LabEx BRAIN report

2012-2013

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Introduction

General presentation of BRAIN and its objectives

The LabEx **BRAIN** (Bordeaux Region Aquitaine Initiative for Neuroscience) is a program from the "Investissement d'Avenir" (investment for the future) national program that has been selected in 2011 by an international jury from a national competitive call. It runs until 2020 and received a total funding of 20 M€.
The core of BRAIN teams represents a subset (roughly 50 % in people) of the Bordeaux neuroscience community, but, importantly, its programs aim to serve the whole community. The totality of Bordeaux neuroscience community is united within the **Bordeaux Neurocampus** federal organization. Bordeaux Neurocampus and BRAIN work hand in hand to promote neuroscience research in Bordeaux.

Understanding brain function in normal and pathological conditions is a major issue in our modern societies due to societal changes (sleep deprivation, addiction...), the ageing of populations and the associated increase in the prevalence of neurological and psychiatric diseases. It is thus of utmost importance to understand deeper these human cognition, behavior and disorders of the nervous system that impose a large financial burden on our societies.

The general **scientific objective** of BRAIN is to put together a multidisciplinary consortium of scientists, featuring world renowned leaders, in order to meet the most important challenges facing neuroscience research. With this aim, BRAIN is built on the diverse and complementary expertise of its teams and partners, in fields ranging from high resolution imaging and cell biology of the neuron to animal and human behavior through the physiology of neural networks and mechanisms of neuro-degenerative and behavioral disorders.

The **strategic objective** of BRAIN is to make of Bordeaux one of the top research center in Europe in the field of Neuroscience. In this perspective, BRAIN is in large part a functional complement of the already instigated **Neurocampus project** funded by the **Regional Council of Aquitaine** that will include the building of 10 000 m² of new lab space for neuroscience research within the next 3 years. The Neurocampus project, so reinforced by BRAIN, also includes an appealing financial mechanism for attracting up to 10 new world-class group leaders in identified strategic areas that are lacking or underrepresented in Bordeaux.

Centered on teams of excellence, BRAIN aims to help accelerate the development of transversal scientific projects, common core facilities and a Europe-leading training center, which together will enable the greatest number of Neuroscience teams in the Aquitaine region to attain the highest international level of excellence.

BRAIN will allow strengthening Bordeaux teams in terms of:

- Productivity and competitiveness through access to infrastructure and high level core facilities required for the genesis of innovative, multidisciplinary and high-tech projects.
- Attractiveness and visibility through the creation of international training programs and the offer of international doctoral and post-doc fellowships and positions.

Neuroscience research in Bordeaux is organized in 5 main independent research centres and institutes and a few smaller teams (represented in squares in the figure 1) encompassing a total of 600 scientists. Scientists have access to 10 core facilities (in circles), and the Bordeaux School of Neuroscience. All these institutes, teams and facilities are federated in **Bordeaux Neurocampus** (in the orange square).

The BRAIN LabEx project gathers 24 teams of excellent international level (blue dotted line square) that have decided to collaborate to create a coherent and comprehensive scientific project addressing a restricted number of the major transversal challenges in modern neuroscience, with teams ranging from molecular to behavioural and patho-physiological/clinical studies. Selection of the teams participating to the core of BRAIN has been performed following the ranking by the AERES evaluation international committee in 2010 (18 teams from the 2 A+ ranked institutes, IINS and NCM, and the A+ teams of the other research centres SanPsy, INCIA and IMN).

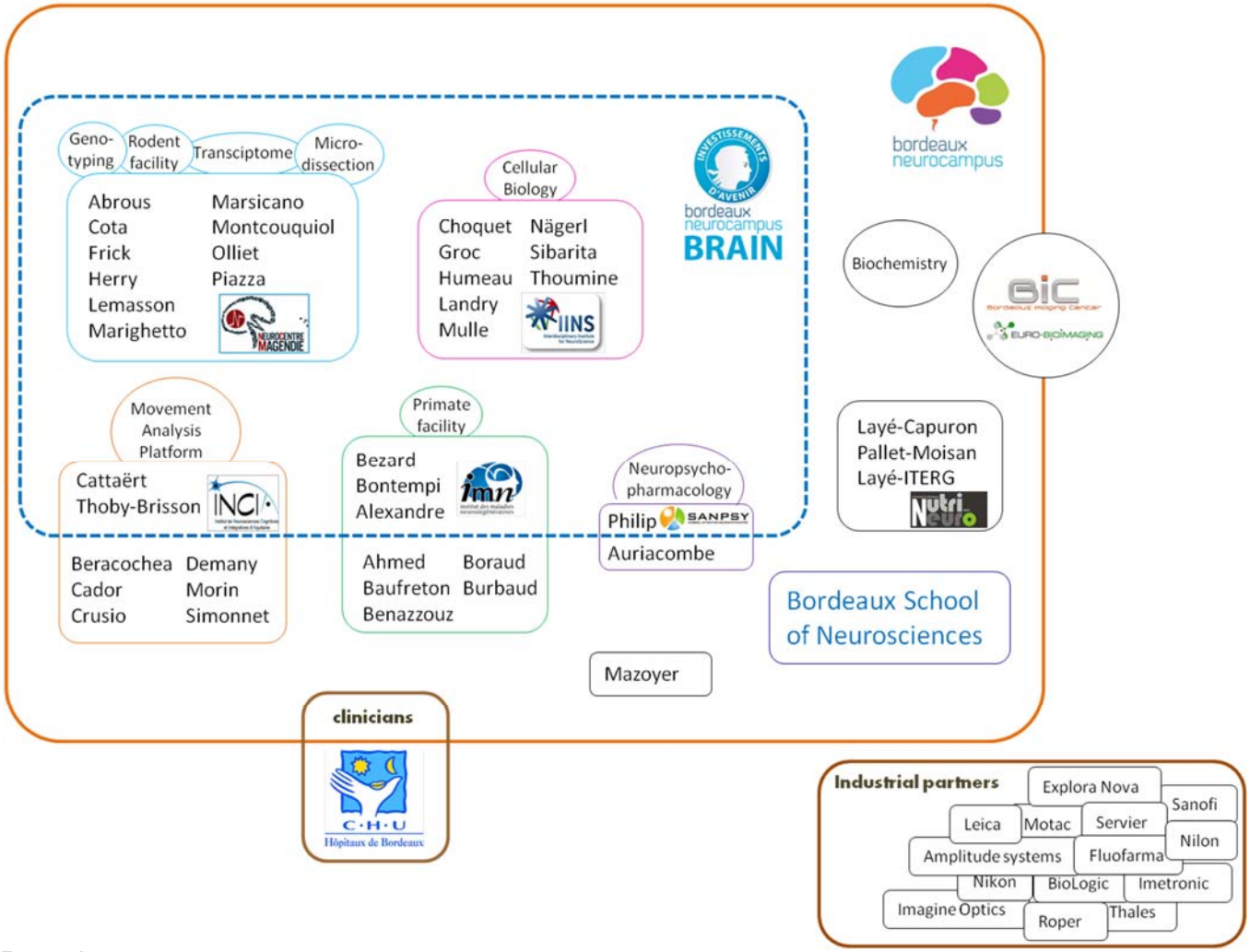


Figure 1

Presentation of the research environment

General relations of BRAIN within the University of Bordeaux

The University of Bordeaux has been successful in the "Investissement d'Avenir" national program with the IdEx (Initiative d'excellence), 5 LabEx (Laboratoires d'excellence), 5 EquipEx (Equipement d'excellence), 1 IhU (Institut Hospitalo-Universitaire), and 1 cohort. The regional transfer agency has also been labelled within the SATT (société d'acceleration et de transfert). Therefore, in the figure 2, the relationships between these programs, particularly the LabEx BRAIN position in this local environment are presented.

We have strong interactions with the 2 EquiEx in neuroscience: Optopath, a rodent platform entirely dedicated to innovation in experimental psychopathology, and Phenovirt, a multiface immersed environment to conduct clinical research. We have interactions with the other LabEx in health, the LabEx TRAIL, dedicated to Medical Imaging, with an important component in neuroscience and the cohort i-share. Some collaborations exist between BRAIN and 2 clusters created at the local level by the IdEx Bordeaux: Laphia (in laser) and CPU (in numerical technology).

For the technological transfer and IP protection, we collaborate with the SATT Aquitaine Science Transfer.

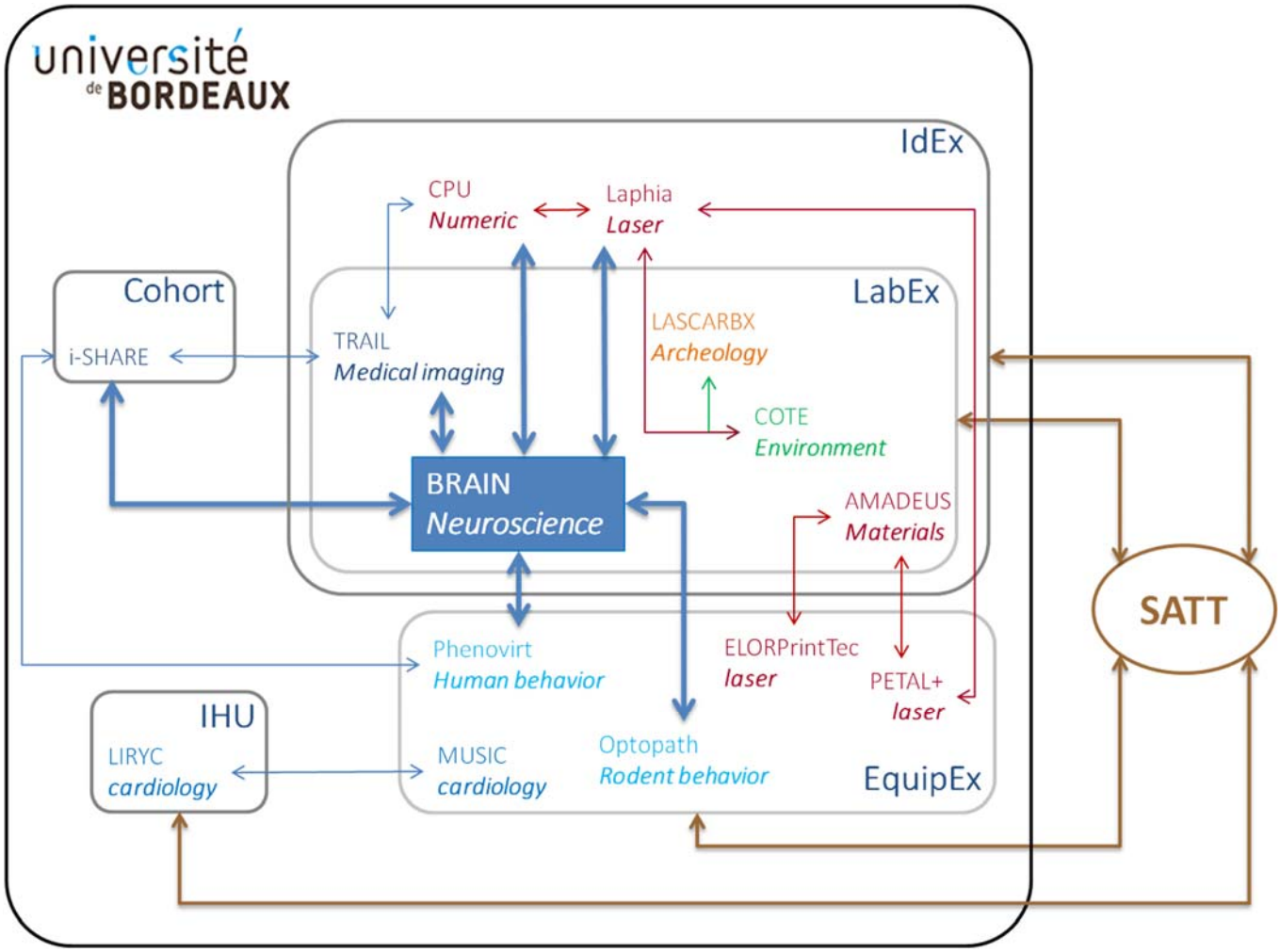


Figure 2

CORE BRAIN LABORATORIES:

The detailed list and description of the teams is in annexe 1

Inserm U862 Research Centre- Pathophysiology of neuronal plasticity (NCM)

Director: Pier Vincenzo Piazza
Date of initiation: January 2007
Main focus: the NCM focuses on integrated study of Neurosciences ranging from neurological and behavioural pathologies to the cellular and molecular mechanisms of neural activity. In particular, the specific aim of the Neurocentre Magendie is the understanding of the pathophysiology of neuronal plasticity.

Members:

- Researcher: 25
- Faculty: 17
- Post-doc: 17
- Student (master +PhD): 26
- ITA: 76

List of the teams involved in the LabEx BRAIN:

- Neurogenesis and pathophysiology, Team leader: Nora Abrous
- Energy balance and obesity, Team leader: Daniela Cota
- Cortical plasticity Team leader: Andreas Frick
- Neuronal circuits of associative learning Team leader: Cyril Herry
- Motor System diseases Team leader: Gwendal Le Masson

- Pathophysiology of declarative memory Team leader: Aline Marighetto
- Endocannabinoids and Neuroadaptation Team leader: Giovanni Marsicano
- Planar polarity and plasticity Team leader: Mireille Montcouquiol and Nathalie Sans
- Glia-neuron interactions Team leader: Stéphane Oliet
- Physiopathology of addiction Team leader: Pier-Vincenzo Piazza

Interdisciplinary Institute for Neuroscience

Director: Daniel Choquet
Date of initiation: January 2011
Main focus: The IINS unites researchers with diverse areas of expertise, and creates a highly synergistic environment to promote the development of innovative methods and investigation tools, especially those based on molecular biology, physiology, optics, chemistry, physics and computer science. The application of such tools to push the boundaries of the study of molecular events underlying the activity of the brain. This will include studying the morpho-dynamic and functional properties of the nervous system to understand the complexity of its molecular assemblies and functions at an integrated level.

Members:
- Researcher: 23
- Faculty: 8
- Post-doc: 23
- Student (master +PhD): 48
- ITA: 49

List of the teams involved in the LabEx BRAIN:

- Dynamic Organization and Function of Synapses Team leader: Daniel Choquet
- Development and Adaptation of Neuronal Circuits Team leader: Laurent Groc
- Synapse in Cognition Team Leader: Yann Humeau
- Central Mechanisms of Pain Sensitization Team leader: Marc Landry
- Physiology of Glutamatergic Synapses Team Leader: Christophe Mulle
- Synaptic Plasticity and Superresolution Microscopy Team leader: Valentin Nägerl
- Quantitative Imaging of the Cell Team leader: Sibarita Jean-Baptiste
- Biophysics of Adhesion and Cytoskeleton Team leaders: Olivier Thoumine and Grégory Giannone

Institute of neurodegenerative diseases

Director: Erwan Bezard
Date of initiation: January 2011
Main focus: The IMN aims to encompass fundamental, preclinical and clinical research in the field of neurodegenerative diseases, with the goal of developing therapeutic approaches to neurodegenerative diseases using both vertical and translational approaches. We are fully aware that such an ambitious objective is often claimed by research units but is seldom satisfied. We consider however that our past achievements, obtained under a less favorable and structured environment, give rise to realistic optimism.

Members:
- Researcher: 12
- Faculty: 10
- Post-doc: 3
- Student (master +PhD): 22
- ITA: 14

List of the teams involved in the LabEx BRAIN:

- Mnemosyne (Mnemonic Synergy) Team leader: Frédéric Alexandre
- Pathophysiology of Parkinson's Syndrome Team leader: Erwan Bezard
- Dynamics of neuronal and vascular networks during memory processing Team leader: Bruno Bontempi

Institute of Aquitaine Cognitive and Integrative Neuroscience

Director: Jean-René Cazalets

Date of initiation: January 2011

Main focus: The INCIA focuses on the mechanisms and development of simple motor functions (such as movement or breathing), as well as more complex phenomena (including memory or addiction) in the Central Nervous System. These research themes are examined at several different levels ranging from molecular research to human clinical studies and with approaches spanning molecular biology, biochemistry, cellular and large-scale extracellular electrophysiology, fluorescence imaging, computational and system neuroscience, animal behavior, human brain imaging, psychophysics and clinical investigations.

Members:

- Researcher: 5
- Faculty: 4
- Post-doc: 2
- Student (master +PhD): 8 (1 PhDstudent, 2 M2, 5 M1)
- ITA: 2

List of the teams involved in the LabEx BRAIN:

- Behavior, development and neural networks Team leader: Daniel Cattaert
- Organization and adaptability of motor systems Team leader: Muriel Thoby-Brisson

Sleep, Attention and Neuropsychiatry

Director: Pierre Philip

Date of initiation:

Main focus: SANPSY's research focuses on establishing links between sleep, sleepiness, fatigue, circadian rhythms, attention and cognitive performance (neuropsychological and experimental tests, real and simulated driving) in healthy subjects (young, middle age and elderly subjects) and patients with sleep or neuropsychiatric disorders (age-related dementia, stroke, multiple sclerosis, head injuries, depression, hyperactivity and attention deficits, addiction).

Members:

- Researcher: 2
- Faculty: 2
- ITA: 9

List of the teams involved in the LabEx BRAIN:

- Sleep, Attention, Attention Deficit Disorder / Hyperactivity Disorder and Aging Team leader: Pierre Philip

Governance

The form of governance within BRAIN reflects the overall objective of the partners involved, i.e. to collaborate constructively with a view to promoting rapid growth and in keeping with a longer term strategy.

COMMITEES

Board of trustees

The Board of Trustees comes under the aegis of the Investissements d'avenir steering committee of the University of Bordeaux, which is responsible for supervising all the Investissements d'avenir projects selected in Bordeaux and for approving BRAIN strategy for growth. The Board of Trustees is thus in charge of assessing the administrative, budgetary and financial actions proposed by BRAIN and that will be specified in the consortium agreement. The board comprises all parties (research bodies, industrial partners, regional government, etc.) whose interests are represented within BRAIN. The board will meet at least once annually in order to assess the progress of BRAIN towards achieving the agreed objectives and review the terms of the consortium agreement.

Steering Committee

The steering committee is the upper board and its members represent the research laboratories comprising BRAIN. The committee meets on a quarterly basis to discuss the growth strategy for BRAIN and to implement the

general guidelines approved by the board of trustees. It makes decisions on the basis of joint initiatives put forward by BRAIN's partners, with particular focus on those initiatives to be funded from its own resources. It monitors the progress of scientific transfer and training projects. It decides upon the addition/removal of teams participating in BRAIN.

The steering committee is composed of representatives of the five partners according to the following:
NCM = 4 seats (Pierre-Vincenzo Piazza, Daniela Cota, Véronique Deroche, Stéphane Oliet)
IINS = 3 seats (Daniel Choquet, Christophe Mulle, Marc Landry)
IMN = 2 seats (Erwan Bézard, Bruno Bontempi)
INCIA = 1 seat (Blaise Yvert – To be replaced)
SanPsy = 1 seat (Pierre Philip)
SFR = 1 seat, director (Jean-Marc Orgogozo)

Daniel Choquet is the Director

In case of the SFR director belongs to one of the partners, therefore, the steering committee is only composed by 11 seats.

The members are nominated for a 4-year period

Board of Directors

For the daily running of BRAIN, the director appoints an executive body called the Board of Directors composed of three adjunct directors in charge of technology transfer, training and clinical relations. In addition, to facilitate smooth communication between Neurocampus and BRAIN, the Neurocampus project coordinator - currently Pier Vincenzo Piazza - is a member of the board of directors.

