Special report

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Generosity

Support the Institute beyond our borders

Portrait

Lars Jørgensen and Stanley Durrleman

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The ambition of Paris Brain Institute, since its creation, has been to bring together researchers with diverse expertise - biologists, clinicians, mathematicians, patients and entrepreneurs, with one goal in mind: understanding the brain and treating the diseases that affect it. The Institute’s model responds to one of the challenges of research: provide the men and women working daily to help nearly one billion patients with the means to achieve it.

As you will discover in the special report of this issue, at the Institute, we are taking action at all stages and at all levels of research to treat brain diseases, such as Parkinson’s. From the most fundamental research all the way to clinical trials, from molecules to complex cognitive functions. We also work on the development of solutions to meet the immediate needs of patients thanks to our Care Lab.

Our ecosystem holds hope for research on the brain and nervous system diseases, and it cannot exist without you. Thank you for your continued support.

More information in the “News” section of our website.

First LIVE conference on depression during Covid

On Tuesday, 20 April 2021, the first live conference of the Circle of Friends of Paris Brain Institute took place on the theme “Depression: What are the repercussions of the pandemic, new therapies and hopes?”, followed by an exclusive discussion with Professors Philippe Fossati and Alexis Brice, and in the presence of Professor Gérard Saillant, Martine Assouline and Maurice Lévy, co-chairs of the Campaign Committee. Watch the replay of this conference at: https://institutucerveau-icm.org/fr/open-brain-school/summer-school-2020/ (in French)


To keep in touch with you and continue to inform you about current research, Paris Brain Institute regularly posts videos on its YouTube channel. The programme consists of all of our donor conferences for which you can ask your questions in advance, but also interviews with our researchers. You can watch the workshops filmed during the Brain Week, which took place from 15 to 22 March simultaneously in a hundred countries and more than 120 cities in France to raise awareness of the importance of brain research: neurons and electricity, digital therapies for neurological pathologies, etc. Hours of quality content in English and in French to be found at: https://www.youtube.com/user/BrainSpineInstitute

CARE LAB
The Healthtech Living Lab
Participatory innovation

At the heart of Paris Brain Institute, the collaborative Care Lab platform (formerly the Living Lab) closely involves players in the care chain (researchers, medical and paramedical staff, patients, etc.) in order to devise and develop innovative medical devices that improve patient care and allow them to remain autonomous. As such, a hackathon, a real accelerator of solutions, is organised each year with international students at the end of their studies. More information at: https://institutucerveau-icm.org/fr/open-brain-school/summer-school-2020/ (in French)

SUNDAY, 20 JUNE

The Heroes’ Course (Parisian edition) at the Saint-Cloud estate. Find all the information to participate at https://www.coursedesheros.com/

MONDAY, 21 JUNE

World Day in the fight against ALS (Amyotrophic Lateral Sclerosis) or Charcot disease. Visit our website to discover the progress of the research carried out at the Institute.

SATURDAY, 26 JUNE

Online donor conference on the genetic transmission of neurological diseases (a link to the video will be emailed to you and will also be available on our website).

Innovative patient support systems developed at the Care Lab and in progress

Secrets of the creative brain

For this new series of podcasts in partnership with the magazine Cerveau & Psycho, discover creativity with Dr Emmanuelle Volle, neurologist and researcher in cognitive neuroscience at Paris Brain Institute. Tune into the exciting exchange at: https://www.cerveauetpsycho.fr/sr/braincast/ (in French)

Nurturing scientific vocations!

The 3rd edition of the International Brain Bee (IBB), an international neuroscience competition for middle and upper school pupils took place online on 20 March. The mission of the IBB is to help pupils become familiar with the brain and its functions, and to teach them about careers in neuroscience. Congratulations to the French winner of this edition, Alexis Vitalis, from Lycée Albert Londres, who will participate in the International Brain Bee competition next September. Find out more: https://openbrainschool.com/en/france-brain-bee-2021-won-by-alexis-vitalis/ (in English)

Paris Brain Institute: 100% digital

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Support.

