

**LET’S TALK ABOUT ALZHEIMER’S DISEASE**

Email us your question or experience on the special feature theme in our next issue on the subject of Alzheimer’s disease, and you may be published in the August issue of Synapse.

contact@icm-institute.org
The emergence of behavioural individuality

Could the keys to our individuality lie in the variability of our brain? Bassem Hassan’s team have identified a random mechanism of neural circuit formation in the fly’s brain that may represent a general principle of how certain aspects of individuality emerge in the brain.

The idea that brain circuits regulate behaviour is a pretty straightforward notion. What is less evident, however, is that if a circuit is different between individuals, then it might influence their behaviour individually. This could explain some of the behavioural individuality present in the population. But how can this idea be demonstrated in an experimental setting?

Bassem Hassan (Inserm/Paris Brain Institute) and his team had previously identified stochastic anatomical and developmental variability in a circuit of the visual system called Dorsal Cluster Neurons (DCN). In each brain, the DCN circuit develops slightly differently. Once development is complete, this pattern is stable throughout the life of the fly. But is the fly’s behaviour as stable and unique as this circuit? The team showed that the behaviour, like each circuit, remained constant in a given fly but differed between flies and that it was more the result of the unique development of each brain than the genetics of each individual. Furthermore, they established that the way the circuit develops causally underlies to a certain significant extent, the way the animal behaves.

The idea that there is something innate in certain aspects of what we would call personality in human psychology, and that it originates in the brain, is a very old idea. For the first time, we can identify a clearly defined brain origin for a parameter of an animal’s personality.

The fact that it is due to development mechanisms that cannot be predicted either by the environment or by the genome alone, but by a random phenomenon during development, is fascinating,” Bassem Hassan concludes.

For the first time ever, we can pinpoint to a clear distinctive brain-based origin for a parameter of what we could call an animal’s personality.”

In the context of the current exceptional health crisis, the Paris Brain Institute is launching a large-scale study to improve our understanding of the possible neurological and psychiatric consequences of the Covid-19 infection. Prof. Jean-Yves Delattre, coordinator of this project with Prof. Jean-Christophe Corvol and Dr. Cécile Delorme, tells us more.

The Covid-Neuroscience Cohort Project

How did the idea for this study come about?

We very quickly suspected that the nervous system could be affected, either directly or indirectly during a Covid-19 infection. Some patients lose their sense of taste or smell, but more severe neurological complications such as encephalitis can occur. We are fortunate at the Pitié-Salpêtrière Hospital to benefit from the expertise of both the Paris Brain Institute and the (DMU) University Medical Department of Neurosciences, which treats a considerable number of patients suffering from neurological or psychiatric illnesses.

What methodology will be implemented for this study?

The methodology consists of developing a database that will be updated every time we see a patient with a neurological disorder, i.e. between 2 000 and 10 000 patients if the pandemic continues in its current dynamics. The entire community will be involved in the project: all of the DMU’s medical and healthcare teams, clinical research professionals, as well as the Paris Brain Institute Centre for Neuroinformatics and basic research teams.

What are the main objectives of the study?

At the end of one year’s work, from April 2020 to April 2021, our goal will be to identify all early and delayed neurological and psychiatric complications of the Covid-19 infection. Obviously, we must draw conclusions that can benefit the patient in real time. A second objective is to provide our researchers with the necessary equipment so that they can improve their knowledge of these neurological and psychiatric complications.

What are the medium- and long term prospects for this research?

The results of this study will help us to be prepared for a pandemic that is bound to occur again in the medium term. We can also consider that this infection in brains already damaged, by a neurodegenerative disease for example, could have as yet unknown effects. It is important to know whether we are going to observe very abnormal long-term developments, for example in patients being treated for Alzheimer’s disease or multiple sclerosis.

Going the extra mile to support Charcot’s disease

Running, walking or jogging in a relaxed atmosphere was the slogan of this sporting event organised by the association Un pied devant l’autre* last November 23rd and 24th, in aid of the Paris Brain Institute, for the second year in a row.

Despite the cold and gloomy weather, more than 1 000 motivated participants gathered in Baguer-Morvan (Brittany, France) during the weekend in November for a common cause: to help people suffering from Charcot’s disease, or amyotrophic lateral sclerosis (ALS) - a progressive and fatal neuromuscular disorder characterised by a loss of motor neurons, neurons that control, among other things walking, talking, swallowing and breathing. On this two-day agenda, a 14 km hike by a team of 4 followed by a dinner dance in the evening; then, the next day, a walk (4 or 7 km) and a run (10 or 14 km).

Last year, the organising team raised €10 000 for the Institute. Last year, the organising team raised €13 000 was raised and once again donated to the research team, ALS causes and mechanisms of motor neuron degeneration, headed by Sérénine Boïlle at the Paris Brain Institute.

The next sports weekend has already been planned (21 and 22 November), with a new feature: a corporate challenge. The date is set!

The Paris Brain Institute extends its warmest thanks to the association Un pied devant l’autre for its loyal support.