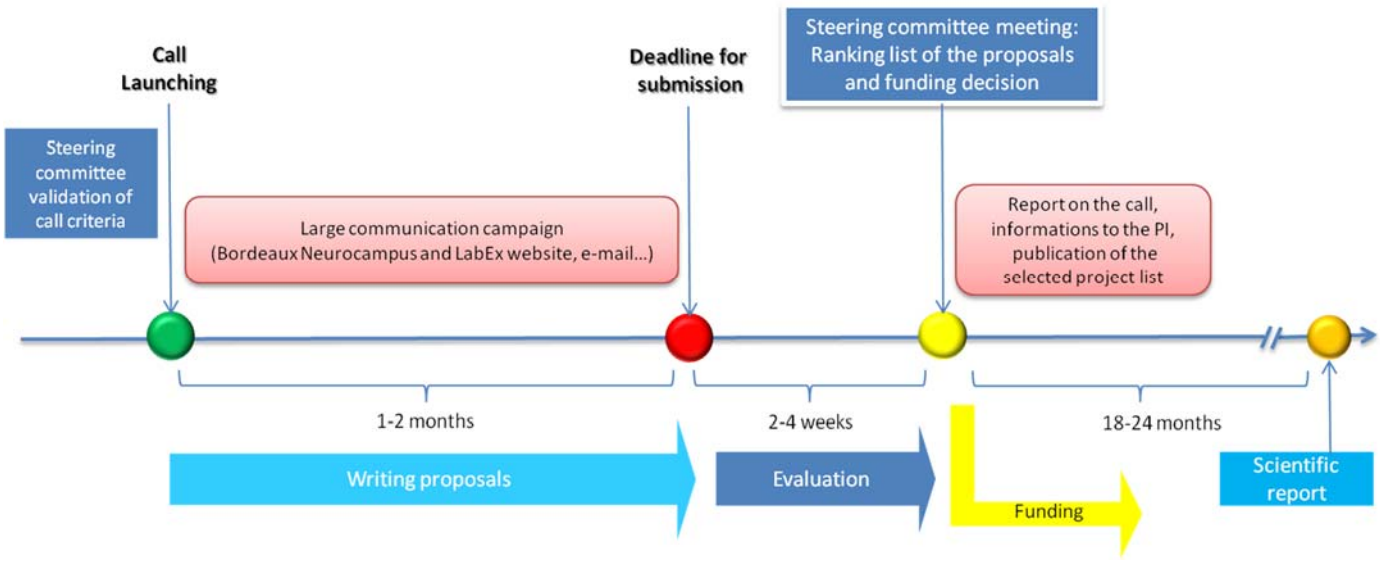
External Scientific Advisory Board (ESAB)

The members of the External Scientific Advisory Board (ESAB) are all highly qualified international academics (currently Arthur Konnerth; Yadin Dudai; Carmen Sandi; Rob Malenka; Claudio Bassetti; Serge Przedborski). They will meet every 2 years upon convocation by the director of BRAIN to discuss the overall policy of BRAIN for the coming years and to assess the annual scientific program with regard to long-term strategic goals. The council will also play an advisory role regarding entry and exit of teams from BRAIN. Recommendations of the ESAB will be transmitted to the steering committee.

PRINCIPLES OF THE CALLS FOR PROPOSALS

Different calls for proposals are launched by the LabEx BRAIN, for the transversal projects, the PhD extension grant, the symposium, etc... The general principles are aimed at favouring a **rapid, efficient and transparent process.**

In order to favour risky and early stage projects, we decided to proceed to an internal evaluation of the proposals. Each grant is independently evaluated by all steering committee members on the criteria mentioned in the call on a scale from 1 to 5. Grants are then discussed for final selection in plenary session as a function of this ranking. Therefore, **to reduce conflicts of interest**, proposals are not evaluated by steering committee members belonging to the same institute as partners. Moreover, when partners are members of the steering committee, they leave the room during the discussion of their submitted proposal.



Main activities of BRAIN

RESEARCH

Transversal projects

Our efforts have been organized and concentrated around 5 major transversal projects corresponding to major challenges in modern Neuroscience. The five scientific projects of BRAIN result from a combination of bottom-up and top down approaches. They all transversally involve teams from different partner research centres and all reflect our motto: "From molecules to behaviour for understanding brain function and its pathologies".

The strengths of these scientific projects lie in their focused and well identified aims, multidisciplinary approaches, critical mass of top level researchers and major potential impacts.

For the first two years, each axis was attributed a lump sum of 95 K€ per year to be allocated to given sub-projects. The first year, a call for proposal within each research axis has been launched and the selection organized by the axis coordinators (2 from 2 different laboratories). The second year, we modified the procedure following discussions with the researchers. We therefore decided to follow a general procedure of an open call (see figure above) and to open a 6th axis called "blue sky axis", allowing proposals in different thematics (pain, chemistry, etc...) to be proposed for selection by the LabEx. For the future, we may wish to introduce more flexibility in between the research axis.

Details in section I

Core facilities

10 core facilities have been selected after an internal audit and according their utilisation rate and the excellence of the service offer, to be supported by the LabEx. Our goal is to propose high-end technical equipment and service to the Bordeaux Neurocampus teams, with a reduced price.

Details in section III

TRAINING

PhD extention grants

The LabEx BRAIN offers to students from Bordeaux a fellowship to complete their Ph.D thesis, either before or after the defense. The fellowship aims at funding either a fourth year of Ph.D or up to one year immediately after a 3 year Ph.D, covering up a period to finish projects before leaving for a post-doc

Details in section II-3

Training programs

We are involved in master and PhD international programs.

Details in section II-3

Bordeaux School of Neuroscience-BSN

Technological innovations and the ability to combine methodological approaches are essential to make significant advances in the understanding of the mechanisms underlying the physiological and pathological functioning of the brain. Modern neuroscience research requires training of high level researchers and technicians from public and private laboratories to meet the technological and conceptual challenges posed by the sophisticated approaches required. In economic terms, the development of biotechnology, the pharmaceutical industry and information technology sectors depends on investment and the creativity of young researchers in neuroscience.

The vocation of the BSN is to **offer the international/European Community a platform of high technological level**, giving the opportunity to organize training for research in neuroscience-based experimental practice, according to the "hand on" principle defended by Georges Charpak.

Unique in Europe, the originality of the project is the ability of the BSN to **provide the infrastructure and logistics for multidisciplinary training** in modern neuroscience research at all stages of initial academic training and professional career.

The BSN will cover a very broad field of methodological approaches and areas in neuroscience. It will also involve partnerships with the core facilities of Bordeaux Neurocampus to take full advantage of the wide range of technological expertise present in Bordeaux.

The BSN will work as a pedagogical transfer unit. By adopting a private sector type approach within the university, the BSN aims to become **financially independent.**

The BSN will have a scientific director who is trained in project management. Together with a team of technicians, he will ensure the organization, communication and logistics of training as part of a quality process where training is constantly evaluated.

The LabEx BRAIN has allowed to secure up to 1.7M€ for the equipment and initial running costs of the Bordeaux School of Neuroscience. Additional support will be sought from the Regional Government and from the IdEx Bordeaux. The University of Bordeaux has decided to provide 500m2 laboratory space in a brand new research building for the Bordeaux School of Neuroscience. This will occur in 2016, upon achievement of the new Neurocampus research building. In the meantime, a temporary laboratory space (200-300m2) will be provided by the University for the organization of hands-on training, in combination with the core facilities which are experienced in training at all levels of the scientific career.

Recently, the **BSN has been selected by FENS/IBRO to be the major partner site of the the CAJAL Advanced Neuroscience Training Program**. This means that BSN will provide infrastructure and logistic support for the organization of 4-6 FENS courses (2-4 weeks/course) per year. The first sessions will start in 2015.

TRANSFER

Knowledge transfer

The LabEx BRAIN supports symposiums organized in Bordeaux. See details section IV.

We also are implicated in popularization, such as conferences, debates, workshops for a general audience, in the context of “the brain’s week” (“la semaine du cerveau”), the “science party” (“la fête de la science).

Technological transfer

We are in close relationship with the transfer agency (SATT Aquitaine Science Transfer) for all the applied projects. Recently, we got closer to venture capital and started a series of meeting to present our team’s skills and some transfer projects.

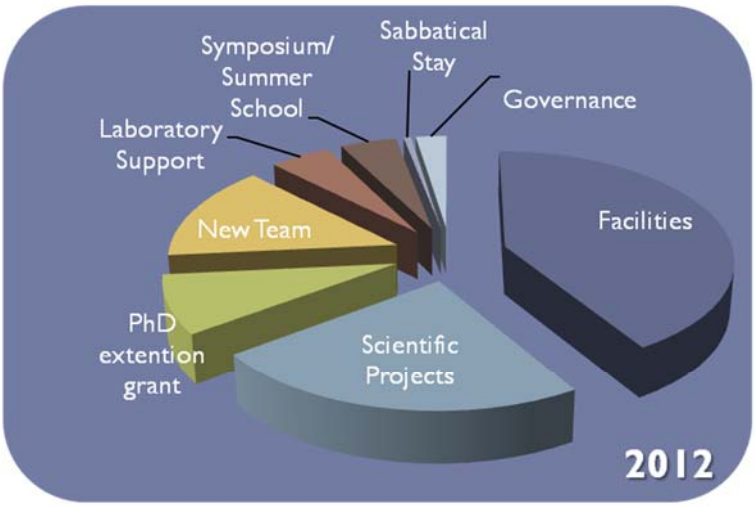
BRAIN Budget

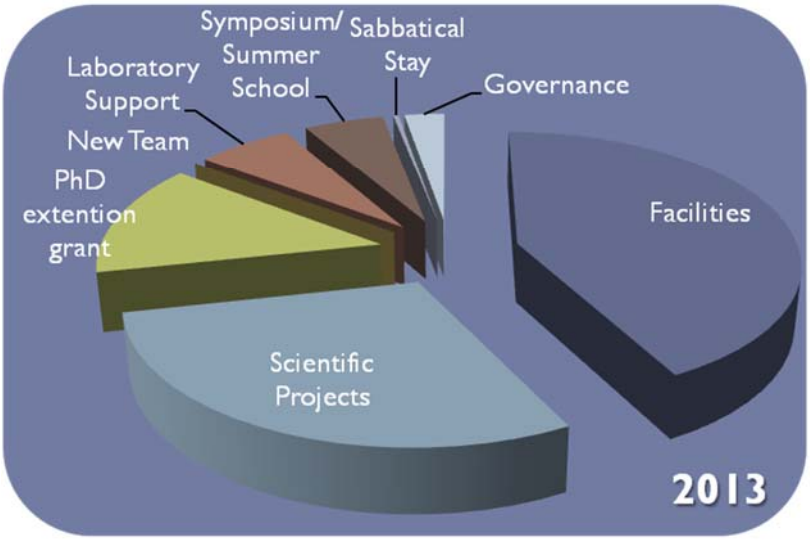
Our resources are dedicated to **increase attractiveness** of Bordeaux for outstanding external scientists and students, to **increase excellence** of the research, to **increase the exploitation and dissemination** of the results produced by the BRAIN teams.

The 20 M€ will be allocated as described in the table below (in k€):

Attractiveness	5 start-up packages	1 700 k€
Excellence	core facilities	5 400 k€
	transversal projects	7 000 k€
Exploitation	translational projects	1 190 k€
Dissemination	education	1 950 k€
	symposia	710 k€
Governance		1 250 k€
Over-heads		800 k€

During the first 2 years of the LabEx, the expanses were spread out as described in the 2 pie-charts below.





Deviation from initial objectives

Overall there has been little deviation from the initial work plan in the first two years. However, we report that:

- More spending has been allocated to the core-facilities than initially planned in order to allow for acquisition of equipment and ramping up of the facilities
- We have not performed a call for proposal regarding translational projects. This is partly taken care of by the SATT.

SWOT analysis

STRENGTHS

Integration:

- Capitalizing on existing competences, we aim to **promote inter-institutes collaborations** in order to generate ambitious and transversal projects. The increased number of publications from intra-LabEx collaborations indicates the success of the call for proposals: **n=10 in 2012 vs n=25 in 2013.**
- Through the call for proposal and the facility program of the LabEx, we could initiate **new collaborations between basic and clinical teams.**
- **Speeding up Bordeaux Neurocampus dynamic**: the structuration of the different teams working in neuroscience in Bordeaux has been initiated with the creation of the federative research structure in neuroscience, (that became Bordeaux Neurocampus). The LabEx BRAIN pursues this effort in the same dynamic and by adding significant funding.

Attractiveness:

- The LabEx BRAIN supported the venue of international symposia in Bordeaux. Therefore, we were partners of 16 symposia each year, with an average of 100-400 international attendees per meeting. The 2/3 speaker are international scientists.
- We are an **international research community**, hosting PhD students, post-docs and researchers from over 20 different nationalities. Among the 45 post-doc working in the LabEx teams, 50% are international.
- We are involved **in international training programs**, with the coordination of the Marie Curie Initial Training Network SyMBaD ("Synapses: from Molecules to higher Brain function and Diseases"), ENI-Net network, ENC network (European Neuroscience Campus), ITN Marie Curie training network, Erasmus Mundus networks at Master and Doctoral levels, the Summer Schools ESCube and NUTRIBRAIN.

Excellence:

- Through the Core-facilities program, we could facilitate access to high-end facilities, permitted the acquisition of equipment and specialized engineers services in fields from molecular and cellular biology to clinical research through animal facility and imaging.

- We opened a new program called "PhD extension grant" to enable the PhD students to finish their work and papers in preparation before to leave for a post-doc. This program received a large success.

WEAKNESSES

- Together with the Neurocampus program and the IdEx, we were able to set-up a start-up package dedicated to host a new team; however we were **not able yet to attract a new team**. One major obstacle is the shortage of space.

- There is a **lack of coherence in the visibility** of the neuroscience community caused by the multiple governance authorities in Bordeaux Neurocampus and a lack of a global communication strategy resulting in a multiple communication actions.

- Overall, the operational organization of the research axis and their mode of funding could be impoved. For example, all research axis may not have the same needs and there is currently a lack of flexibility that should be corrected.

- No international PhD program

- Weakness of the support of the University and IdEx.

- No specific transfer program

OPPORTUNITIES

- Increase capacity: the **Neurocampus Project**: 75 M€ (delivery in 2016) to build 10 000 m² of new lab space to rationalize animal facilities and the imaging center

- **Bordeaux School of Neuroscience**, opening 2015 is a unique hands-on training center in Europe, with a partnership with IBRO and FENS.

- BIC as a European level facility

- Investment funds: IdEx program to reinforce inter-labEx collaborations, attractiveness program, CPER (regional support to infrastructure), Investment funds…

THREATS:

- Decrease in local (IdEx and CRA) and national support
- Unbalanced focus on applied research from governing bodies (national and local)

Strategy

- Depending on SAB advices, **pursue successful programs** and steer towards more call for projects, increasing the non-thematic call for projects, pursue the phD extension grants, support to facilities and symposium

- Reinforce the potential and KETs (Key enabling Technologies) by **attracting New Teams**: we dedicate a package to attract 6-8 new and/or emerging team composed by 1,8 M€ from LabEx BRAIN. The Neurocampus project involvement has to be secured. The main criterion is excellence, and we will try to fill gaps in the several thaematics including, in particular but not exlusively: *in vivo* imaging, development, model organisms, clinical research, physical chemistry, biosensors.

- **Reinforce innovative and transversal projects,** by stimulating inter-labex programs (e.g. ExtraBrain) and developing new facilities (Protein production, Stem cells, Optopath/phenovirt)

- **Increase European visibility and training**, with the creation of the Bordeaux School of Neuroscience and the European labeled of the BIC. We wish to increase our presence at carreer fairs. Moreover, we need to reinforce links with patient associations and we have to identify representative icons. A large work of Lobbying has to be done to improve governing bodies' awareness on neuroscience.

- **Attract new funds**: we need to develop a strategy for a better communication and fund raising. Therefore, we plan to reinforce access to European funds, stimulate IP protection, and structure interactions with venture capital and creation of start-ups.

I- Transversal Research Projects

Axis 1: Patho Dyn Syn- Mechanisms and patho-physiological consequences of the dynamic organization of synapses

MORPHO-FUNCTIONAL PLASTICITY OF THE TRIPARTITE SYNAPSE

LabEx support (2012): 58 000€
Teams: Giovanni Marsicano (NMC), Valentin Nägerl (IINS), Stéphane Oliet (NMC)

Objectives of the project:
Aim 1: Characterize morphological organization of tripartite synapse using STED
Aim 2: Investigate activity-dependent structural plasticity of tripartite synapse.
Aim 3: Study role of astrocytic coverage
Aim 4: Study role of endocannabinoid signaling
Aim 5: Study impact of CB1 signaling on behavior

Main results:
*We imaged hyperfine astrocytic processes in proximity of dendritic spines using STED in living brain slices
*We described structural changes in astrocytic coverage of dendritic spines after LTP
*We identified a form of LTP in vitro that depends on astroglial CB1 receptors
*We found that this is likely mediated by control of co-agonist occupancy of NMDA receptors
*We found that astroglial CB1 receptors are necessary for object recognition memory.

Working plan to continue:
*concluded

Additional grant obtained:
Funding agency: ANR
Name of the project: SUPERtri
Total amount: 53 6720 Euro
Date and duration of the grant 01-04-2013 until 01-04-2016

Published publications:
Publications in preparation:
1. LTP withdraws perisynaptic astroglia boosting glutamate escape by Christian Henneberger*&, Aude Panatier*, Nikolay I. Medvedev*, Stefanie Anders, Daniel Minge, Igor Kraev, Lucie Bard, Stephane H.R. Oliet, Michael G. Stewart&, Valentin Nagerl&, Dmitri A. Rusakov&
*equal contribution & correspondance
2. Endocannabinoid control of gliotransmission mediates recognition memory. In preparation

CYTOPLAN: IMPACT OF PLANAR POLARITY ON SHAPING NEURONS AND SYNAPSES

LabEx support (2012): 36 000€
Teams: Mireille Montcouquiol (NMC), Olivier Thoumine (IINS)

Recruited personnel:
- Nicolas Piguel, post-doc (6 months)
- Cedric Landmann, Master 2 (6 months)

Objectives of the project:
Our main objective was to understand the impact of Planar Cell Polarity (PCP) signaling on the dynamic organization of the actin cytoskeleton during neuronal growth cone motility and dendritic spine morphogenesis. We

looked at the impact of Vangl2, one of the most upstream components of PCP signaling, on the actin cytoskeleton, which is recognized as a major determinant of the morphology and function of axonal growth cones and dendritic spines.

Main results:

We focused on the study of growth cones, comparing cultures from homozygote animals bearing a Vangl2Lp mutation, with WT animals. We first analyzed the morphologies of axonal growth cones and found that Vangl2Lp neurons had more filopodia-like structure than Vangl2WT. SptPALM allowed the tracking of hundreds of individual actin-mEOS2 molecules within growth cones. We showed a clear directed motion of actin filaments from the tip to the rear of the growth cones, called actin retrograde flow. Our data also showed a reduction in the speed of actin retrograde flow in growth cones from Vangl2Lp mutants (0.07 µm/s) compared to Vangl2WT (0.1 µm/s). We also generated the Vangl2-mEOS construct in order to track the dynamics of Vangl2. Our results show that Vangl2 exists in two distinct dynamic pools: one vesicular/punctuate pool moving slowly and one fast moving pool, at the cell plasma membrane. These results are the first showing a direct impact of PCP signaling on cytoskeleton dynamics in neurons, and strongly suggest that at least part of the phenotype observed in the mutants is due to a dynamic deregulation of the actin cytoskeleton

Working plan to continue:

We will apply a similar experimental strategy to examine the impact of PCP signaling disruption on the dynamics and organization of the actin cytoskeleton in dendritic spines. We hypothesize that deregulation of the actin cytoskeleton in neurons defective for Vangl2 or Scrib1 leading to defects in spine morphology is the cause of learning and memory defects in PCP mutants. Deciphering the control of the actin cytoskeleton by PCP proteins in dendritic spines will provide new insights into the morphogenesis and structural plasticity of synapses.