These difficult times remind us every day of the importance of scientific and medical research. Vaccines, developed in record time, give us a glimpse of light at the end of the tunnel and hope for a return to more normal life soon. Their development shows us the incredible determination and perseverance of researchers when they join forces towards a common goal and are financially supported to achieve it.

In the news

More information in the “News” section of our website.

- Parkinson’s disease: Empowering patients during their deep brain stimulation treatment
- Obesity and the response to food marketing
- New diagnostic tool for post-stroke motor neglect

Videos

- Multiple sclerosis online donor conference of 20 March 2021
- The voice of neurons, a podcast in partnership with the magazine Cerveau & Psycho, with Dr Emmanuelle Volle, neurologist and researcher in cognitive neuroscience at Paris Brain Institute (in French)

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INNOVATIVE PATIENT SUPPORT SYSTEMS DEVELOPED AT THE CARE LAB

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IN PROGRESS

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CITIVE INNOVATION

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Analyzing research results: a major challenge in neuroscience

What is data analysis and is there a specific approach in the field of neuroscience?

L. J. We have a large amount of data from research projects and we need to extract information by analyzing them. To do so, we must combine computer engineering, statistics, and scientific and medical research.

S. D. As research at the Institute focuses on neurosciences, the knowledge and data sets have certain specificities. The brain is a very complex organ, which is difficult to study. The data we generate include genomics, electrophysiology, imaging and behaviour. This heterogeneity complicates an analysis integrating, for example, a genetic mutation, the dysfunction of a region of the brain and a particular behaviour. This is one of the main challenges that we have to overcome with this platform.

Lars, you recently joined the Institute. What are your background and your expertise?

L. J. I studied computer science at university. Before joining the Institute, I worked in different places: Denmark, the United Kingdom and Canada. I specialised in bioinformatics to provide support to researchers who process large quantities of heterogeneous data.

What are the platform’s goals and how do they fit into the Institute’s overall strategy?

L. J. The platform is already very efficient and the main objective is to broaden support for researchers and clinicians, and deal with the variety of data available. To do so, we must answer more complex questions requiring integrative analysis combining the results of many different types of research projects.

S. D. We must adapt and develop analytical tools responding to the questions raised by the translational and transdisciplinary research strategy carried out at the Institute.

The Institute invested in the neuroinformatics centre to increase the capacities of data storage and management servers, harmonise procedures and train researchers in the latest data analysis techniques. Lars joined the Institute to develop the analytical activity so that it meets the needs of all scientists.

The platform must be the hub where all forms of expertise can communicate and share tools, methods and knowledge. This strategy is accompanied by the creation of a new research domain dedicated to computational modeling, i.e. to the analysis of data resulting from research combining biology, computer science and statistics. More information on page 11.
Gain understanding of biological mechanisms to better target treatments

Parkinson’s disease is the second most common neurodegenerative disease after Alzheimer’s disease. It currently affects 6.2 million people in worldwide and the number of cases is estimated to rise with the ageing of the population.

Age is an important risk factor, with a prevalence of 0.04% in persons between 40 and 49 years old and increasing to 2% in those over 80 years old.

Parkinson’s disease is said to be multifactorial: the risk of developing the disease is slightly increased by genetic predisposing factors and environmental factors as yet unknown. Only 5% of cases are hereditary and carry a known mutation.

Men are more affected than women, with a ratio of 2 men to 1 woman over 40 years old.

Parkinson’s disease is characterised by degeneration of dopaminergic neurons in the substantia nigra of the brain, the upper part of the brainstem.

The best-known signs are tremors at rest, but the disease appears when 50% of dopaminergic neurons are impaired. 

α-synuclein aggregates, which also accumulate outside the substantia nigra, explain the heterogeneity of non-motor symptoms seen in patients. These symptoms are difficult to treat today, but the recent discovery of the key role of α-synuclein opens new therapeutic avenues.