Choosing to support the Paris Brain Institute is a meaningful choice. After a first negative experience in this field, we felt that we could have confidence in Professor Gérard Saillant and this state-of-the-art structure with its numerous research teams.”

Martine Aubry, President of the association Un pied devant l’autre

About 800 people in France die from Charcot’s disease every year. The next 42 teams of 4 people doing this major challenge will have to work hard and mobilise its 150 volunteers to raise €23 000.

*Un pied devant l’autre is an association founded in 2018. Its objective is to raise awareness, inform and collect donations to help people with Charcot’s disease (ALS).

Contact: Martine Aubry, President of the association - martine.aubry35@orange.fr
The multi-annual letter of commitment: provides the time and resources to conduct research

First of all, simplicity. Easier to implement than an agreement, the multi-annual commitment letter allows you to choose the annual amount of your contribution, the duration (between 3 and 5 years) as well as the due date of the payment so that the latter is in line with your habits, notably fiscal (year-end or IWI wealth tax period). It also allows you to express your wish to have your generosity allocated to all of the Paris Brain Institute’s missions or to a particular pathology or team.

... and because the researchers, know in advance what resources they have at their disposal, they can plan for the long term, without worrying about a hold up in their projects. They also have access to more research resources thanks to the savings made on collection fees.

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A means of support with many advantages for you...

And it is also a tangible expression of the donation, as attested by Jacques Garaïalde, a member of the Cercle des Amis, who has twice made a 3-year commitment in 2014 and 2016 to support research in neuroinformatics and microscopy.

“Once a year, I meet with the researchers who receive my donations. This is particularly rewarding and necessary. Not only because you can see the results of the research in tangible terms, but also because by interacting and contributing my own thoughts, I feel more involved. The scientific teams are welcoming, motivated, and efficient. Although I live in London, I choose to donate in France with the assurance of having a global impact. Signing a multi-annual commitment is common sense: the Paris Brain Institute cannot begin with a clean slate every year. I am providing it with a form of essential budgetary sustainability.”

Yes, the Paris Brain Institute is authorized to receive property (apartment, house, commercial premises, building, land…). At the succession, our legal department shall proceed with the sale of the property with the help of trusted professionals (property agencies, notary property department…). The proceeds from the sale help finance the Institute’s research programs of excellence, contributing directly to the discoveries and advances of our researchers for the benefit of the millions of patients affected by neurological diseases.

Reminder: the donation is made by drawing up a will that can be modified at any time.

YOUR PERSONAL CONTACT
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“Mme Carole Clément, in charge of donor relations, bequests and life insurance at the Paris Brain Institute

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The «Cercle» Breakfasts hosted at Publicis’ headquarters.

°F.A.Q.

Do I still own my apartment even if I leave it to the Institute?

Yes, of course, you still own all the property you plan to donate, the will only becomes effective on your demise.

As a company executive, I would like to donate to the institute on behalf of my company. Is this possible?

Absolutely. With or without an agreement, your donation can be received by the Institute and allows you to enjoy a fiscal advantage in terms of Corporation tax up to 60% of its amount and at your choice, within the limit of €20 000 or 0.5% of the Turnover. It should be noted that within the framework of the health crisis, the Government has adjusted the tax due dates in May: payment of the tax balance is postponed to June 20, 2020. The Cercle des Amis Office can be reached at +33(0) 1 57 27 40 32 or via cercle@parisbraininstitute-icm.org.

As a donor member of The Cercle des Amis, can I visit the Institute with a friend who doesn’t yet know the institute but who may be interested in getting to know it?

Of course you can. The Paris Brain Institute regularly organizes private tours for individuals or small groups (max. 8 people) for its major donors. These tours last about one hour and can also be themed according to your wishes and interests, e.g. for a specific disease. Simply contact the Cercle des Amis office at +33(0) 1 57 27 40 32 or via cercle@parisbraininstitute-icm.org.

I look forward to the Cercle des Amis breakfasts that take place three times a year at Publicis, I learn a great deal about life at the Institute and can confirm that my donations are being put to good use. Above all, the guest researchers have the art of making their work, however complex, easily understood. It is fascinating. For example, during the last breakfast on brain tumours, Professor Jean-Yves Delattre explained how the Institute had set up a “therapeutic motorway” to enable a more efficient selection of the most promising drugs to be offered to patients in clinical trials. I came out of it even more motivated to fight alongside him against diseases of the nervous system!”

Philippe C., major donor and member of the Paris Brain Institute Cercle des Amis

“In this unprecedented health context, we cannot schedule the next Cercle’s breakfasts, however, we will be pleased to welcome you again as soon as possible.”
I would like to receive free information on bequests and donations.

Please make your cheque payable to the Institut du Cerveau and send it with this form to the Institut du Cerveau - Hôpital Pitié-Salpêtrière - 47, boulevard de l'Hôpital - 75646 Paris Cedex 13 - France

I am sending a donation of: €

(name and contact information)

The Paris Brain Institute Foundation adheres to the rules of ethics of the Comité de la Charte du don en Confiance (Committee for the protection of donors).