Additional grant obtained:

Funding agency: ANR
Name of the project: MossyPCP
Total amount: 598 360 Euros
Date and duration of the grant: 2013-2016

Publications in preparation:

Piguel N, Garcia M, Landmann C, Chazeau A, Giannone G, Sans N, Thoumine O* & Montcouquiol M*. Vangl2 affects actin dynamic during axonal growth, in preparation.

MEMBRANE DYNAMICS OF ASTROCYTIC GLUTAMATE TRANSPORTER AND ITS FUNCTIONAL IMPACT ON SYNAPTIC FUNCTIONS

LabEx support (2013-2014): 31 666€ /year for 2 years
Teams: Laurent Groc (IINS) ; Stéphane Oliet (NCM)

Recruited personnel:

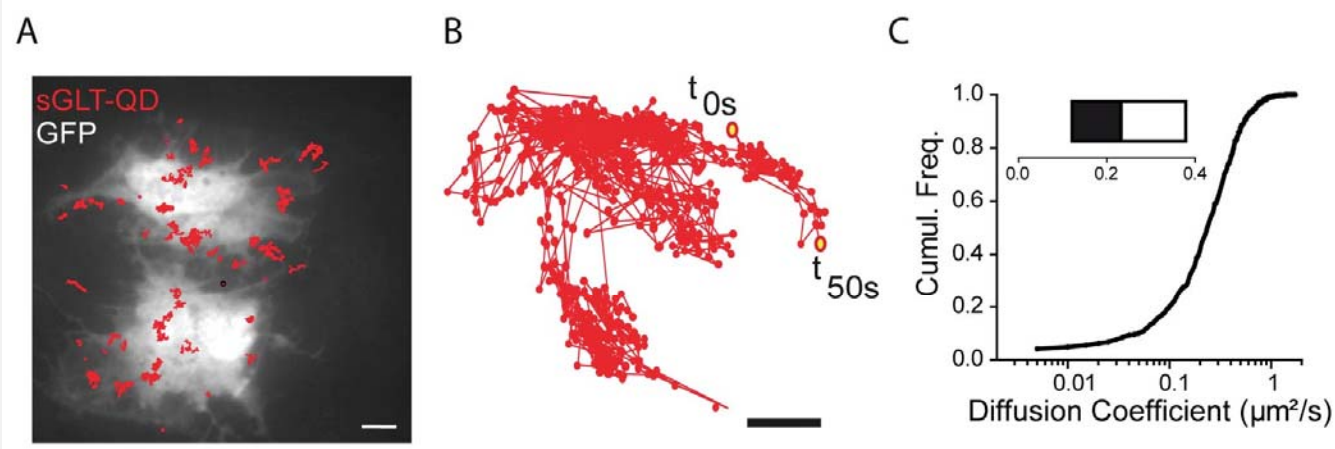
Ciaran Murphy Royal

Objectives of the project:

We want to test the possibility that GLT-1 dynamics at the surface of astrocytes shape the glutamatergic synaptic transmission and control glutamate receptor location. Cutting edge single nanoparticle tracking and electrophysiological approaches will be used to measure, in vitro and in vivo, the impact of a pharmacologically-altered GLT-1 surface dynamics on synaptic transmission, plasticity, and receptor locations in hippocampal glutamate synapses.

Main results:

Preliminary and unpublished observations revealed that GLT-1 are highly dynamics at the surface of astrocytes (Murphy Royal et al, Soc Neurosci Abstract 2012). Such a mobility is activity-dependent since it is sensitive to changes in neuronal and/or transporter activity as revealed by the use of selective pharmacological compounds. Remarkably, GLT-1 is highly retained in the vicinity of spontaneously-active glutamate synapses, suggesting that astrocyte can dynamically control the location of GLT-1 and ensure efficient glutamate buffering in synaptic areas. Finally, cross-linking the transporters to experimentally induce its immobilization affects the kinetics of excitatory postsynaptic currents. These data thus suggest that GLT-1 mobility is an important contributor to glutamatergic transmission.



(A) eGFP expressing astrocyte with 50s long QD trajectories overlaid (scale bar 5 µm).
(B) Representative single trajectory of GLT-1flag surface diffusion (scale bar 320 nm).
(C) Cumulative distribution of GLT-1 diffusion coefficients. Inset: instantaneous GLT-1 diffusion coefficient distribution.

Working plan to continue:

All the work carried out so far was performed in vitro. We are now assessing whether GLT-1 mobility is also shaping excitation at CA3-CA1 synapses in vivo. To this end, we are targeting the endogenous GLT-1 by injecting antibodies directed against the transporter in vivo in order to induce cross-linking. Slices form such animals are presently undergoing electrophysiological analysis.

Publications in preparation:

Murphy-Royal C, Dupuis J, Pinson B, Baufreton J, Groc L* and Oliet SHR*. Surface dynamics of astroglial glutamate transporter GLT-1 shapes excitation.

Communications:

- Society for Neuroscience, New Orleans 2012
- FENS Forum satellite workshop, Barcelona 2012
- Symposium of the Mediterranean Institite for Applied Science, Marseille 2013
- 3rd International Astrocyte School, Bertinoro 2013
- COST meeting, Palermo 2013
- 4th annual conference of CIPKeBiP,Ljubljana 2013
- UAB minisymposium, Birmimgham USA, 2013
- EuroGlia, Berlin, 2013
- Societe des Neurosciences, Lyon 2013
- Gordon Conference on Glial Biology, Ventura CA 2013

Role of Planar Polarity proteins on the Cytoskeleton dynamics of dendritic spines

LabEx support (2013-2014): 31 666€ /year for 2 years

Teams: Mireille Montcouquiol (NCM); Olivier Thoumine (IINS)

Recruited personnel:

- Kevin Richards, Master 1 (5 months)
- Hortense Fanet, Master 2 (6 months)
- Jerome Ezan, Postdoc (6 months)

Objectives of the project:

Our objective is to understand the impact of PCP proteins, mainly Vangl2 and its associated protein Scribble-1 (Scrib1), on the dynamic organization of actin and actin regulatory proteins (Rac1, Arp2/3, WAVE, IRSp53) during spinogenesis and morpho-fonctional plasticity. We expect to identify clear and important roles for PCP genes in the control of the spines actin cytoskeleton, providing new insights into both fundamental and pathological changes in dendritic spine morphology.

Main results:

Using single protein tracking (sptPALM) and combining PALM and dSTORM to generate dual color super-resolution images of actin regulatory proteins and PSD-95, we recently unraveled the nanoscale organization and dynamics of branched F-actin networks in dendritic spines (Chazeau et al., to be submitted). Specifically, we revealed a zone of high convergence between diffusing Arp2/3 complex and its activators (the WAVE complex, IRSp53 and Rac1), which colocalizes with the PSD, consistent with the nucleation of branched F-actin close to the PSD. This organization is opposed to classical motile structures such as the lamellipodium where branched F-actin nucleation and elongation are triggered at the tip of membrane protrusions. We are applying a similar experimental strategy to examine the impact of PCP signaling disruption (Vangl2 looptail or Vangl2, Scrib1 and Rac1 cKO) on the dynamics and organization of the actin cytoskeleton in dendritic spines. We expect to find that Vangl2 and Scrib1 are implicated in synaptogenesis and regulate synapse morphology and that these effects depend on the control of actin regulatory proteins. We hypothesize that deregulation of the actin cytoskeleton in neurons defective for Vangl2 or Scrib1 leading to defects in spine morphology is the cause of learning and memory defects in PCP mutants. Deciphering the control of the actin cytoskeleton by PCP proteins in dendritic spines will provide new insights into the morphogenesis and structural plasticity of synapses.

Working plan to continue:

To determine the PCP proteins sub-spine dynamics and organization, we will transfect neurons with constructs coding for PCP proteins fused to mEOS2 (Vangl2, Scribble-1, Rac1) and will perform single protein tracking and super resolution imaging after mEOS2 photo-activation (sptPALM). To determine if PCP proteins control the dynamic organization of actin regulatory proteins in dendritic spines, we will transfect PCP mutant neurons (Vangl2, Scribble-1, Rac1) with constructs coding for actin and actin regulatory protein fused to mEOS2 (already available) and will perform sptPALM. We will combine PALM and dSTORM to generate dual color super-resolution images of actin regulatory proteins and PCP proteins within spines, to determine their respective localization and potential interactions within spines.

ROLE OF NEURONAL AND ASTROGLIAL CB1 RECEPTORS IN MORPHO-FUNCTIONAL PLASTICITY OF THE TRIPARTITE SYNAPSE

LabEx support (2013-2014): 31 666€ /year for 2 years

Teams: Giovanni MARSICANO (NCM); Valentin NAGERL (IINS)

Objectives of the project:

*Aim 1: Morphological organization of tripartite synapse with or without cannabinoid treatments?

*Aim 2: Activity-dependent structural plasticity: Do synaptic activity and endocannabinoid signaling modulate the morphological interaction of the three synaptic elements?

*Aim 3: Role of astrocytic coverage: Does CB1-control of astrocytic morphology influence synaptic function and plasticity?

*Aim 4: Behavioral analysis

Main results:

*We optimized the STED microscope to perform nanoscale imaging in acute brain slices

*We carried out STED time lapse imaging together with pharmacological experiments (using agonists and antagonists of CB1 signaling) in acute brain slices to screen for morphological effects in tripartite synapse structures

*We found that the object recognition memory impairment of the GFAP-CB1R-KO mice (described in the previous LabEx grant) depends on alterations in NMDARs activity

*We showed the necessity of the NMDARs activity of the hippocampus in object recognition memory and enhanced its activity to rescue the phenotype of the GFAP-*CB$_1$R*-KO mice

*We identified a form of NMDAR-dependent LTP in vivo that depends on astroglial CB1 receptors

*We found that the Endocannabinoid system on astrocytes may likely control this form of LTP through the availability of D-serine, a NMDAR co agonist.

Working plan to continue:

We will address whether the impact of astroglial CB1 receptors on synaptic plasticity and memory consolidation is linked to endocannabinoid-dependent control of astroglial morphological plasticity. A similar approach will be adopted for neuronal CB1 receptors.

Published publications:

1. Bethge, Avignone, Marsicano & Nägerl, Biophysical Journal (2013)
2. Soria-Gómez E*, Bellocchio L*, Reguero L, Lepousez G, Martin C, Bendahmane M, Ruehle S, Remmers F, Desprez T, Matias I, Wiesner T, Cannic A, Nissant A, Wadleigh A, Pape HC, Chiarlone AP, Quarta C, Verrier D, Vincent P, Massa F, Lutz B, Guzmán M, Gurden H, Ferreira G, Lledo PM, Grandes P*, Marsicano G* (2014) Nature Neuroscience 17(3):407-15
Publications in preparation: Endocannabinoid control of gliotransmission mediates recognition memory. In preparation

Communications:
Poster presentation at Neurophotonics meeting 2013. Poster presentations at International School on Astrocytes (2013) and oral presentations at GRC Conferences on Cannabinoids (2013), on GPCR Physiology (2013) and on Neuron-Astrocyte Interactions (2013)

Axis 2: Ipsynet- Integrative physiology of synapses and neural networks

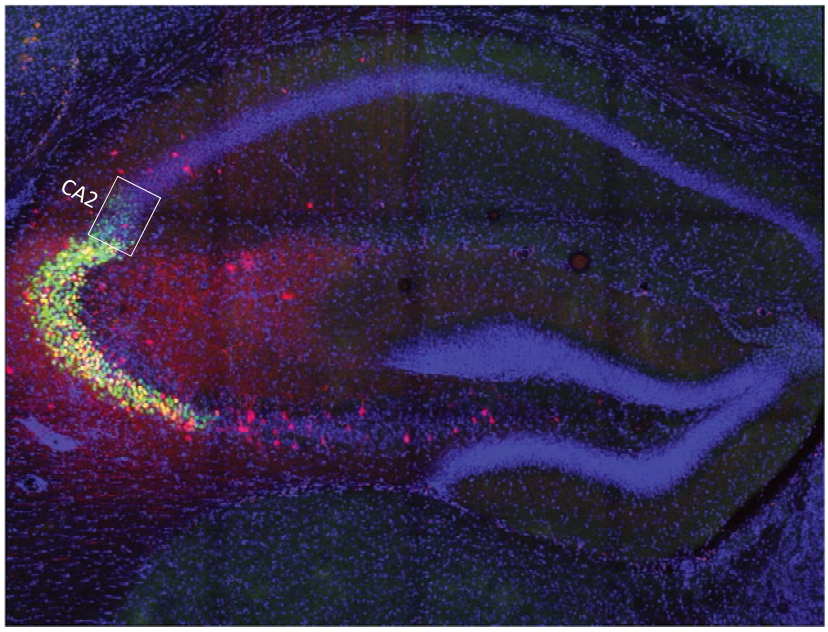
UNRAVELING THE ANATOMICAL WIRING DIAGRAM TO UNDERSTAND THE PHYSIOLOGY AND PATHOPHYSIOLOGY OF THE HIPPOCAMPUS AND NEOCORTEX

LabEx support (2012): 47 000€
LabEx support (2013-2014): 58 000€/year for 2 years
Teams: Christophe Mulle (IINS), Andreas Frick (NCM)
People involved in Mulle's team: Dr. Melanie Ginger, Dr. Mario Carta, Bernat Gonzales, Silvia Vianna da Silva, Amalia Callado Perez; in Frick's team: Dr. Melanie Ginger, Dr. Guillaume Bony, Matthias Haberl, Enoch de los Rios Mera.

Recruited personnel:
Dr. Melanie Ginger, IR, Bordeaux University.
Amalia Calloda-Perez, M1 Neurasmus student

Objectives of the project:
An understanding of how the brain processes information requires knowledge of the architecture of its underlying neuronal circuits. The aim of this collaborative project is to investigate the architecture, and ultimately also the physiological function of hippocampal and neocortical circuits. To do this, we are using a sophisticated tool-box comprising novel recombinant rabies virus-based tracing approaches and whole-brain imaging techniques.

Main results:
The previous year has seen a number of technological advancements that have greatly aided the development of the project.
1. Development of a novel anterograde RABV-based tracer.
We described and characterised a novel pseudotyped form of RABV ΔG, capable of infecting the cell bodies of neurons and imparting intense labelling of all morphological features of these neurons along the entire length of their projections (see publication below).
2. Development of improved methodology for targeting mono-trans-synaptic tracing to a hippocampal CA3 starter cell population and mono-transynaptic tracing approaches to correlate the morphological input map with the receptive field properties of pyramidal neurons of layer 2/3 of the somatosensory cortex.
Working plan to continue (5 lines):
We will use the tools developed so far to 1) examine the link between structure and function of neuronal circuits in the hippocampus and the neocortex (receptive fields of somatosensory cortex, pairs of connected neurons in the hippocampus and 2) study remodelling of neural circuits following learning or in physiopathological conditions (Fragile X, Alzheimer's disease). Overal, as soon as possible, we will combine the RABV- base tracing with brain clearing and ultramicroscopy.



Targeting monosynaptic-trans-synaptic tracing to the CA3 (*Cornus Ammonis* area 3) of the hippocampus. Maximum projection from a confocal image stack. Initially infected "starter" cells denoted by expression of nuclear-localised eGFP. Post-synaptic secondarily infected neurons, yellow. Presynaptic neurons, red. Image counterstained with DAPI (blue). Image acquired using equipment provided by the Bordeaux Imaging Centre.

Additional grant obtained:

Funding agency: FRM

Total amount: 2 years for the recruitment of an Engineer for the production of viral tools

Date and duration of the grant: 2014-2016

Published publications:

Haberl, M.G.,Viana da Silva, S., Guest, J.M., Ginger, M., Ghanem, A., Mulle, C., Oberlaender, M., Conzelmann, K-.K. and Frick, A. (2014) An anterograde rabies virus for high-resolution large-scale reconstruction of 3D neuron morphology. Brain Structure and Function. *In Press*.

PROGRAMMING SUPPORT FOR HYBRID SYSTEMS APPLICATIONS

LabEx support (2012): 48 000€

LabEx support (2013-2014): 34000€ /year for 2 years

Teams: John Simmers (INCIA), Gwendal Lemasson (NCM), Daniel Cattaert (INCIA)

Recruited personnel:

The recruitment of an engineer is planned for this year (2014), since all the project's equipment has now been established in the three participating teams. A profile for this position has been defined and posted in several Bordeaux engineering schools.

Objectives of the project:

The project's long-term objective is to establish a centralized facility in the Bordeaux site that will be principally engaged in the updating, customization and development of hybrid interfacing soft- and hard-ware. In a first step towards this objective, the project's aim is to set up computing/programming support for one of the principal hybrid neurobiological technologies –the dynamic clamp - used in the three partner laboratories.

Main results:

The project's first step was to acquire dynamic clamp hardware that was in common accordance with our research goals. To this end, we have been in close communication with an international company (Cambridge Electornic Designs – CED) that has developed such a system. To satisfy our specific requirements, the company has recently developed

a new system version that we acquired in late 2013 and have now successfully installed in our laboratories. Amongst our different hybrid projects, this technology has already been successfully employed on *in vitro* neuronal preparations to selectively replicate or suppress membrane and synaptic plasticity induced by appetitive operant learning. Specifically, this study has provided fundamental data on the causal relationship between these types of plasticity and the expression of different behavioral components of reward-induced compulsive-like behavior. A manuscript reporting these findings has been recently accepted for publication in *Current Biology* (see below).

Working plan to continue:

The development of our hybrid systems requires the assistance of a computing software engineer (to be recruited in 2014). The goals for this next year are also to develop a library of ion channel mechanisms, and an extension of the system (1) to include the calcium dynamics underlying KCa membrane channel operation and (2), to interface the dynamic clamp with computer simulations of individual neurons and network assemblies (using the NEURON simulation environment). This development will improve our capacity to analyze the cellular and network properties of motor output genesis and its sensory-induced adaptability.

Publications:

Sieling F, Bédécarrats A, Simmers J, Prince AA, Nargeot R (2014). Differential roles of nonsynaptic and synaptic plasticity in operant reward learning-induced compulsive behavior. *Curr. Biol.* In press.

Publications in preparation:

Communications: Nargeot, R. (2013) Reward-induced, dopamine-dependent plasticity in electrical coupling and neuronal excitability regulates rhythmogenesis in a motor pattern-generating network in *Aplysia*. Minisymposium, Annual Meeting of the Society for Neuroscience (San Diego).

Axis 3: MAD- Molecular Basis of the Transition to Addiction- From behavioral to molecular characterization of drug addiction

1- Psychobehavioral characterization of addiction

LabEx support (2012): 20 000€
LabEx support (2013): 36 000€
Daniela Cota and Véronique Deroche Gamonet

Objective measure of motivational and hedonic states in humans

Daniela Cota (NCM), Pierre Philip (SanPsy)

Recruited personnel:

Clinical research technician

Objectives of the project:

The experimental methods currently used for assessing hedonic and motivational processes in humans have some limitations primarily derived from subjective assessments. Here we propose a novel experimental computer-based tool for a quantitative and objective measurement of both hedonic and motivational states in humans. Two tasks evaluating the discrimination of size or presentation time between a food stimulus (food picture in color) and its devalued counterpart (same image in grayscale) were developed and tested in healthy subjects under satiety or fasting. Geometric figures in color or grayscale were used as controls.