Molecular and cellular research at Paris Brain Institute

The main molecular player in Parkinson’s disease is α-synuclein.

As the disease progresses, this protein aggregates in the cell body of dopaminergic neurons located mainly in the substantia nigra. The death of neurons linked to α-synuclein aggregates leads to a deficit in the production of dopamine, a neurotransmitter allowing communication between neurons, and leads to a loss of nerve transmission in the cerebral circuits controlling movements resulting in the appearance of motor symptoms.

One estimates that the first symptoms of Parkinson’s disease appear when 50% of dopaminergic neurons are impaired.

The “Molecular pathophysiology of Parkinson’s disease” team seeks to identify mutated genes in familial cases of Parkinson’s disease and to understand the cellular dysfunctions induced by these mutations.

This team is particularly interested in the dysfunction of mitochondria, whose role is to supply energy to neurons and ensure their survival.

In certain forms of Parkinson’s disease, the death of dopaminergic neurons is caused by toxins that target the mitochondria or by the mutation of genes, such as parkin, whose function is to preserve mitochondrial quality. The proper functioning and survival of neurons involve, among other things, the degradation and replacement of defective mitochondria.

The “Experimental therapeutics of Parkinson’s disease” team seeks to identify the role of α-synuclein aggregates in cerebral inflammation observed in areas of degeneration of dopaminergic neurons and suspected of being toxic.

The molecular and cellular studies of both research teams carried out in close collaboration with the other research teams of the Institute, and in particular with doctors, aim to identify and characterise molecules or cell types that can be used as biomarkers and therapeutic targets to protect dopaminergic neurons and reduce or even stop the disabling symptoms of the disease.

This work is carried out with the support of experts from the Institute’s sequencing, culture and cell imaging platforms.

At Paris Brain Institute, two teams, including one co-directed by a neurologist, are studying the biological mechanisms of Parkinson’s disease.

PROGRESSION OF PARKINSON’S DISEASE

At Paris Brain Institute, two teams, including one co-directed by a neurologist, are studying the biological mechanisms of Parkinson’s disease.

Prof. Catherine Lubetzki
Medical director of Paris Brain Institute and neurologist, team leader, director of the Pitié-Salpêtrière Department of the Neuroscience Medical-University Hospital.

“Both clinical and fundamental research are by essence research! In both cases, an issue is raised and the methodology must be strict in order to achieve interpretable results.

Paris Brain Institute strives to enable clinicians and researchers to collaborate.”
Currently, 16 therapeutic trials and 29 pathophysiological trials, i.e. relating to the clinical and biological symptoms of the disease, are coordinated by clinician-researchers at Paris Brain Institute. They are underway at the Clinical Investigation Centre located in the building. Examples include:

Researchers, clinicians, engineers and entrepreneurs at Paris Brain Institute work daily to:

- Identify clinical signs or biological markers to predict the onset or severe progression of the disease

The ICEBERG study, conducted by the “Mov’It: Movement, Investigations, Therapeutics” team. Normal and abnormal movement: physiopathology and experimental therapy”, showed that the cognitive symptoms of Parkinson’s disease, such as paradoxical sleep disorders or abnormal eye movements, begin early and start before motor symptoms. This study also identified a progression marker for the loss of dopaminergic neurons characteristic of Parkinson’s disease; on the right: patient with a lengthy disease progression (MRI in the substantia nigra. On the left: a healthy individual).

The best-known side effects of treatments based on L-Dopa or dopamine agonists are impulsive-compulsive disorders expressed by addiction to games, shopping, eating disorders, hypersexuality or risky behaviour. A study coordinated by Professor Jean-Christophe Corvol, director of the Clinical Investigation Centre and team leader at Paris Brain Institute, carried out on 400 patients, showed that the appearance of behavioural disorders increased with the duration of Parkinson’s disease. Among the patients without tremors at the start of the study, nearly 50% developed them within five years of follow-up. These findings indicate that regular follow-up of patients on Parkinson’s disease therapy is essential and should be monitored regularly.