Main results:

Relative to their devalued counterparts, the food images were judged significantly greater in size and shorter in time of presentation in fasting than in satiety. In fasting, the size and the time of presentation for the food images were respectively estimated significantly greater and shorter than for the control images when compared to their respective devalued counterparts. Conversely, there was no overall change in the perception of size or duration of presentation for the control images between fasting and satiety conditions.

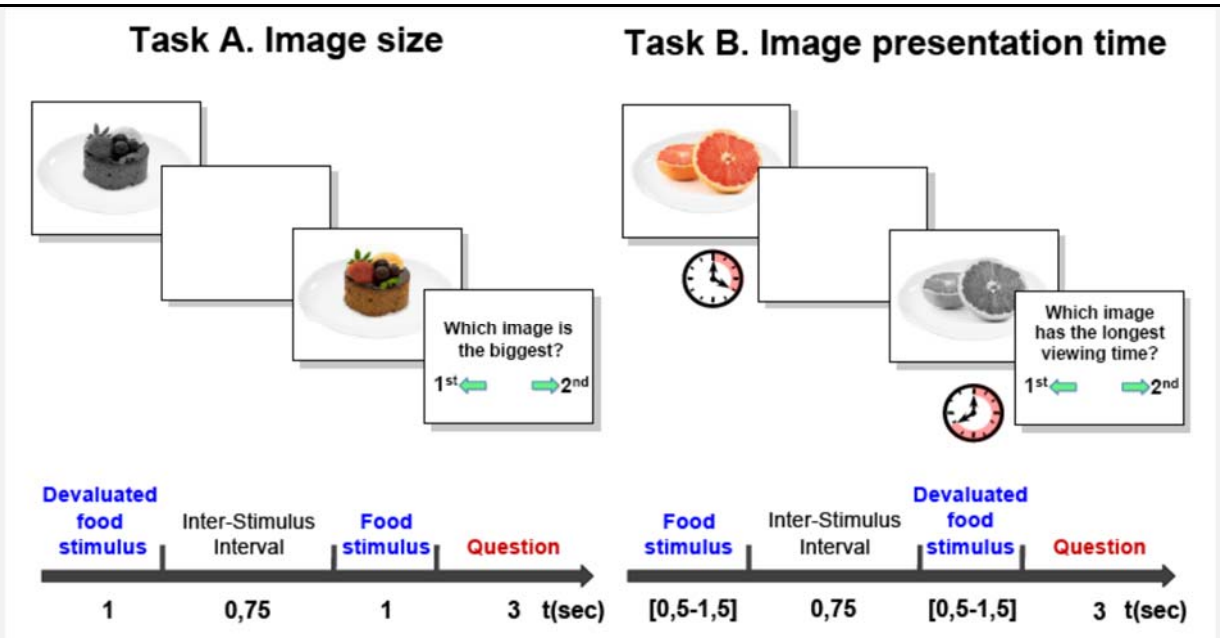


Figure 1. Illustrations of the two computer-generated tasks A (on the left) and B (on the right) developed for the assessment of hedonic and motivational states in humans. At each trial, the subject has to view and compare two subsequently presented stimuli, a food picture in original colors and its devalued counterpart in grayscale according to either their size for the task A or their presentation time for the task B.

Working plan to continue:

The present work highlights the relevance of a novel computer-based test that we have developed for the study of the hedonic and motivational processing of food images, allowing assessing changes in visual and time perception in humans. This computer-based test could therefore contribute to the characterization of disturbances in reward processes with their biological substrates and responses to standard therapeutic strategies currently proposed in subjects suffering from obesity.

Additional grant obtained:

Funding agency: French Foundation Eating-Health (French "Fond Français Alimentation-Santé")

Name of the project: A new method of characterization of pleasure for food. Relationships with the endocannabinoid system

Total amount: 45000 €

Date and duration of the grant: January 2013 – Duration: 2 consecutive years

Publications (submitted):

Aouizerate, B., Gouzien, C., Doumy, O., Philip, P., Semal, C., Demany, L., Piazza, P.V. and Cota, D. A new computer-based tool for the objective measurement of hedonic and motivational states in humans (submitted)

Communications:

Aouizerate, B., Gouzien, C., and Cota, D. A new method for the characterization of pleasure for food in obesity and relationships with the endocannabinoid system. The 8th edition of BIOVISION, the World Life Sciences Forum, March, 24-26, 2013 - Lyon (2013 Biovision Catalyzer Award winner)

Aouizerate B. A new method for the characterization of pleasure for food in obesity. Relationships with the endocannabinoid system. The 6th Meeting of Nutrition and Neurosciences, March, 18, 2013 - Bordeaux.

Measures of motivational and hedonic states in rats

Martine Cador (INCIA)

Objectives of the project:

The project was aimed at setting the taste reactivity test (Berridge, 2000) in order to be able to get an objective evaluation of the hedonic perception of an animal as a function of its drug state.

Main results:

We have studied to which extent the hedonic perception is influenced by the sweetness of the solution (using different concentrations of sucrose), the metabolic state of the animal (using deprived vs satiated animals), the caloric value of the solution (saccharine vs sucrose). In parallel, we have developed the Licking test which is also sensitive to the hedonic properties of the solution. This will provide a way to compare hedonic perception using two different paradigms.

Working plan to continue:

We plan to use the taste reactivity test and the licking test in animals which have overconsumed either natural rewards (sucrose) or/and drugs such as alcohol, nicotine, cocaine. A next step will be to implement physiological recordings which will quantify markers of the emotional reactivity of the animal (Heart rate, temperature..).

Additional grant obtained:

Funding agency Fonds Francais Alimentation Santé

Name of the project Un modèle neurocomportemental du plaisir alimentaire: l'exposition à des aliments sucrés à l'adolescence et ses conséquences

Total amount 130KEuros

Date and duration of the grant November 2012-november 2015

Published publications

Baldo B.A., Pratt WE, Matthew J W, Hanlon EC, Bakshi VP, Cador M, Principles of motivation revealed by the diverse functions of neuropharmacological and neuroanatomical substrates underlying feeding behavior. Neurosciences Biobehavioral Reviews 2013 Nov;37(9 Pt A):1985-98.

Communications:

Cador M., De la surconsommation de sucre à la dépression: l'adolescence comme période critique. Journées Francophones de Nutrition, Lyon, 12-14, 2012

Cador M. Hedonic vs motivational properties of food in rodents: interaction between palatabiliy and homeostatic states in food intake and food selection. 6th symposium Nutrition-Neuroscience, Bordeaux, le 18 Mars 2013

Alteration in learning strategies associated with drug addiction

Véronique Deroche Gamonet et Vincent David

Objectives of the project:

Drug addicts show alterations in memory processes and learning strategies. Whether these cognitive alterations are symptoms of prolonged drug use or are specific of addiction is unknown. The addiction model implemented by VDG and the expertise of VD in drug-induced influence on learning processes, are keys to answer this issue. VD evidenced that morphine compromises spatial-guided and promotes cue-guided learning. The two partners will evaluate whether this drug-induced effect on learning is also observed for cocaine and differently affects addicted and non-addicted-like rats.

Main results: The project is in the planning phase.

Additional grant obtained: The Labex grant is used to get preliminary results in order to apply to national or European grants.

2-CHARACTERIZATION OF NEURONAL CIRCUITS INVOLVED IN ADDICTION

LabEx support (2012): 40 000€
LabEx support (2013): 22 500€

Cyril Herry

Specifying the brain circuits involved in pathological incentive responses and the loss of control over drug taking during the development of addiction

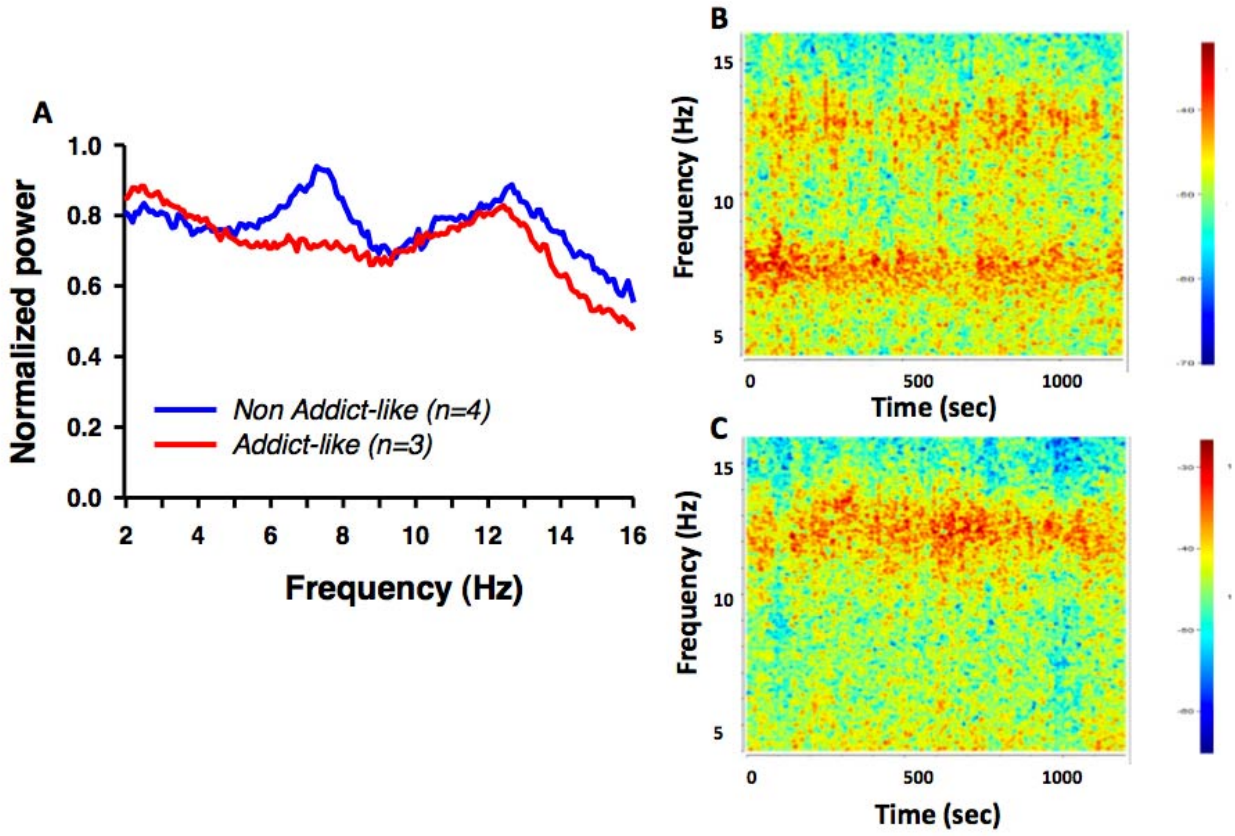
Véronique Deroche Gamonet, Cyril Herry

Objectives of the project:

Distinct, but interconnected, circuits appear at the core of pathological incentive processes and difficulties to control cocaine taking. Our goal is to characterize the function, connectivity and plasticity of dedicated nucleus accumbens (NAc), medial prefrontal cortex (mPFC) and basolateral amygdala (BLA) circuits involved in transition to cocaine addiction. For this, CH will record the same neurons from early to late cocaine use in rats resistant and vulnerable to cocaine addiction-like behavior issued from the addiction model implemented by VDG.

Main results:

We have performed simultaneous single unit and local field potential recordings in NAc, mPFC and BLA in rats behaviorally characterized as addicted or non-addicted-like after 3 months of cocaine self-administration. Our results indicate reduced functional connectivity between these neuronal structures in addicted compared to non-addicted-like rats, as assessed by long-range neuronal correlations and LFP coherence analysis. These preliminary results support the notion that cocaine addiction is associated with functional alterations of specific neuronal circuits.



Neuronal oscillations in the theta frequency range, recorded in the hippocampus, during cocaine self-administration. Neuronal oscillations, such as theta rhythm, are LFP oscillations in the 6-12Hz frequency range suggested to promote the synchronization of neuronal ensembles during emotion and motivational states. (**A**). Normalized power spectral density for a LFP recorded in the dorsal CA1 region of the hippocampus, in *Addict* and *Non Addict-like* rats. Whereas *Non Addict-like* rats display two distinct peaks between 5 and 9 Hz and 10 and 14Hz, *Addict-like* rats only display the second peak. Spectrogram analysis of hippocampal theta power during a self-administration session in *Addict* (**B**) and *Non Addict-like* (**C**) rats.

Working plan to continue:

Additional experiments are performed to comfort the identified alterations in functional connectivity in addicted-like rats. To test the involvement of relevant identified neuronal circuits on addiction-like behavior, we plan to manipulate these neuronal circuits using optogenetics. Finally, the identified relevant circuits will be tested from early to late training to identify their role in the pathological process.

Additional grant obtained:

Funding agency: Eranet Neuron grant / ANR
Name of the project: COCADDICT
Total amount: 720 000 euros

Date and duration of the grant: Starting 15 May 2014 (3 years)

Publications in preparation:

Martín-García E, Courtin J, Renault P, Fiancette JF, Wurtz H, Simonnet A, Levet F, Herry C, Deroche-Gamonet V. Frequency of Cocaine Self-Administration Influences Drug Seeking in the Rat: Optogenetic Evidence for a Role of the Prelimbic Cortex. Neuropsychopharmacology. 2014 Mar 17. doi: 10.1038/npp.2014.66. .

Communications:

Simonnet A. et al., Functional connectivity of neuronal circuits involved in cocaine addiction. French Neuroscience Society meeting, Lyon, France, 2013.

Simonnet A. et al., Functional connectivity of neuronal circuits involved in cocaine addiction. FENS, Milan, Italy, 2014.

Identifying the contribution of distinct neuronal circuits in the encoding of affective memories after drug withdrawal

Martine Cador

Objectives of the project:

Understand how affective memories associated with appetitive or aversive drug effects are encoded and retrieved within limbic structures. For this we performed multi-site single-unit and local field potential (LFP) recordings in the PFC, BLA, and NAc of behaving animals following opiate withdrawal. The objective is to evaluate the dynamics of PFC-NAc-BLA neuronal synchronisation involved in the coding of opiate withdrawal memories and their role in memories retrieval.

Main results:

We have evidenced that retrieval of opiate withdrawal memories is associated with specific local field potentials oscillations and synchronization. More particularly NAc and BLA LFP show a concurrent increase in the amplitude and the synchronization of gamma band oscillations at the time of memory retrieval. Interestingly the contexts respectively associated with withdrawal (aversive) or the absence of withdrawal (safe) present different gamma profiles. Aversive memory retrieval is associated with fast gamma (~80 Hz) whereas safety is linked to slow gamma (~60 Hz). The sorting of slow and high gamma is under the control of cortical inputs that dynamically allocate slow and high gamma to their specific emotional contexts.

Working plan to continue:

We plan to follow up on the study of single neuron activity in relation to gamma oscillations and emotional learning. Preliminary results show that conditioning results in an increase in context related information content at the level of single NAC neurons at the time of memory retrieval. Our next step is to link this spatial selectivity with gamma oscillatory process and to apply this approach to neurons of the PFC and the BLA.

Additional grant obtained:

Funding agency: FRM Innovative project
Name of the project: Neural networks and synchronization in addiction:
development of multi-sites multi-unit recordings in behaving animals
Total amount: 80 000 € for the salary of an IE in signal processing
Date and duration of the grant: November 2013 for 2 years

Probing the role of dedicated valuation neuronal circuits in the development of pathological decision making in addicted individuals

Serge Ahmed

Recruited personnel: Audrey Durand (October 1, 2013 - March 31, 2014)

Objectives of the project:

To dissect the neural circuits that underlie pathological decision-making in cocaine addiction by comparing non-addicted versus addicted rats.

Main results:

When faced with a choice between two competing actions, taking cocaine or drinking sweet water, most rats prefer the nondrug activity, even after prolonged drug use. Only few rats prefer the drug, suggesting that, like in people, addiction would only affect a minority of rats. We first sought to image brain activity in nondrug-preferring rats in response to cocaine *versus* sweet water (the preferred activity), using large-scale Fos mapping. Rather surprisingly, the preferred activity induced little specific brain activity, except in the thalamocortical gustatory pathway. In contrast, cocaine taking elicited more brain activity; particularly in brain regions involved in reward omission and frustration (e.g., the lateral habenula and the tail of the VTA). This result is unlikely due to a direct aversive effect of self-administered cocaine; it more likely reflects the frustration of not having access to the preferred reward during testing.

Working plan to continue:

We plan to extend this work in 2 directions: i) we will image brain activity in nondrug-preferring rats in experimental conditions that rule out the involvement of preferred reward omission and frustration; and ii) we will compare and contrast the obtained pattern of brain activity to that observed in addicted rats. This work will define brain regions and circuits involved in individual cocaine preferences for future interventional studies.

Additional grant obtained:

Funding agency: ANR

Name of the project: Pathological decision-making in cocaine addiction: role of the orbitofrontal cortex and its projections to the dorsal striatum

Total amount: 472 000 euros

Date and duration of the grant: March 2011, 48 months

3- CHARACTERIZATION OF MOLECULAR PATHWAYS IN VULNERABILITY TO DRUG ADDICTION

LabEx support (2012): 40 000€
LabEx support (2013): 31 500€

Jean-Michel Revest

Recruited personnel:

Recruitments were not planned.

Objectives of the project:

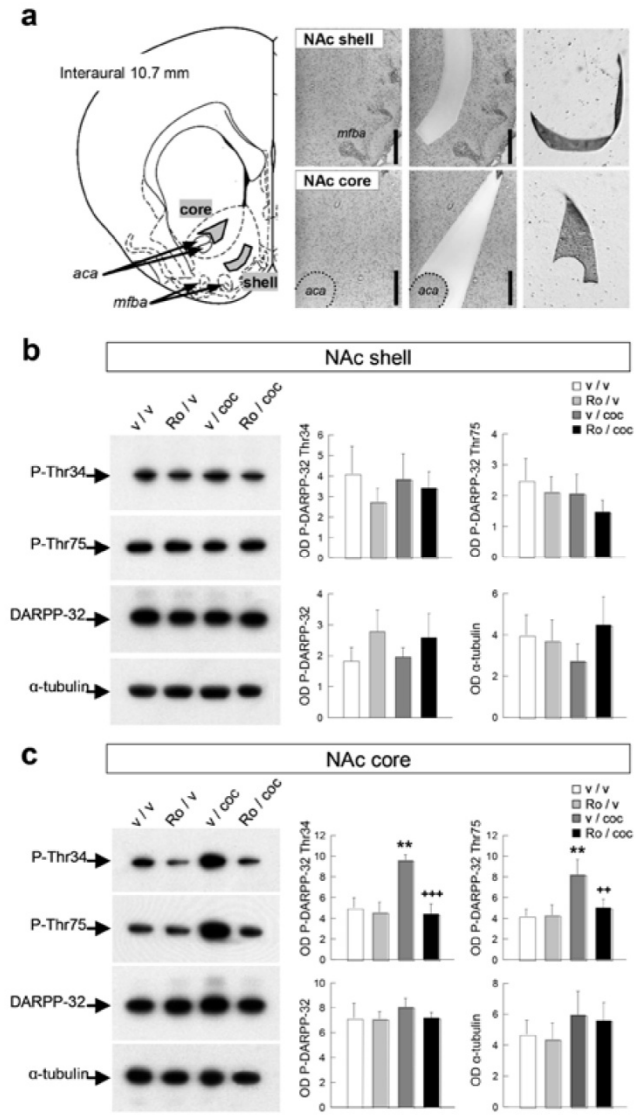
Cocaine by interfering with the dopamine transporter (DAT) leads to elevated levels of dopamine (DA). DA activates D1- and D2-like G protein-coupled DA receptors inducing a complex network of intracellular signaling mechanisms that were shown to be deregulated following acute cocaine administration. Among these signaling pathways protein kinases appear to play a pivotal role in vulnerability to cocaine abuse. Our goal is to characterize these molecular pathways underlying cocaine addiction by comparing non-addicted versus addicted rats.