**SYMPTOMS OF PARKINSON’S DISEASE**

- **APATHY**
  - disturbances in REM sleep, memory, object recognition, depressive syndrome

- **ASYMMETRIC REGULAR TREMORS AT REST**
  - mainly affect the upper limbs, disappearing during voluntary movements and while sleeping

- **HYPOKINESIA**
  - slowness of movement, “freezing”, difficulty in initiating walking

- **MUSCLE STIFFNESS**
  - reduced facial expression, eye disturbances, monotonous speech

**To study and understand is to heal. Research and care are inseparable and fully integrated.**

**Study the disease symptoms to better predict its progression, and provide relief and treatment**

**C**urrently, 16 therapeutic trials and 29 pathophysiological trials, i.e. relating to the clinical and biological symptoms of the disease, are coordinated by clinician-researchers at Paris Brain Institute. They are underway at the Clinical Investigation Centre located in the building. Examples include:

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We observe in patients a decrease in neuro-melanin, which is accentuated over time, due to the degeneration of dopaminergic neurons.

- The ICEBERG study, conducted by the “Mov’It: Movement, Investigations, Therapeutics” team. Normal and abnormal movement: physiopathology and experimental therapy”, showed that the cognitive symptoms of Parkinson’s disease, such as paradoxical sleep disorders or abnormal eye movements, begin early and start before motor symptoms. This study also identified a progression marker for the loss of dopaminergic neurons visible on MRI: neuro-melanin. This protein plays a protective role in neurons by capturing toxic molecules, such as iron, for example.

MRI performed by the CENIR imaging platform of Paris Brain Institute - Quantity of neuro-melanin observed by MRI in the substantia nigra. (On the left: a healthy individual; in the centre: a patient at the onset of Parkinson’s disease; on the right: patient with a lengthy disease progression)
A study conducted by Liane Schmidt (Inserm researcher and team leader at Paris Brain Institute) and Hilke Plassmann (INSEAD’s Octapharma Chair in Decision Neuroscience) established, for the first time, a link between weight loss, nervous system connectivity and the hormonal regulation of satiety.

Obesity is a multifactorial disease, with environmental, hormonal, psychological and physiological dimensions. One dimension remains little explored: neurobiological bases and to what extent these can predict variations in weight.

Liane Schmidt, Hilke Plassmann and their collaborators, in particular from the Nutrition Department of the Pitié-Salpêtrière Hospital (AP-HP/Sorbonne University), conducted a study in 44 participants, 14 with obesity before and after bariatric surgery (digestive system surgery to restrict food absorption), and 30 age-matched controls, also examined twice over the same period.

They demonstrated that two connectivity networks of the reward and cognitive regulation system vary between obesity and non-obese subjects: firstly between the ventromedial prefrontal cortex and the ventral striatum and secondly between the ventromedial and dorsolateral prefrontal cortex. However, only the connectivity of the first network was able to predict weight changes in obese participants after bariatric surgery.

After surgery, leptin levels decrease and are better able to signal satiety. The team showed that the resting activity of the brain reward system correlated with the decrease in leptin resistance after bariatric surgery.

The more the activity of the resting reward system varies over time, the greater the weight loss. The activity of this network, therefore, seems to be a good predictive factor. – Liane Schmidt

A fifth research domain, dedicated to computational modelling in neuroscience has just been created to develop computational methods to better understand the complex relationships between the brain’s structure and function.

This new domain gives researchers using modelling an opportunity to share their expertise with three main objectives:

- Mathematical and computational modelling of brain mechanisms on multiple scales, ranging from molecular and cellular processes, and the large-scale integrated structure and its dynamics (e.g. interactions between anatomy and function), cognition and behaviour;

- Development of data exploration methods, including network science, signal and image processing, machine learning and artificial intelligence, for data interpretation and analysis leading to better diagnosis and prognosis of neurological and psychiatric diseases, and personalised treatment;

- Development of scientific software and engineering tools for neuroscience applications.

Until now, Paris Brain Institute’s research has been organised in four domains:

• Cellular and molecular neurobiology, which study genetics, molecular mechanisms and the role of different types of cells to understand complex cellular interactions in the normal or pathological state.

• Integrative neurophysiology, which allows us to understand the principles by which neuron activity induces normal or abnormal behaviour.

• Cognitive neuroscience, which studies the link between brain dysfunction and specific patient behaviour.

• Clinical and translational neurosciences, which study the development of predictive or progression markers and therapeutic solutions for neurological and psychiatric diseases.
The ALBA network, composed of more than 150 international scientific organisations, aims to defend equity and inclusiveness by fighting against implicit prejudices and discriminatory culture.

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“Braincare Plan Lab”: a joint laboratory for epilepsy

In France, epilepsy affects more than 600,000 people. This chronic disease is diagnosed and treated variably throughout the country. Many deaths linked to this disease could be avoided with a better organisation of healthcare. For this reason, Paris Brain Institute and the start-up BioSerenity are joining forces to develop a telediagnostic network for this disease.

The joint laboratory created by the Paris Brain Institute and BioSerenity, “Braincare Plan Lab”, will develop a digital platform for doctors to facilitate the exchange of expertise for better treatment of epileptic patients.

This platform will help practitioners to improve diagnostics on the different forms of epilepsy, but will also facilitate access throughout the country to cutting-edge technological expertise in electrophysiology. It will support health professionals in the management and improvement of treatment plans.

This strategic partnership will also accelerate joint research on “biomarkers” to characterise the different forms of epilepsy, and ultimately to anticipate seizures.

This new knowledge will help to better understand and treat this disabling disease, which continues to suffer from unwarranted stigma and insufficient research budgets.

In this societal and economic context, imprisoned in unconscious prejudices and gender stereotypes, information and training for both women and men are essential to escape these biases.

Neurosciences have shown that 90% of cerebral connections are gradually built based on social influences, family, social structures, culture, etc. Society, therefore, perpetuates among other things such biases.

In this societal and economic context, imprisoned in unconscious prejudices and gender stereotypes, information and training for both women and men are essential to escape these biases.

This is the objective set by the committee for equity between women and men, the “XX Initiative Committee”, an integral part of the governance system of Paris Brain Institute, which has since its creation allowed collective and individual consciousness.

The recommendations of this committee have led to an increase in the number of women on the Institute’s statutory committees, the establishment of “self-confidence” training for female researchers, better promotion of their work and increased attention to equal opportunities for recruitments or promotions.

Hydrocephalus is a severe disease that results in excessive intracranial pressure. The standard treatment is a shunt tube to drain excess cerebrospinal fluid. Adjustment of the drainage flow sometimes leads to numerous additional examinations and hospitalisations: on average, one in three patients requires a reoperation after 18 months.

Neurallys is developing a connected implant that measures intracranial pressure and transmits the information to the surgeon, who remotely assesses the correct functioning of the valve.

This year, Neurallys was ranked in the top 5 most innovative start-ups in neurology globally (StartUs Insights) and is currently starting a new fundraising campaign.
Donate from abroad: support the Institute’s research beyond borders

A sovereign domain par excellence, tax is controlled by each State that defines the tax rules applicable in its territory and the tax reductions granted for philanthropy. What is the impact of the principle of territoriality for donations? What happens when a foreign donor wishes to contribute to the Institute’s missions? Does he/she benefit from French taxcuts or the ones provided for by his/her country of residence?

If you or your company is subject to tax in France, you can benefit from one of the most advantageous tax systems in the world

The French tax system is one of the most generous in the world with the adoption in 2003 of the Aillagon law. The benefit of the tax reduction is open to any donor (individual or company) subject to tax in France, whether it is the solidarity tax on wealth, income tax (BNIC, BIC or BA) or corporate tax.