Main results:

We found in particular that among these signaling pathways the extracellular-regulated kinase ($Erk1/2^{MAPK}$) and protein kinase C gamma (PKCγ) were downregulated in rats behaviorally characterized as addicted-like after 3 months of cocaine self-administration in comparison to non-addicted rats. In contrast, cAMP-dependent protein kinase (PKA), cyclin-dependent kinase 5 (Cdk5) and DA and c-AMP regulated phosphoprotein of Mr 32kDa (DARPP-32), as some of the cytoskeletal and chaperone proteins were not modified in addicted rats.

Working plan to continue:

Since, most of these kinases induce the activation of immediate early genes coding for transcription factors (TF), our plan is now to study how the TF such as ΔFosB, a Fos family member, Egr-1 (Zif268) and CREB (cAMP response element binding protein) are modulated in addicted rats. Thus, these TF will lead to altered gene transcription and protein synthesis that ultimately contribute to long-term changes in synaptic function and neural networks observed in addiction.



Effect of Ro 60-0175 on cocaine-induced stimulation of DARPP-32 signaling pathway in the shell and core subregions of the nucleus accumbens (NAc). Ro 60-0175 (Ro, 1 mg/kg, i.p.) was injected 15 min prior to cocaine (coc, 15 mg/kg, i.p.). (**a**) Schematic diagram, taken from the Paxinos and Watson atlas (1986), showing representative pictures of the Laser Microdissection and Pressure Catapulting (LMPC) treatment of NAc. Shell and core subregions before, after LMPC, and captured zones are shown. Scale bar = 300 µm, *aca*: anterior part of the anterior commissure, *mfba*: medial forebrain bundle. Western blot analysis and densitometric quantification of (**b**) NAc shell and (**c**) NAc core expressions of P-DARPP-32^{Thr34}, P-DARPP-32^{Thr75}, DARPP-32, and α -tubulin proteins. Histograms represent the mean ± SEM optical density (OD) (n= 6 animals/group). DARPP-32 and α-tubulin values did not differ across the different experimental groups in both the shell (ANOVA, DARPP-32: $F_{(3,20)}$ = 0.63, NS; α-tubulin: $F_{(3,20)}$ = 0.48, NS) and the core subregion (ANOVA, DARPP-32: $F_{(3,20)}$ = 0.35, NS; α-tubulin: $F_{(3,20)}$ = 0.58, NS). **p<0.01, *versus* the corresponding vehicle/vehicle (v/v) groups; $^{++}$p<0.01, $^{+++}$p<0.001, *versus* the corresponding v/coc groups (Fisher's PLSD test). From Cathala et al., *Addiction Biology* 2014.

Publications:

Serotonin$_{2C}$ receptors modulate dopamine transmission in the nucleus accumbens independently of dopamine release: behavioral, neurochemical and molecular studies with cocaine. Adeline Cathala, Céline Devroye, Marlène Maitre, Pier Vincenzo Piazza, Djoher Nora Abrous, Jean-Michel Revest, Umberto Spampinato. *Addiction Biology*. 2014. In press.

Publications in preparation:

Serotonin$_{2C}$ receptor stimulation inhibits cocaine-induced c-Fos expression and DARPP-32 phosphorylation in the rat striatum independently of dopamine outflow. Céline Devroye, Adeline Cathala, Marlène Maitre, Pier Vincenzo Piazza, Djoher Nora Abrous, Jean-Michel Revest, Umberto Spampinato.

Time-course effect of cocaine on DARPP-32 phosphorylation in the rat striatum and nucleus accumbens. Céline Devroye, Adeline Cathala, Marlène Maitre, Pier Vincenzo Piazza, Jean-Michel Revest, Umberto Spampinato.

Axis 4: Itera-AMC- Transversal pathophysiology and innovative therapeutics for aging, memory and cognition

DIPPAL: DIAGNOSTIC PRECOCE ET PLEOTHERAPIE DE LA MALADIE D'ALZHEIMER

LabEx support (2012): 45 000€

Teams: JM. Orgogozo, P Philip, J-F Dartigues

Recruited personnel:

One part time Neurologist, Dr Pascale Cowpply Boni, MD, PhD, Payed by the University of Bordeaux.

Compensation to the University of Bordeaux for the extra work of the PAQUID research team for the selection of 100 normal controls to provide 100 plasma samples matched with the AD (100) and non-AD (20) other neurological diseases provided by the CHU of Montpellier.
Compensation to the ADERA for the administrative work over 2 years.

Objectives of the project
Contribute to a research on plasmatic proteomic biomarkers in AD, run by Pharnext, a private biotech company in Issy les Moulineaux, together with BSI, a private company, then by Pharnext alone after the withdrawal of BSI. Unlike the reasonably well validated ABeta and Tau markers in the CSF, the plasma biomarkers approach is not invasive, much less costly and is actively looked after.

Main results:
In total, 88 potential markers were identified, statistically differentiating controls from AD patients. Of those. Work is in progress to combine them in optimal signatures of AD versus true normals (who did not develop AD during the 5-10 years after plasma sampling) and other neurological diseases. Of those 8 are more discriminating individually and work is in progress to determine which combination could be the most discriminative as an AD "signature".
Further, 2 phase 1 clinical trials were conducted, measuring the level of these biomarkers before and after treatments based on the same rationale in order to explore the validity of these biomarkers to parralel a treatment effect, which could be of great interest for future molecules and combinations screening.

Working plan to continue:
This phase of the research is terminated on our side, except for complementary statistical analyses which are being done free of charge. The best combination of plasma biomarker signature for AD will be tested in subjects from the PAQUID cohort who became demented AFTER the plasma sampling. This additional phase is being financed by Pharnext (100 000 €).

Additional grant obtained:
Funding agency: Oséo, for 120 000 € (total budget of Oséo for DIPPAL: 10,4 M€)
Name of the project: DIPPAL
Total amount: 285 000 €, including the 50% co-financing of the University to Oséo
Date and duration of the grant 7 July 2011 – end of 2013

Publications in preparation: patent applications
Communications: only to the research team: Pharnext, University of Bordeaux & Inserm 897 and CHU of Montpellier, because of the constraints of intellectual and industrial property of Pharnext.

FUNCTIONAL CONTRIBUTION OF NEWLY BORN NEURONS TO THE FORMATION OF REMOTE MEMORIES DURING NORMAL AGING

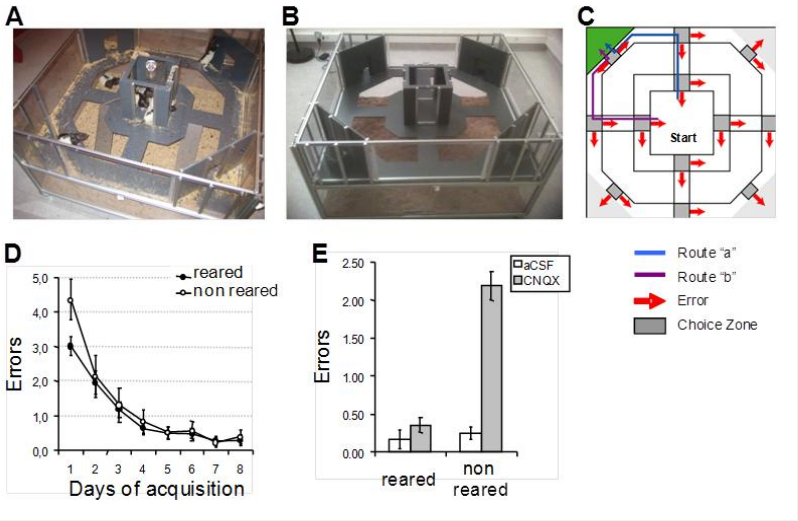
LabEx support (2012): 50 000€+20 000€ (2013)
Teams: Nora Abrous (NCM), Bruno Bontempi (IMN)

Recruited personnel:
Thibault Maviel, post-doc.

Objectives of the project:
By using innovative memory paradigms coupled to region-specific inactivation and imaging of newly-born hippocampal neurons in adult and aged rats, its core objective is to decrypt the nature and dynamics as well as the neuronal constraints within the hippocampal-cortical interface responsible for the formation and stabilization of enduring declarative memories, and to determine how these parameters can be altered during normal aging.

Main results:
We have addressed the potential change in the format of spatial/episodic memory representations (memory transformation due to loss of details and/or flexibility) as they mature and consolidate over time in the cortex by using a behavioral apparatus named the "village", a new maze in which rats can be reared for extended period of time (up to 2 months), thus making it possible to study spatial navigation in a complex, but familiar environment. During the first year of the project, we: 1) made a series of changes to the training procedure and structure of the village prototype and successfully validated the maze by establishing that rats were adopting a hippocampal-dependent strategy to solve

this goal-directed spatial task. 2) unravel a new property of the cortex, that is, the ability not only to store richly detailed familiar spatial information but also to ensure their retrieval flexibly (use of alternate spatial routes) independently of the hippocampus The contribution of the hippocampus is however required to express flexibly unfamiliar cortical memories.



(A) The complex village environment during the rearing period and (B) the spatial testing phase. (C) Schematic illustration of the village showing the start point, the baiterd corner (green), the choice zones, the most direct routes leading to the reward (a and b) and the possible errors. (D) Perfromance during acquisition of reared (1 month in the village) and non reared rats equipped with guide canulas in the dorsal hippocampus. (E) Silencing hippocampal activity with CNQX 1 hour prior to retention testing 1 day after acquisition impaired non reared rats. In contrast, reared rats were spared, indicating that the memory was no longer dependent on the hippocampus but dependent on extrahippocampal strcutures, most likely cortical regions. Sham controls were injected with aCSF as vehicle.

Working plan to continue:

We now seek to 1) identify specific cortical sites involved in memory storage of familiar information. Their inactivation should impair trials with or without obstacle on the familiar route to the baited corner of the maze only in rats reared in the village. Candidate regions are the parietal and cingulate anterior cortices; 2) examine the functional implication of newly born hippocampal neurons in the flexible expression of consolidated memories. We will examine the proportion of new neurons involved in the retrieval of recent and remote familiar and unfamiliar memories, and determine to what extent these neurons are crucial for the establishment of richly detailed cortical cognitive maps in adult and aged rats.

Additional grant obtained:

No grant obtained. One ANR grant "MemoryTrack" submitted in 2013 based on our preliminary findings. Ranked 2 in the complementary list. Will be resubmitted in 2014.

Publications in preparation:

Unraveling a new property of the cortex: the flexible expression of consolidated memories.

TRANSLATIONAL STUDY OF THE CEREBRAL SUBSTRATES INVOLVED IN PATHOLOGICAL FEAR RECOVERY

LabEx BRAIN support (2013-2014): 35 000€/ year for 2 years

Cyril HERRY (NCM); Mélissa BONNET (UMS CNRS 3428)

Recruited personnel:

Simon Ulrich-AI- 6 months. To perform analyses on single unit recordings and local field potentials collected in mice.

Objectives of the project:

The objective of this translational research project was to identify the changes in functional connectivity occurring between neuronal structures involved in emotional processing during relapse of fear behavior in animals and humans. This project combines fMRI and electroencephalography in humans as well as single unit extracellular recordings in mice.

Main results:

Within the first year of the project we have processed all the administrative requirement for studies in healthy humans subjects and obtained the necessary authorization (Agence Nationale de Sécurité du Médicament (ANSM); local ethical committee). We have successfully developed an equivalent of the animal model of auditory fear conditioning in healthy humans and validated the protocol in a cohort of 10 volunteers. In mice 7 animals have been

recorded simultaneously in several neuronal structures during auditory fear conditioning, extinction and fear retrieval. Our preliminary results indicate that coherent activity is increased in the theta range between the prefrontal cortex and the amygdala in animals showing low fear recovery during fear retrieval.

Working plan to continue:
The next steps of this project will be to perform fear conditioning in healthy humans while performing fMRI as well as post-extinction sleep monitoring using electroencephalography. This has been schedule for April 2014. In mice we plan to finalize our recordings and analyses in 7 additional animals.

Publications in preparation:
Dejean C. et al., Temporal encoding of fear behavior in prefrontal neuronal circuits. In preparation

Communications:
Dejean C. et al., Medial prefrontal cortex neuronal ensembles encode conditioned fear behavior, FENS, Milan, July 2014.

Axis 5: Itera-MSA- Transversal pathophysiology and innovative therapeutics for motor, sleep and attention disorders

SLEEP, COGNITION AND ALZHEIMER (SCOAL)

LabEx support (2012): 47 500€
Teams: P. Philip (SanPsy)

Recruited personnel:
Patricia Sagaspe – Researcher - 8 months in 2012

Objectives of the project:
- To study nocturnal sleep architecture (micro- and macro-architecture), sleep/wake rhythms, prevalence of sleep disorders in patients with isolated memory complaints or mild cognitive impairment at inclusion T0 and followed-up 1 year later T1
- To assess whether the presence of sleep disorders accelerates cognitive decline and psycho-affective disturbances after 1 year.

Main results:
Development of an ecological tool of virtual reality MemoShop, based on an usual activity of daily life (i.e., shopping at the supermarket). Memoshop seems reliable to assess episodic memory compared to the reference neuropsychological test in healthy elderlies (n=30) and in patients with isolated memory complaints or mild cognitive impairment.
34 patients with isolated memory complaints or mild cognitive impairment are included in the study. Follow up period (after 12 months) is running.
Intermediate analysis (on 18 patients) shows that 82 % patients with mild cognitive impairment presented respiratory disorders during sleep and 47 % presented periodic leg movement during sleep.

Working plan to continue:
Inclusion of patients is running to November 2014. Follow up period is running to November 2015. At the end of study we can evaluate if sleep-related changes affecting prodromal AD patients could contribute to cognitive and psycho-affective disturbances.

Additional grant obtained:
Funding agency: ANR
Name of the project: SCOAL
Total amount: 225 K€
Date and duration of the grant: October 2011, 4 years

ESTABLISMENT OF A BIOLOGICAL RESSOURCES COLLECTION

LabEx support (2012): 47 500k€
Teams: Erwan Bezard (IMN), Wassilios Meissner (IMN)

Recruited personnel:
Sandrine Villars, clinical research assistant and bioexpert (6 PM)

Objectives of the project:
Setup of a repository for body fluids (cerebrospinal fluid, plasma/serum, urine) of patients with neurodegenerative disorders.

Main results:
Establishment of a repository including standard operating procedures (sample type and circuitry, preanalytics, quality control and storage) by the bioexpert. Beyond funding parts of the salary of the bioexpert, the LabEx has provided support for the necessary acquisition of a centrifuge for preanalytics and software for recording and handling of the samples. Altogether, the LabEx support has allowed creating the infrastructure necessary for the successful conduction of the BIOAMS and BIOPARK cohort studies (see below) and additional studies to come.

Working plan to continue:
The collection of samples of the BIOAMS and BIOPARK cohorts is ongoing. The declaration of the repository at French regulatory authorities is underway, as is the repository accreditation according to AFNOR norm. The first scientific results based on the analysis of samples of the repository are expected for 2015/2016.

Equipments for conduction of biomarkers cohort studies

Additional grant obtained:
Funding agency: PHRC (French Health Ministry), PSP-France
Name of the project: BIOAMS and BIOPARK
Total amount: 200000€
Date and duration of the grant: BIOAMS (2012-2015, BIOPARK 2013-2016)

Publications in preparation:
Review article entitled "Biomarkers in multiple system atrophy"

Communications:

1. Update on MSA - Natural history and biomarkers, Joint Meeting EFAS-ISAN, Giessen, Germany, 31/07/2013.

2. Update on biomarkers for the diagnosis of MSA. 4th International Congress on MSA, Toulouse, France, 20/03/2012.

DOES THE OREXIN SYSTEM CONTRIBUTE TO INDIVIDUAL DIFFERENCES IN SLEEP DEPRIVATION-INDUCED CHANGES IN NEUROBEHAVIORAL FUNCTION?

LabEx support (2013): 45 000€ for 1 year

Pierre PHILIP (Sanpsy) ; Sophie LAYE (NutriNeuro)

Recruited personnel:

Camille Loisseau, engeneer student ISBS (Paris), Victor Bibène, IR , Aurélien Boiseau, AI

Objectives of the project:

Our main objective was to test whether the orexin system could contribute to individual differences in sleep loss induced impairment of neurobehavioral performance.

Main results:

Animal study: After sleep deprivation (SD), we found that the reaction time was increased for some mouse (sensitive to SD) but not others (resistant to SD). After at least 3 days of normal sleep, the two subgroups of animals (sensitive or resistant to SD) received an oral dose of the orexin receptor antagonist (Almorexant) right after the SD period. We found that animals sensitive to SD had a reaction time similar to resistant animals when exposed to Almorexant.

Human study: 6 narcoleptics with cataplexy (low level of orexin) and 6 healthy subjects (high level of orexin) have been sleep deprived during one night. Subjective sleepiness during SD is higher in narcoleptics but constant during all SD. In healthy subjects, Subjective sleepiness is lower at the beginning of SD and higher (same level than narcoleptics) at the end of SD.

Our data thus indicate that orexin may be a key player in sensitivity to sleep loss

Working plan to continue:

Both experiments need to be replicated in larger population (animal and humans) to confirm these data. In human, we must complement these results with an objective assessment of excessive daytime sleepiness measure.

STUDY OF MIRNA EXPRESSION PATTERN AS DIAGNOSTIC AND PROGNOSTIC BIOMARKER IN AMYOTROPHIC LATERAL SCLEROSIS

LabEx support (2013-2014): 44 000€ per year for 2 years

Alexandre FAVEREAUX (IINS) ; Gwendal LE MASSON (NCM) ; Anne-Cécile WIELANEK-BACHELET (Centre référence SLA)

Recruited personnel:

2013 Vanessa Charrier (AI), 2014 Maria José Lopez Gonzalez (Post-doc)

Objectives of the project:

Amyotrophic Lateral Sclerosis (ALS) is an adult-onset neurodegenerative disease leading to muscle wasting, palsy and death due to respiratory failure within 3 to 5 years. Our principal goal is to demonstrate that a specific pattern of miRNA expression in patient's cerebrospinal fluid or blood can be correlated with the definite diagnosis of ALS. A second objective is to correlate the miRNA pattern to the severity and/or progression rate of the disease.

Main results:

The clinical study protocol has been approved by the Centre Hospitalier Universitaire de Bordeaux and the Ethic committee. Therefore, the clinical study was launched on September 2013 and patients' inclusion has started. On January 2014, the clinical study design was improved by adding MRI of all patients in addition to biological sample collection. MicroRNAs' extraction and quantitative PCR protocols have been set up on test samples as well as data collection, transfert and analysis by the Unité de Soutien Méthodologique à la Recherche Clinique et Epidémiologique du CHU de Bordeaux.