For example, if your company is liable for corporate tax through one of its subsidiaries. 60% of the amount of its donation to Paris Brain Institute is deductible as philanthropy up to a limit of €20,000 or 0.5% of turnover. Above 2M € of cumulative donations, the deduction is 40%. When the amount of the tax reduction exceeds the annual limit, the unallocated balance can be carried forward to the payment of tax due for the following five years.

If you or your company is not liable for any tax in France, the Transnational Giving Europe (TGE) network can allow you to benefit from the advantages of your country of residence

Since 2009, Paris Brain Institute has developed an agreement with the TGE, which brings together prestigious philanthropic institutions from 21 countries (including Belgium, Luxembourg, Switzerland and the United Kingdom) and provides a secure and fiscally efficient framework. Concretely, it allows donors, individuals or companies to support a non-profit organisation in one of the countries covered by the network while directly benefiting from the tax advantages of their country of residence. To date, it should nevertheless be noted that the TGE is limited to donations from individuals and companies, but does not cover, for example, bequests or donations of immovable assets.

The FCDDV is the French Central File of the Dispositions of Last Wills, also called the file of wills. Notaries register the civil status of persons who submit their wills to them. After their passing, this file is systematically queried to find out whether the deceased had filed a will and with which notary it is located.

For any questions, please contact:

Ms Carole Clément, bequests, donations and life insurance manager at Paris Brain Institute
+33 (O) 1 57 27 41 41
carole.clement@icm-institute.org

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Why Paris Brain Institute?
All generations can suffer from a neurological disease that affects the brain. This noble organ is essential to our life: speech, creativity, reading, vision, smell, touch, feelings, memorisation, etc. Like a conductor, it coordinates and harmonises all moments of our life: it is the centre of our emotions. The brain deserves our full attention. Moreover, we say that when your head is together, your body is healthy. Gaining an understanding of how it works will one day allow us to better anticipate its dysfunctions. For this, we need research and expert doctors, who work day after day for our well-being and that of future generations. For this reason, bequeathing to Paris Brain Institute is the right choice, and also a way of express our gratitude to all the people who are working for us.

Thank you to all of you professors, researchers, doctors, surgeons and neurologists. You are our future!
I am honoured to be by your side on this exciting adventure.

“ I am considering making a bequest to Paris Brain Institute. What is the FCDDV? ”

For more information, the Circle of Friends Office is at your disposal on +33 (O) 1 57 27 40 32 or via cercle@icm-institute.org

If I make a bequest to Paris Brain Institute, will you pay inheritance tax?
No. As a foundation recognised of public utility, Paris Brain Institute is exempt from inheritance tax: 100% of your bequest will go to research, without any State levy.

Madeleine has organised her estate and has decided to make a universal bequest to Paris Brain Institute. She shares with us her testimony and her motivations.

YOUR DEDICATED CONTACT
at the Circle of Friends Office
Ms Marielle Lethrosne
+ 33 (O) 1 57 27 45 72
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 am donating ____________________________ €

☐ Mrs  ☐ Mr  ☐ Mr and Mrs

Last name: ___________________________________________ First name: ___________________________________________

Address: ____________________________________________________________________________________________

Post code: _______________________________________________________________________________________

Email: ___________________________________________@______________________________

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

Paris Brain Institute Foundation adheres to the rules of ethics of the Confidence Donation Charter Committee.

The information collected on this form is recorded in a computerized file under the responsibility of Paris Brain Institute in order to be able to send you your tax receipt, report on the use of your donation, invite you to conferences or events, appeal to your generosity and sometimes for study purposes to get to know you better, collect your opinion and improve our practices. These data, intended for Paris Brain Institute, can be transmitted to third parties that it mandates to print and send your receipts, our fundraising campaigns or studies. You have a right of access, rectification, deletion, opposition, limitation or portability of personal data concerning you, by contacting the Circle of Friends Office at the following address: Bureau du Cercle des Amis de l’Institut du Cerveau - Hôpital Pitié-Salpêtrière - CS 21414 - 75646 Paris Cedex 13 - France.

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