Working plan to continue:

Patients' inclusion should be completed within the next year. A first batch of samples will be analyzed when half of the patients will be recruited. Final data analysis will define a specific pattern of miRNA expression that correlates to ALS diagnostic, thus enabling earlier diagnosis and medication. We should also be able to identify specific miRNA as prognostic markers of the ALS disease. This should improve patient management strategies.

Additional grant obtained:
A grant was submitted to the PEPS-IDEX-CNRS call, the project is entitled: "Analyse intégrative de données de grandes dimensions (miRNA et radiologique) appliquée à l'étude MIRSLA: Etude de l'expression des micro-ARN comme biomarqueur diagnostique et pronostique dans la Sclérose Latérale Amyotrophique (SLA).

Axis 6: Non Thematic projects

DECIPHERING THE MECHANISMS OF CENTRAL PAIN SENSITIZATION IN VIVO USING INNOVATIVE HEAT-SHOCK LOCAL DELETION OF THE L-TYPE CALCIUM CHANNEL CAV1.2 GENE IN THE MOUSE LUMBAR BULGE

LabEx support (2013-2014): 43 300€/year for 2 years
Teams: Christel BAUDET (IINS); Pascal FOSSAT (INCIA); Bruno QUESSON (CNRS UMS 3428,TRAIL); Klaus PETRY (INSERM U1049); Erik DUMONT (Image Guided Therapy)

Recruited personnel:
One Master 2 student has been recruited from January to May 2014

Objectives of the project:
- Objective 1: Adapting the existing HIFU technology to our specific aim: a lumbar bulge targeted deletion of the Cav1.2 gene in mice
- Objective 2: Creation and characterization of the Cav1.2 heat-inducible knock-out mouse
- Objective 3: Analyzing the effect of the lumbar bulge targeted deletion of the Cav1.2 gene in neuropathic pain model mice

Main results:
We have tailored a bench-top HIFU system with degassed-water circulation around an ultrasonic transducer to overcome the constraint of animal immersion necessary in existing systems. This apparatus is composed of a programmable single channel electrical generator that allows us to control the power delivery in the transducer. A graphical interface allows simple programming of the generator (frequency, pulse duration, duty cycles…). We then tested several transducers to find the most appropriate (focal length, frequencies, versatility). The relevant apparatus configuration includes an Imasonic transducer characterized by a 1,5Mhz frequency and a 1cm focal length.
We then performed experiments to empirically define the optimal parameters combination allowing a tightly controlled hyperthermia. Using biological tissues substitutes (Phantom gel and/or chicken breast) we could set the "not-burning" parameters. Inserting a thermal sensor in the spinal cord of wild-type adult animals we could empirically correlate power delivery and temperature increase in the spine at the level of the lumbar bulge. We then started to investigate which heating pulse duration and duty cycles should be use to obtain Cre recombinase activity while preserving the tissues integrity. These tests are performed on reporter mice (hsp-Cre/R26-YFP). We are currently running histological analyses of HIFU-treated animals.

Working plan to continue:
Once we will have shown a focalized YFP label in the lumbar bulge of the reporter mice, we will create the hsp Cre/Cav1.2$^{DH-/DH-}$ animals submitting hsp-Cre/Cav1.2$^{flox/flox}$ mice (soon available) to the non-invasive HIFU stimulation previously established to produce the mild hyperthermia necessary and sufficient to obtain the gene deletion. These animals will then be thoroughly characterized at the molecular, biochemical and electrophysiological level. Once characterized, these animals will be subjected to sciatic nerve lesion, a neuropathic pain model, in order to decipher the role of the L-type calcium channel Cav1.2 gene in the mechanisms of central pain sensitization.

RELATIVE CONTRIBUTION OF THE HYPOTHALAMIC PROLIFERATIVE AND NEUROINFLAMMATORY RESPONSES TO THE OBESE PHENOTYPE

LabEx support (2013): 49 000€
Teams: Daniela COTA (NCM); Nora ABROUS (NCM); Sophie LAYE (INRA)

Recruited personnel:
Elodie Ladeveze (AI)

Objectives of the project:
In this project, we propose to investigate whether the relative balance between neurogenesis and neuroinflammation is critical for the CNS regulation of energy balance and if the alteration of the cell-proliferative response resulting from the adaptation to a hypercaloric diet is sufficient to cause rapid changes in food intake and body weight.

Main results:
We investigated whether adult neurogenesis within the hippocampus and the hypothalamus are regulated by high-fat (HF) diet and mTORC1 pathway using S6K1 KO. We found that HF-diet or CNTF treatment did not modify cell proliferation in the DG. In contrast, cell proliferation was reduced in S6K1 KO mice indicating an important role of mTORC1 pathway. Using Dcx as a surrogate of immature neurons we found a reduction of adult neurogenesis in the KO mice and no effect of HF-diet or CNTF treatment. In the hypothalamus, HF-diet increases cell proliferation. We therefore examined the impact of the chronic central administration of Arabinofuranosyl Cytidine (Ara-C) on cell proliferation and energy balance. We found that Ara-C abrogated cell proliferation in mice, an effect that led to decreased food intake, persistent fat mass loss and reduced plasma leptin levels in response to the exposure to a HF-diet, but not to chow. Such treatment inhibited the mRNA expression of orexigenic peptides, while inducing the activation of the mTORC1 pathway in the hypothalamus of HFD-fed mice only. Additionally, AraC treatment decreased Iba-1 and GFAP-positive cells in the hypothalamic arcuate nucleus of HFD-fed mice. Immunological profile of macrophages and microglia assessed by FACS analysis also showed that inhibition of cell proliferation by AraC impairs the number of CD86 and CD36-positive brain macrophages independently of the diet. This last result suggests that AraC induces the polarization of microglia in a M1 phenotype.

Working plan to continue:
To determine the hypothalamic cellular population affected by the AraC treatment, we plan to perform neuroanatomical studies using specific neuronal, astrocyte and microglia markers as well as markers for hypothalamic cell proliferation, apoptosis, neurogenesis and microglia activation to establish the role of such temporal neuroanatomical changes. We also plan to use golgi staining to analyze the morphology of the neurons after Ara-C treatment. To inducibly and selectively fate-map new neurons and their progeny in the hypothalamus, we also plan to use Ai6 x Nestin Cre ERT2 mice for fluorescent labeling of newborn cells.

Additional grant obtained:
Funding agency: Mexican post-doctoral fellowship (D. Cota)
Name of the project: Relative contribution of the hypothalamic proliferative and neuroinflammatory responses to the obese phenotype
Total amount: 40 000 euros
Date and duration of the grant: Sept 2013-Sept 2014 (renewable for 1 more year)

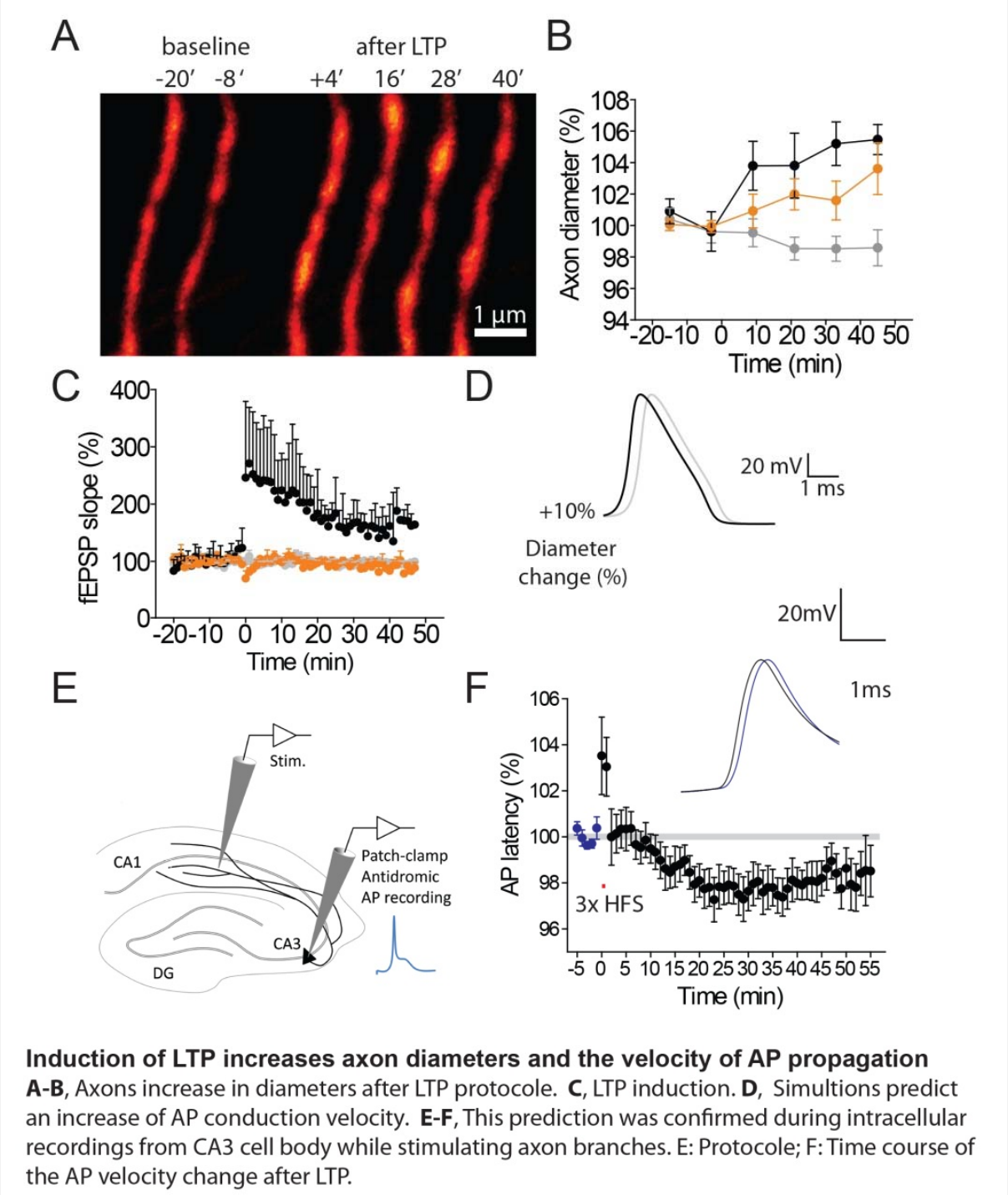
THE IMPACT OF STRUCTURAL CHANGES IN AXONS ON INFORMATION TRANSFERT IN CA3 NEURONS:A COMBINED COMPUTATIONAL AND NANOSCALE IMAGING STUDY

LabEx support (2013-2014): 10 000€/year for 2 years
Teams: Daniel CATTAERT (INCIA); Valentin NAGERL(IINS)

Objectives of the project:
Using a multidisciplinary approach combining STED microscopy, calcium imaging and computer simulations, this project aims at: 1) understanding the basic rules that govern information distribution in axonal arbors of CA3 pyramidal neurons; 2) analyzing the functional significance of axon morphology and structural changes induced by LTP/LTD.

Main results:
The induction of LTP increases CA3 axon diameters and the velocity of action potential (AP) propagation. Our findings indicate 1) that CA3 axons become wider upon LTP induction, 2) that AP conduction velocity is increased upon LTP induction. Before LTP, diameter of CA3 branches was measured with STED microscopy after targeted infection of CA3 pyramidal neurons using Sinbis-GFP in organic mouse hippocampal slice culture. After electrical field stimulation of Schaffer collateral – CA1 synapses that induced a LTP monitored by the slope of field EPSP in CA1, the same axonal branches significantly increased their diameters. Note that in the presence of the NMDA blocker APV, LTP was prevented but the stimulation still evoked a significant CA3 axonal branches diameter increase. Realistic

simulations using the NEURON software, had predicted that such diameter changes would result in velocity increase in CA3 axonal branches. This prediction was confirmed by measuring antidromic spike propagation during the above experiments. These results indicate that axons dynamically tune AP propagation by changing their diameters, and thereby alter the timing of information transfer in neural circuits, suggesting a novel and powerful structural mechanism for neural plasticity.



Induction of LTP increases axon diameters and the velocity of AP propagation
A-B, Axons increase in diameters after LTP protocole. **C**, LTP induction. **D**, Simultions predict an increase of AP conduction velocity. **E-F**, This prediction was confirmed during intracellular recordings from CA3 cell body while stimulating axon branches. E: Protocole; F: Time course of the AP velocity change after LTP.

Working plan to continue:

In a next step, similar experiments and simulations will be used to explore the effects of LTD-induced changes in diameters. This question is crucial because decreasing axon diameters could result in propagation failure. This possibility will be analyzed both experimentally and using simulations to assess the risk of failure and analyze the involved mechanisms.

Communications:

CHEREAU R, CATTAERT D, NAGERL VU (2013) Activity-dependent structural plasticity of hippocampal axons revealed by STED microscopy Annual Meeting of the Society For Neuroscience, San Diego, USA, Novembre 2013.

CHEREAU R, CATTAERT D, NAGERL VU (2013) Induction of LTP increases axon diameters and the velocity of AP propagation Frontiers in Neurophotonics Meeting, Bordeaux, Octobre 2013.

THERMO-SENSITIVE NANOPARTICULES AS A CARRIER OF BIOACTIVE PEPTIDE AGAINST PAIN SENSITIZATION DETERMINING THE MODE OF BINDING OF PSD-95 TANDEM PDZ DOMAINS

LabEx support (2013-2014): 43 300€/year for 2 years

Teams: Marc LANDRY (IINS); Valérie Heroguez (UMR CNRS 5629); Klaus PETRY (INSERM U1049)

Recruited personnel:

Recruited personnel:

Loïc Pichavant, post-doc, 1 year

Objectives of the project (5 lines max):

Our general objective is to perform a proof-of-concept study that validates a non-invasive approach to target the 14-3-3□/GABAB interaction in the spinal cord. The expected outcome is to prevent GABAB dedimerization and to alleviate pain. Our project will therefore test the therapeutical potential of combining Polynorbornene (PNb)-nanoparticles (NPs) and Highly Focused Ultra Sounds (HIFU) stimulation in an animal model of neuropathic pain.

The specific objectives aim (1) to assess the efficiency of -PNb thermo-sensitive NPs to encapsulate, and subsequently deliver CPP-conjugated anti-14-3-3ζ peptides, (2) to improve the penetration of NPs through the brain blood barrier (BBB), (3) to trigger focal drug delivery *in vivo* upon HIFU-mediated elevation of temperature, (4) to assess the antalgic potential of this protocol in animal models of pain.

Main results:

We evaluated and compared two systems of polymeric NPs to entrap a model peptide labeled with a fluorochrome (FITC): a system including linear PNb chains and a system including a cross-linked PNb network (5 w% of a reticulating agent added for the NPs synthesis). We have already shown that (i) more than 2200 and 3800 peptide molecules can be loaded in non-reticulated and cross-linked NPs, respectively, (ii) the peptides are preferentially loaded in the PNb core that undergoes contraction when NPs are solubilized in water, thus preventing peptide leakage.

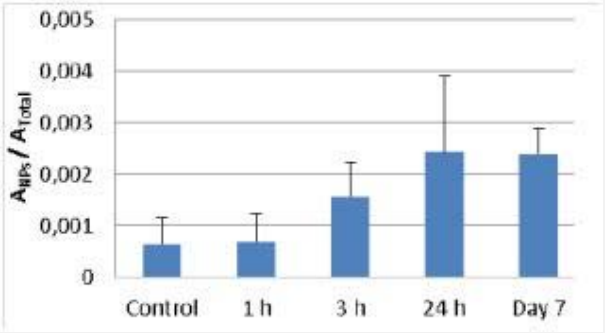


Figure 1 : Quantification of rhodamine-NPs accumulation in the brain after intra-venous injection, at different time points.

In a preliminary study, a Rhodamine B fluorochome has been attached to Nb-chain extremity in order to assess NPs crossing the BBB by fluorescence microscopy and spectroscopy. This experiment has demonstrated NPs time-dependent penetration with a maximum at 24h after injection in the blood stream

Pilot experiments with a prototypical HIFU system have permitted to define the range of conditions for HIFU shots to increase body tissue temperature. They have been successfully carried out *in vitro* on biological substitutes mimicking the spinal cord environment, including the column bones, but also *in vivo* in rats and mice implanted with a thermocouple to monitor temperature increase.

Working plan to continue:

We will further improve the NPs accumulation in the spinal cord. Here again, we will take advantage of the HIFU properties that can temporarily and reversibly increase BBB permeability without long-term tissue damage when used in combination with preformed gas microbubbles, a phenomenon known as acoustic cavitation. We will then establish the sonication protocol to achieve a high yield of release for shorter time of exposure at elevated temperatures, around 43°C. Control experiments will assess possible tissue damage, and alterations of the motor behaviour.

Then, anti-14-3-3ζ peptide-containing PNb NPs will be injected in Sham and neuropathic rats. HIFU exposure will be used to activate thermally the NPs and to trigger peptide release. Pain behavior will be finally tested after NPs activation, and after subsequent application of Baclofen.

DETERMINING THE MODE OF BINDING OF PSD-95 TANDEM PDZ DOMAINS

LabEx support (2013-2014): 47 000€/ year for 2 years
Teams: Matthieu SAINLOS (IINS); Cameron MACKERETH (IECB)

Recruited personnel:
Dolors Grillo-Bosch

Objectives of the project:

We aim at undertaking structural NMR-based studies to understand the precise mode of binding of the tandem PDZ domains of PSD-95-like proteins and biomimetic divalent ligands that we have recently developed. Indeed, these divalent ligands derived from the C-termini of Stargazin, an AMPAR auxiliary subunit, and GluN2A show a remarkable efficiency to acutely disrupt the synaptic anchoring of both types of endogenous receptors in a sequence-specific manner. Our goal is therefore to fully characterize the mode of binding of these synthetic biomimetic ligands and ultimately provide a molecular model for the PDZ domain-mediated interactions involved in the anchoring of Stargazin-containing AMPARs and GluN2A-containing NMDARs.

Main results:

Structural determination of PSD-95 tandem PDZ domains. The first step has consisted in the extensive characterization of the PSD-95 tandem PDZ domains (domains 1 and 2) in order to later be able to analyze the various complexes. We took advantage of the fact that the tandem is composed of two stable domains to employ a bottom-up approach in assigning first the backbone nuclei of the isolated domains in order to simplify assignment of the tandem.

Analysis of the complex with biomimetic divalent ligands. We have focused on two of our most efficient and best characterized divalent ligands, which are derived from Stargazin and GluN2A subunit respectively. We have studied the complexes formed by each monovalent ligands with both the isolated domains and the tandem and identified the specific residues involved in their binding.

Interactomics. In parallel, we have determined the dissociation constants between the various ligands and the PDZ domains and precisely identified by proteomics the cellular targets of the ligands.

Working plan to continue:

Next, we will investigate by NMR the multivalent complexes and compare these ensembles of dataset to determine the mode of interaction of each peptide constructs. The results of our analysis will be verified by production of relevant mutants and binding affinity measurements in order to strengthen and validate our model. Besides the definition of a precise molecular model, the studies will enable us to design ligands with improved efficiency.

Additional grant obtained:

Funding agency: ANR
Name of the project: CheMoPPI
Total amount: 434 747 €
Date and duration of the grant: 01/10/2013-30/09/2016 (36 months)

Publications in preparation:

When the results of the multivalent complexes are obtained, we anticipate one publication on the structural model/interactomics and one on the design of an improved generation of ligands.

Communications:

Poster in the 2nd Meeting of the RSEQ Chemical Biology Group in Bilbao (February 2014)

II- Training Activities

Master program

ISIS: Euro-Mediterranean master's degree in Neurosciences and Biotechnologies

Scientific director: Marc Landry

Description of the master:

ISIS is a Euro-Mediterranean master's degree in Neurosciences and Biotechnology based on the courses offered by 5 European universities, all leaders in neurosciences (Bordeaux, Marseille, Nice, Turin and Valencia) and 6 Universities in the southern Mediterranean area (Alexandria and Senghor Universities in Egypt, Beirut and Jounieh in Lebanon, Tetouan and Marrakech in Morocco). It is a part of a TEMPUS project (2010-2014) financed by the European Commission and coordinated by Bordeaux University. It aims at ensuring standardisation of teaching of neurosciences within the Euro-Mediterranean area and the acquisition of high level competences, knowledge and know-how. The ISIS Master offers innovative pedagogical organization combining on-site and on-line teaching through a Moodle platform, and videoconferences. Particular attention is paid to deliver a unique, common teaching to all students through these pedagogical tools. Student assessment is also common. (See more at: http://www.univ-bordeauxsegalen.fr/en/studies/international-programmes-of-courses/isis-master-s-degree.html#sthash.NQ1LADDj.dpuf).

Number of candidates:
Nb of international students: 5 (2012-2013); 6 (2013-2014)
Nb of local students: 10 (2012-2013); 11 (2013-2014)

Number of selected students:
Nb of international students: 1 (Algeria) (2012-2013); 1 (Switzerland) (2013-2014)
Nb of local students: 6 (2012-2013); 8 (2013-2014)

The data presented here concern only the students registered in Bordeaux. Other students enrolled in the ISIS programme are registered in the partner Universities. The programme has started in 2011 in Morocco, but only in 2012 in Bordeaux; Then, the first class of students is not yet graduated.

Neurasmus

Scientific director: Marc Landry

Description of the master:

Neurasmus is developped through the active cooperation of 6 partner universities and 4 Associated Members.

The 6 Neurasmus academic partners (Université de Bordeaux, Vrije Universiteit Amsterdam, UMG Universitätsmedizin Göttingen, Charité - Universitätsmedizin Berlin, Universidade de Coimbra, Université Laval) are sites of excellence in neuroscience and have a proven track record of close collaboration. Most of them are part of the European Neuroscience Campus Network, a new organization of Neuroscience Centres in Europe, with the aim to organize - and formalize - research collaborations, align grant acquisition strategies and create exchange opportunities at all levels of education and professional work.

In order to boost future brain research in Europe, Neurasmus offers a stimulating, interdisciplinary training environment for young neuroscientists with the goal to prepare them for future challenges in neuroscience research.

Number of candidates: 2011-2013;
Nb of international students: 105, main countries are China, Ethiopia, India, Pakistan…
Nb of local students: 1

Number of selected students: 2011-2013;
Nb of international students: 15

Nb of local students: 0

Number of candidates: 2012-2014;
Nb of international students: 352, main countries are China, Ethiopia, India, Pakistan, Ghana, Bangladesh…
Nb of local students: 3

Number of selected students: 2012-2014;
Nb of international students: 20
Nb of local students:0

What is the future of the 2012-2013 students:
PhD:9
USA School of Medecin:1
Specialization in Medicin:2

BIO-IMAGING

Scientific director: Valentin Nägerl & Eric Thiaudière

Description of the master:

The students will receive high-level training in Bio-Imaging, both theoretical and practical. They will acquire scientific and technological knowledge and experience in the main imaging techniques used in Biology or Biomedicine. The Master program covers a wide range of applications, from cell biology research to maintenance and service. The program will provide expertise in modern bio-imaging approaches to understand pathophysiological processes from cellular and molecular mechanisms to whole body level of integration.

Number of candidates:
Nb of international students:2 (2012-2013); 4 (2013-2014)
Nb of local students: 8 (2012-2013); 12 (2013-2014)

Number of selected students:
Nb of international students: 2 (Lebanon, Germany) (2012-2013); 1 (Bénin) (2013-2014)
Nb of local students: 3 (2012-2013); 7 (2013-2014)

What is the future of the 2012-2013 students):
Three students are pursuing PhD studies in Bordeaux (2) and Laval University (1). One student did not achieve the Master. The last student was looking for a job (no more info).

The bioImaging is on the process to be co-accredited with Laval University in Quebec City (Canada). Selected students will have the opportunity to study one year in the partner University and to get awarded the diploma of both Universities. The "pedagogical agreement" has been written and approved by the scientific and pedagogical coordinators (Marc Landry & Paul de Koninck). Discussions are still pending with the administration to provide the formal frame that will allow opening the co-accredited programme for the next class, starting in September 2014. The University of Mons (Belgium) may be also interested in joining the programme (they are already teaching) and develop co-accreditation procedure.

The programme is still very young and is targeting a very specific segment at the interface between academics and industrials. We need to develop specific tools to support the student search for hosting labs/companies for their internship, and also their professional insertion.

PhD program

SyMBaD Synapses: from Molecules to higher Brain function and Diseases

Description of the program:

The program has started on the 1st of December 2009, as part of the Marie Curie Initial Training Network. It deals with the study of synapses and extends from molecules through higher brain function to diseases.

The SyMBaD program offers PhD students:

- an outstanding training in scientific basic research in academic laboratories;
- the possibility to apprehend research in private companies for some months (up to 6);
- network-wide training activities (workshops and summer schools) and the opportunity to attend the international conferences in Neuroscience;
- the possibility to integrate European and International collaborative networks.

The SyMBaD consortium includes:

- 6 academic institutions: Alicante (SP), Bordeaux (FR), Bristol (UK), Göttingen (GE), Geneva (CH) and Milan (IT);

- 6 private companies: Amplitude Systèmes (FR), BioXtal (CH), Explora Nova (FR), GSK (UK and CHINA), Noscira (SP) and Neurosearch (DA);

- 3 associate private companies: Aptuit (IT), Femtonics (HUNG) and Lilly (UK).

Number of candidates: 150

Number of selected students: 23. They come from 14 countries: 9 EU (France, Germany, Greece, Hungary, Italy, Poland, Portugal, Spain, United-Kingdom) and 5 third countries (Brazil, China, India, Korea, Sudan). The SyMBaD network includes also 9 associated PhD students, hired by local partners.

Number of students in Bordeaux: 7

What is the future of graduated PhD: some SyMBaD students have already negotiated a post-doc position in renowned research institutes in Europe as well as in US and Japan. They could also focus their career in industry following the opportunity that some of them had within SyMBaD to work in the private sector.

EScube

http://www.escube.u-bordeaux2.fr/index.php

The Bordeaux neuroscience community has organized a series of six FENS-IBRO Training Centers since 2006, the European Synapse Summer School, focused on different aspects of synaptic research. The European Synapse Summer School is based on a mix of theoretical lectures (by renowned scientists), methodological demonstrations (carried out also by the Bordeaux Imaging Centre) and hand-on training in the Neuroscience laboratories.

Comparing the number of good candidates applying to the Schools to the number of young scientists that we can select, we conclude that there is a real need for this type of training in Europe.

EScube is highly appreciated by the students and all its editions demonstrated a remarkable success.

See more on the website above.

Number of candidates: 80-170 students have applied every year, from more than 30 countries with a large majority of mid-term PhD students and some young post-doc.

Number of selected students: 20-24 students participated in each edition, coming mostly from Europe, but also from Russia, Japan, US and Latin America.

NUTRIBRAIN

Coordinator: Sophie Layé
Calendar: September 3-14, 2012
LabEx BRAIN support: 15 000€

The 1st edition of the International NutriBrain Summer School was organized in Bordeaux in September 2012. The aim of this new Summer School was to bring young researchers in nutrition to be informed on integrative neuroscience research, but also that students in neurobiology avail themselves of nutritional expertise. NutriBrain welcomed 22 PhD students and post-docs coming from all around the world (USA, Turkey, South Africa, Latvia…). With high-level conferences given from renowned scientists, workshops and practical projects completed in collaboration with four laboratories of the Bordeaux Neurocampus, students have been given access to two weeks of extensive theoretical and practical training. Conferences which dealt with "nutrition and obesity", "cognitive aspects of food intake" and "lipids and brain function" gathered around 500 persons together as it was freely accessible to the scientific community and Master's students of Bordeaux. The second edition of the International NutriBrain Summer School is already planned for 2014.
See more at: http://www.nutribrain.univ-bordeauxsegalen.fr/

Number of candidates: 41

Number of selected students: 22. Nine came from the EU (Belgium, Italy, Latvia, Poland, Spain, The Netherlands), 9 from America (Canada, Mexico, USA) and 4 from Africa (Morocco, South Africa, Turkey)
Students of Bordeaux (Master Nutrition and Master Neurosciences) were offered to assist to the conferences without registering at the school

PhD extension Grants

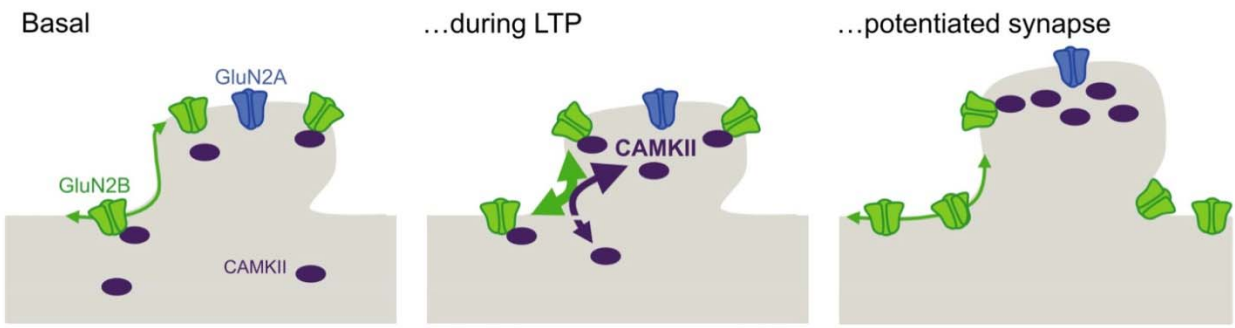
"Role of NMDA receptor surface trafficking during synaptic maturation and plasticity"

Laurent Ladepeche, supervision Laurent Groc, IINS.
LabEx BRAIN support: 10 months-2012

Objectives of the project:
During my PhD I unraveled an unexpected regulation of NMDA receptor surface dynamics by ambient neuromodulators and coagonists, which plays a major role in the plastic range of synapses. We then wanted to investigate the differential mechanisms underlying these processes during maturation (ex. coagonist and subunit dependence), their potential implication in pathophysiological conditions (ex. neurotoxicity) and test them in more integrated models.

Main results:
Using high resolution dynamic imaging techniques (e.g. single particle tracking, FRAP) and high specificity molecular tools (e.g. antibodies, competing peptides), we thus discovered that:

- GluN2B-NMDAR are dynamically redistributed away from glutamate synapses through increased lateral diffusion during LTP in immature neurons.
- NMDAR coagonist switch from glycine to D-serine at maturing synapses drives the replacement of GluN2B- by GluN2A-NMDARs by selectively impacting the surface diffusion of NMDAR (collaboration Dr. Oliet).
- direct interaction with tissue plasminogen activator (tPA, acts as a neurotoxic factor in strokes) modulates extrasynaptic NMDAR dynamic (collaboration Dr. Vivien).
- Blocking NMDAR mobility prevented *in vivo* LTP in CA1 and memory of temporal association between discrete stimuli (collaboration Dr. Marighetto).



Schematic model of the dynamic interplay between surface GluN2B-NMDAR and CaMKII during synaptic long-term potentiation (LTP).
In basal conditions, GluN2B-NMDAR surface diffusion is regulated by the activity of CaMKII. During activity-dependent changes in glutamatergic synaptic transmission, the surface dynamics of GluN2B-NMDAR increase favoring a redistribution of CaMKII through their direct interaction, promoting the accumulation of CaMKII in spines.

Ladepeche et al, EMBO J, 2014

Working plan to continue:

Some experiments are still ongoing in the lab concerning the publications in preparation and to keep further the investigation on the detailed mechanism that is responsible for the selectivity of the effect of the coagonists as well as the modulation by the dopaminergic receptors. I recently joined a group in Barcelona to characterize the influence of the dynamic of NMDAR in psychotic disorders looking at the distribution of receptors at the nanoscale using super-resolution techniques.

Published publications:

Ladepeche L.[#], Dupuis J.P.[#], Seth H., Bard L., Varela J., Mikasova L., Bouchet D., Rogemond V., Honnorat J., Hanse E. and Groc L. *Surface dynamics of GluN2B-NMDA receptors controls LTP of maturing glutamatergic synapses*, EMBO J. 2014 ; in press. doi:10.1002/embj.201386356.

[#]*Equal contribution*

Ladepeche L., Dupuis J.P., Bouchet D., Dounikoff E., Yang L., Campagne Y., Grea H., Bezard E., Hosy E. and Groc L. *Single molecule imaging evidence of the functional crosstalk between surface NMDA and dopamine D1 receptors*, PNAS 2013 ; 110(44):18005-10.

Ladepeche L., Yang L., Bouchet D. and Groc L. *Regulation of dopamine D1 receptor dynamics within the postsynaptic density of hippocampal glutamate synapses,* PloS ONE 2013 ; 8(9): e74512. doi:10.1371/journal.pone.0074512.

Ladepeche L., Dupuis J.P. and Groc L. *Surface trafficking of NMDA receptors: gathering from a partner to another,* Semin. Cell. Dev. Biol. 2013 ; pii: S1084-9521(13)00110-9. doi: 10.1016/j.semcdb.2013.10.005.

Publications in preparation:

Papouin T., **Ladepeche L.**, Yao A., Langlais V., Dulong J., Sacchi S., Mothet J.P., Pollegioni L., Paoletti P., Groc L. and Oliet S.H.R. *Co-agonist availability controls NMDA receptor composition at synapses,* in preparation.

Potier M., Georges F., Brayda-Bruno L., **Ladepeche L.**, Mikasova L., Lamothe V., Bonnet C., Groc L., Marighetto A. *Temporal memory requires surface trafficking of hippocampal NMDA receptors,* in preparation.

Lesept F., Chevilley A., **Ladepeche L.**, Jezequel J., Macrez R., Bertrand T., Hommet Y., Maubert E., Cobo S., Galea P., Groc L. and Vivien D. *The extracellular Serine protease tissue plasminogen activator (tPA) promotes the dynamic of neuronal extrasynaptic NMDA receptors and subsequent signaling through direct NTD-GluN1 (Lys178) coupling,* in preparation.

Communications:

Ladepeche L., Dupuis J.P., Seth H., Bard L., Varela J., Mikasova L., Bouchet D., Rogemond V., Honnorat J., Hanse E. and Groc L. *Surface NMDA receptors dynamic modulation of glutamate synapse plasticity.*
Barcelona, Spain, November 2013. **Invited seminar**

Ladepeche L.#, Dupuis J.P.#, Seth H., Bard L., Varela J., Mikasova L., Bouchet D., Rogemond V., Honnorat J., Hanse E. and Groc L. *Plasticity of maturing glutamate synapses requires NMDA receptors lateral mobility.* Frontiers in Neurophotonics, Bordeaux, October 2013. **Selected talk**

Ladepeche L., Dupuis J.P., Papouin T., Mikasova L., Bouchet D., Bard L., Rogemond V., Imperiali B., Honnorat J., Sainlos M., Oliet S. and Groc L. *Surface dynamics of glutamate receptors: lateral shaping of synaptic plasticity.* Tsukuba, Japan, April 2013. **Invited seminar**

Ladepeche L.#, Dupuis J.P.#, Seth H., Bard L., Varela J., Mikasova L., Bouchet D., Rogemond V., Honnorat J., Hanse E. and Groc L. *Plasticity of maturing glutamate synapses requires NMDA receptors lateral mobility.* #*Equal contribution* 4th European Synapse Meeting, Bordeaux, August 2013. **Poster**

Ladepeche L., Dupuis J.P., Bouchet D., Dounikoff E., Yang L., Campagne Y., Grea H., Bezard E., Hosy E. and Groc L. *Single molecule crosstalk between surface NMDA and dopamine D1 receptors tunes plasticity at excitatory synapses.* 4th European Synapse Meeting, Bordeaux, August 2013. **Poster**

"Cannabinoid type 1 receptor (CB1) deletion in discrete hypothalamic nuclei: its role in energy and glucose homeostasis"

Pierre Cardinal, supervision Daniela Cota, NCM.

LabEx BRAIN support: 10 months-2012

Objectives of the project:

The endocannabinoid system impacts energy balance regulation at both central and peripheral level. The hypothalamus is one of the main regions involved in the control of food intake and body weight. Different hypothalamic nuclei exert specific functions in this context. The main objective of this project was to determine the role of the cannabinoid type 1 (CB1) receptor in the regulation of energy balance when its expression is deleted in specific hypothalamic nuclei.

Main results:

Our studies on the role of the CB1 receptor in the ventromedial hypothalamus (VMN) demonstrate that this receptor regulates the organism's metabolic flexibility to environmental dietary changes by orchestrating peripheral use of energy substrates and behavioral and metabolic responses to the adipocyte-derived hormone leptin.

Differently, the studies carried out in mice specifically lacking CB1 receptors in the paraventricular nucleus (PVN) have shown that deletion of CB1 protects from diet-induced obesity by inducing increased sympathetic nervous activity (SNS), with consequent heightened energy expenditure.

Working plan to continue:

The manuscript on the role of CB1 receptor in the VMN is currently under review at The Journal of Clinical Investigation.

Concerning the study on the role of CB1 in the PVN, additional experiments will be performed to better clarify the SNS activity changes induced by the deletion of CB1 in PVN neurons, and the manuscript will then be resubmitted.

Publications:

Cardinal P, Bellocchio L, Clark S, Cannich A, Klugmann M, Lutz B, Marsicano G, Cota D. Hypothalamic CB1 Cannabinoid Receptors Regulate Energy Balance in Mice. Endocrinology, 2012 Sep;153(9):4136-43.

Bermudez-Silva FJ, Cardinal P, Cota D. The Role of the Endocannabinoid System in the Neuroendocrine Regulation of Energy Balance. J Psychopharmacol 2012 Jan; 26(1):114-24. (revue)

Dubreucq S, Matias I, Cardinal P, Häring M, Lutz B, Marsicano G, Chaouloff F. Genetic Dissection of the Role of Cannabinoid Type-1 Receptors in the Emotional Consequences of Repeated Social Stress in Mice. Neuropsychopharmacology 2012 July; 37(8):1885-900.

Bellocchio L, Soria-Gomez E, Quarta C, Metna-Laurent M, Cardinal P, Binder E, Cannich A, Delamarre A, Häring M, Martín-Fontecha M, Vega D, Bartsch D, Monory K, Lutz B, Chaouloff F, Guzman M, Pagotto U, Cota D, Marsicano G. Activation of the sympathetic nervous system mediates hypophagic and anxiety-like effects of CB1 receptor blockade. PNAS, 2013, March 9;110(12):4786-91

Bosier B, Bellocchio L, Metna-Laurent M, Soria-Gomez E, Matias I, Cannich A, Maitre M, Verrier D, Leste-Lasserre T, Cardinal P, Mendizabal-Zubiaga J, Canduela MJ, Reguero L, Chaouloff F, Hermans E, Grandes P, Cota D, Marsicano G. Critical role of astroglial CB1 cannabinoid receptors in the regulation of leptin-mediated functions. Mol Metab. 2013 Aug 9;2(4):393-404.

Publications in preparation:

Cardinal P, Bellocchio L, Quarta C, Clark S, Elie M, Leste-Lasserre T, Maitre M, Cannich A, Pagotto U, Marsicano G, Cota D. Diet-dependent bidirectional regulation of energy balance by CB1 cannabinoid receptor in the ventromedial hypothalamus. Under review at The Journal of Clinical Investigation.

Cardinal P, Bellocchio L, Clark S, Elie M, Leste-Lasserre T, Cannich A, Marsicano G, Cota D. Cannabinoid type 1 (CB1) receptors on Sim1-expressing neurons regulate energy expenditure via the sympathetic nervous system. To be resubmitted.

Mancini G, Srivastava RK, Aparisi Rey A, Quarta C, Cardinal P, Tedesco L, Zingaretti CM, Sassmann A, Conrad A, Schwitter C, Wettschureck N, Monory K, Cinti S, Marsicano G, Offermanns S, Nisoli E, Cota D, Pagotto U, Lutz B. Adipocyte cannabinoid CB1 receptor is a key regulator of body energy homeostasis. To be resubmitted to Nature Medicine.

Communications:

Cardinal, P, Bellocchio L, Clark S, Elie M, Marsicano G, Cota D." The role of CB1 located in the ventromedial nucleus in energy and glucose homeostasis." TOS meeting in Orlando (USA), October 2011

Cardinal, P, Bellocchio L, Clark S, Elie M, Marsicano G, Cota D." The role of CB1 located in the ventromedial nucleus in energy and glucose homeostasis." Neurocentre Magendie Symposium in Bordeaux (France), December 2011

Cardinal, P, Bellocchio L, Clark S, Elie M, Marsicano G, Cota D." The role of CB1 located in the ventromedial nucleus in energy and glucose homeostasis." European Congress of Obesity in Lyon (France), May 2012

"Dietary omega-3 deficiency and emotional behaviors: role of hypothalamic-pituitary-adrenal axis"

Thomas Larrieu, thèse sous la direction de Sophie Layé, NutriNeuro.

LabEx BRAIN support: 10 months

Objectives of the project:

The nutritional omega-3 deficiency observed in Western countries could have huge consequences, as it has been associated with many diseases, including mood disorders. Nowadays, mechanisms underlying the effects of omega-3 deficient diet on mood disorders remain largely unknown. In the present project we unravel molecular and cellular mechanisms by which nutritional disturbances lead to impaired emotional behaviour in mice.

Main results:

In this work, our findings can be summarised in two major observations:

1- Dietary omega-3 deficiency induces a chronic stress state reflected by hypothalamic-pituitary-adrenal (HPA) axis hyperactivity. This, lead to neuronal atrophy in the dorso- and ventro-medial prefrontal cortex (mPFC) and mood-related behaviours alteration, similarly to chronic social defeat stress.

2- Dietary omega-3 supplementation induces resilience to the effects of chronic social defeat stress on emotional behaviours by preventing HPA axis hyperactivity and neuronal atrophy in mPFC.

Working plan to continue:

One possible molecular candidate to explain these alterations is fatty acid amide hydrolase (FAAH) which is involved in the degradation of endocannabinoids. Indeed, it has been nicely shown that increase FAAH activity, is crucial for chronic stress-induced anxiety and neuronal plasticity. It will be interesting to measure FAAH activity and see if suppression of FAAH can normalize the behavioural and structural plasticity changes observed in the n-3 deficient animals.

Additional grant obtained:
Postdoctoral fellowship from the "société française de nutrition (SFN)"

Publications in preparation:
Nutritional omega-3 deficiency induces a chronic-stress phenotype in mice.
Thomas Larrieu, Muna L Hilal, Célia Fourrier, Véronique De Smedt-Peyrusse, Nathalie Sans, Lucile Capuron and Sophie Layé

« Nanoscale functional organization of branched F-actin networks and N-cadherin adhesion during dendritic spine motility"

Anael Chazeau, supervision Grégory Giannone, IINS.
LabEx BRAIN support: 10 months

Objectives of the project:
The objective of my Ph.D. project was to unravel how actin-binding proteins and N-cadherin adhesion regulate the organization and dynamics of F-actin network in dendritic spines.

Main results:
In a first study, by performing quantitative live imaging experiments and computer simulations, we demonstrated that engagement of a mechanical connection between trans-synaptic N-cadherin adhesions and the actin/myosin network stabilizes dendritic spines.
In a second study, using single protein tracking and super-resolution imaging we revealed the dynamic nano-organizations of branched F-actin regulators within spines. Branched F-actin nucleations occur at the PSD vicinity, while elongations occur at membrane protrusion tips.

Working plan to continue:
The first study will be submitted beginning of June, while the second one will be resubmitted in March. To widen our first study, we plan to focus on the intracellular signaling pathways leading to spine head expansion during the transition from a filopodium to a spine. To go beyond our second study, we want to understand how the nanoscale organization and dynamics of branched F-actin networks in dendritic spines are reorganized during synaptic plasticity protocols. To do so we are developing a new microscope to be able to perform super-resolution microscopy on organotypic slices. Finally we are also developing a new simulation program to reach a detailed understanding of actin, actin regulators and adhesion protein dynamics within a variety of subcellular structures.

Publications in preparation:
Chazeau A, Garcia M, Czöndör K,Argento A, Perrais P, Levet F, Giannone G, Thoumine O. A mechanical coupling between N-cadherin adhesions and F-actin flow stabilizes dendritic spines. To be submitted to Mol. Biol. Cell.
Chazeau A., Nair D., Gautier J., Leduc C., Thoumine O., Choquet D., Gautreau A., Sibarita J.B., Giannone G. Nanoscale organizations and dynamics of branched actin network regulators within dendritic spines. To be submitted to EMBO J.

Communications:
Poster presentations: "Evidence for a mechanical coupling between N-cadherin adhesions and F-actin in stabilizing dendritic spines". Journée de l'école doctorale Arcachon (Mars 2010, 2011, 2012); EMBO Workshop Heraklion (Mai 2011); FENS Barcelone (Juillet 2012); 10th Göttingen Meeting (Mars 2013).

Oral presentation: "Nanoscale organization and dynamics of branched actin network regulators within dendritic spines" Frontiers in Neurophotonics Bordeaux (Octobre 2013).

"Alterations of dendritic electrogenesis in layer 5B pyramidal neurons in a mouse model of Fragile X Syndrome"

Audrey Bonnan, supervision Andreas Frick, NCM
LabEx support: 8 months

Objectives of the project:
The aim was to use the LabEx support to have the opportunity to 1) complete our experiments on the dysfunction of dendritic excitability in *Fmr1*KO mice; 2) to wrap up our project in collaboration with Prof. R. Kramer on the

photocontrol of dendritic excitability using a small molecule photoswitch (QAQ) and 3) to write and submit the corresponding publications.

Main results:

For the first project, we were unfortunately unable to perform the calcium imaging experiments of populations of pyramidal neuron dendrites in response to sensory stimulation *in vivo* which were originally planned in collaboration with Dr. M. Larkum, due to issues with the animal transfer agreement. However, we performed *in vivo* electrophysiological recordings from single layer 5 pyramidal neurons in anesthetized mice in our own laboratory and find changes in the same dendritic/cellular parameters as in our *in vitro* recordings from these neurons. We also used western blots experiments to probe the mechanisms of h-channel dysfunction in the dendrites of *Fmr1*KO mice. We found a reduction in the expression level of HCN1 but not HCN2 in the somatosensory barrel cortex, which is consistent with our electrophysiological and calcium imaging data. For the second project, we performed new experiments showing that the use of QAQ can allow photocontrol of a form of short-term plasticity. More specifically, we showed that we can control DSI (Depolarization-Induced Suppression of Inhibition) with light in CA1 pyramidal with QAQ in the recording pipette. Finally, the paper from the first project is submitted, and the paper from the second project is almost ready for submission.

Working plan to continue:

The two projects mentioned above are now completed and I moved to Dr. Jason Christie's laboratory (MPFI, Florida) for a post-doctoral training. The working plan concerning these projects is now to work on the papers until publication.

Publications:

Szlapczynska, M., Bonnan, A., Ginger, M. & Frick, A. Plasticity and Pathology of Dendritic Intrinsic Excitability. *Horizons in Neuroscience Research*. **14,** (Nova Publishers) 2014, *In Press*.

Publications in preparation:

-Yu Zhang*, Audrey Bonnan*, Isabelle Ferezou, Guillaume Bony, Melanie Ginger, Nathalie Sans, Jean Rossier, Ben Oostra, Gwen LeMasson and Andreas Frick. The Cellular Basis of Sensory Hypersensitivity in the Fmr1 Knockout Mouse Model of Fragile X Syndrome. *Submitted*.

-Audrey Bonnan, Yu Zhang, Alexis Fedorchak, Richard Kramer, Andreas Frick. Optical control of dendritic excitability with an intracellular photoswitch molecule. *In preparation.*

Communications:

"Channelopathies in neocortical dendrites in Fragile X Syndrome", Max Planck Florida Institute (July 12th, 2013)

Role of the endocannabinoid system in morphological plasticity probed by two-photon excitation STED microscopy

Philipp Bethge, supervision Valentin Nagerl, IINS
LabEx BRAIN support: 12 months

Objectives of the project:

- Optimize the homebuilt two-photon excitation STED microscope
- Use the microscope to study the role of the endocannabinoid system on morpho-functional plasticity using pharmacological tools
- Apply the microscope to *in vivo* STED imaging of spines in the murine cortex
- Advance collaborative projects
- Train new team members to use the microscope
- Write and defend the PhD Thesis and find a post-doctoral position

Main results:

- The custom two-photon excitation STED microscope has been updated with critical optical components (new scan- and tube lens combination) to reduce chromatic aberrations and thus improve optical performance over larger fields-of-view. Extensive troubleshooting has reduced mechanical vibrations and image artifacts due to electrical interference (ground-loops) affecting the beam scanner.
- Preliminary experiments suggest that bath application of a cannabinoid receptor 1 (CB1) agonist leads to acute changes in spine morphology of CA1 pyramidal neurons.

- *In vivo* imaging of dendritic spines in the barrel cortex has been established.
- More data for a collaborative project on the morphology of dendrites in the dentate gyrus has been collected and a new project has started with the group of Christophe Mulle, IINS Bordeaux, investigating Alzheimer related morphological alterations in CA3 of the hippocampus.
- Two new PhD students are being trained to operate the microscope.
- I finished writing my PhD thesis (defense date is March 27th, 2014).
- I interviewed for postdoc positions and obtained an offer by Fritjof Helmchen at the University of Zürich, which I accepted (starting Fall 2014).

Working plan to continue:
- The number of experiments using agonists will be increased and supplemented with the treatment of antagonists
- Experiments and analysis for collaborative projects will be finished before the end of the funding period
- Optimization of the microscope and development of surgical skills for *in vivo* experiments.

Additional grant obtained: N/A

Published results:
- Springer Book: Nanoscale Imaging of Synapses: New Concepts and Opportunities. U. Valentin Nägerl and Antoine Triller (Eds.) Chapter 11: Two-photon STED microscopyCommunications:

Adolescence, a period of vulnerability to the effects of obesity on memory: a focus on hippocampus and amygdala

Chloé Boitard, supervision Guillaume Ferreira, NutriNeuro
LabEx BRAIN support: 10 months

Objectives of the project:

During my PhD work, I evidenced the vulnerability of the juvenile period (compared to adulthood) to the detrimental effects of high-fat diets on endocrinology, neurophysiology and memory. We now need to achieve the peer-review process on our submitted articles and to publish our recent work, obtained at the end of my PhD, on the mechanisms explaining how the diet can impact on brain functioning as well as on the reversibility of the detrimental effects induced by high-fat diet (HFD) when animals are shifted back to standard diet.

Main results:

We evidenced that juvenile high-fat diet exposure leads to impaired hippocampal function together with enhanced amygdala function, a bidirectional pattern that can be induced by glucocorticoids action (PhD work). Interestingly, glucocorticoid release is modified in obese, and we demonstrated that juvenile high-fat diet exposure protracts the normal corticosterone release after stress. Moreover, we were able to demonstrate this protracted corticosterone release was responsible for amygdala-dependent memory enhancement since blockade of glucocorticoid action directly in the basolateral nucleus of the amygdala was sufficient to restore normal memory in juvenile high-fat fed rats.

In another study, we also demonstrated that shifting adult rats back to control diet after exposure to high-fat during the juvenile period was sufficient to restore all the detrimental effects (i.e. on memory, neurophysiology and endocrinology) induced by the high-fat diet.

Working plan to continue

It should now be assessed how the detrimental effects we described after juvenile high-fat diet exposure interact with each other. If we demonstrate that modified glucocorticoid release is responsible for amygdala enhancement, we did not assess its role on hippocampal impairment. Moreover, juvenile high-fat diet exposure appears to rapidly decrease hippocampal neurogenesis, which can be responsible for protracted glucocorticoid release. Thus the temporal pattern of emergence of the detrimental effects of juvenile high fat diet exposure and the causality between those effects remains to be assessed (see Fig. 1).

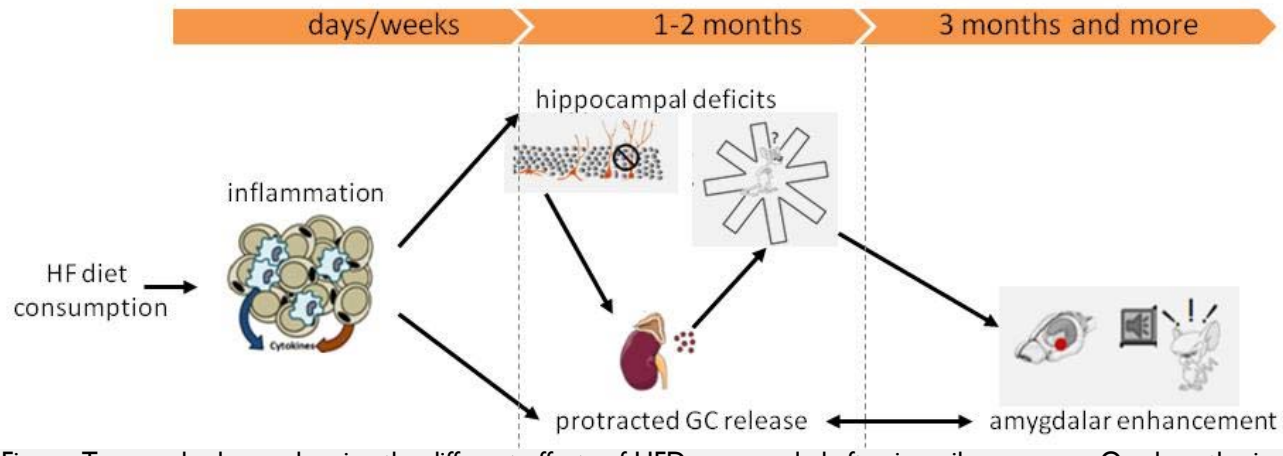


Figure: Temporal scheme showing the different effects of HFD we revealed after juvenile exposure. Our hypothesis concerning the causality of these effects is represented by the black arrows.

Published publications:

Boitard C, Etchamendy N, Sauvant J, Aubert A, Tronel S, Marighetto A, Layé S & Ferreira G (2012). Juvenile, but not adult, exposure to high-fat diet impairs relational memory and hippocampal neurogenesis in mice. Hippocampus 22(11):2095-100.

Publications in preparation:

Boitard C, Cavaroc A, Sauvant J, Aubert A, Castanon N, Layé S & Ferreira G. Impairment of hippocampal-dependent memory induced by juvenile high-fat diet intake is associated with enhanced hippocampal inflammation in rats. Special Issue "Diet, Inflammation and the Brain" in Brain, Behaviour and Immunity, Submitted.

Boitard C, Maroun M, Tantot F, Cavaroc A, Sauvant J, Coutureau E, Marchand A, Capuron L, Castanon N, Darnaudéry M, Layé S, Vouimba RM & Ferreira G. Juvenile obesity enhances emotional memory and amygdala plasticity through glucocorticoids. In progress

Boitard C, Cavaroc A, Sauvant J, Layé S & Ferreira G. Endocrinology, neurophysiology and memory disruptions induced by juvenile high-fat diet exposure are restored following a shift back to control diet exposure at adulthood. In progress

Communications:

My PhD work was already presented through 16 posters and 2 invited lectures during my PhD internship. Additional work supported by the LabEx BRAIN was presented during the 3rd "Doc/post-doc day" of NutriNeuro's lab (28/01/2014, Bordeaux), "Endocrinology, neurophysiology and memory disruptions induced by juvenile high-fat diet exposure are restored following control diet exposure".

This work may also be presented to the 7th Nutrition & Neurosciences Symposium (14/03/2014).

Role of prefrontal parvalbumin interneurons in the expression of conditioned fear behavior

Julien Courtin, supervision Cyril Herry, NCM

LabEx BRAIN support:12 months

Objectives of the project:

The main objective of the research project was to evaluate if the neuronal changes occurring in specific population of cortical inhibitory interneurons was causally related to expression of conditioned fear behavior in mice. To this purpose we used a combination of extracellular recordings, optogenetic manipulations and behavioral approaches.

Main results:

Thanks to the Labex Brain support we have been able to demonstrate using optogenetics that neuronal inhibition of a subpopulation of prefrontal inhibitory interneurons –expression the calcium binding protein parvalbumin (PV) was

causally related to fear expression in behaving mice. Inhibition of prefrontal PV interneurons disinhibits projection neurons to drive fear expression. Moreover, we observed that inhibition of these interneurons during fear behavior is also associated with the genesis of cortical oscillations in the theta range that allow the synchronization of principal neuron activity during fear expression. These results identify two complementary mechanisms mediated by PV interneurons that precisely coordinate and enhance the neuronal activity of prefrontal projection neurons to drive fear expression.

Working plan to continue:

It is still unclear how inhibition of prefrontal PV interneurons can be associated with the genesis of theta oscillations. This could rely on the existence of two neuronal oscillators that could compensate each other under baseline conditions, PV interneurons would be in this configuration one of the two oscillators. Alternatively, prefrontal principal interneurons could also be directly involved in the genesis of theta oscillations. We are currently using optogenetic approaches in behaving animals to disentangle these possibilities.

Published publications:

Courtin, J., Chaudun, F., Rozeske, R.R., Karalis, N., Gonzalez-Campo, C., Wurtz, H., Abdi, A., Baufreton, J., Bienvenu, T.C.M., and Herry, C. (2014). Prefrontal parvalbumin interneurons shape neuronal activity to drive fear expression. Nature, 505: 92-96. IF: 38.597

Publications in preparation:

Karalis, N., Courtin, J., Dejean, C., et al., 4 Hz oscillations synchronize prefrontal-amygdala neuronal circuits during fear behavior. In preparation

Communications:

Courtin, J., Wurtz, H., and Herry, C., Prefrontal interneurons in fear behavior, FENS meeting, Milan, July 2014

Development of novel micro-patterned substrates for axonal growth and synaptogenesis

Mikael Garcia, supervision Olivier Thoumine, IINS

LabEx BRAIN support: 12 months

Objectives of the project:

The objectives of my project are to characterize the role of the mechanical coupling between the actin motile machinery and N-cadherin adhesions in two important brain developmental processes, namely axonal outgrowth and synaptic morphological plasticity. To reach these objectives, I am performing high resolution live imaging experiments in hippocampal neurons expressing fluorescently-tagged adhesion and cytoskeletal proteins.

Main results:

Since the grant started, I have performed Fluorescence Recovery After Photobleaching (FRAP) experiments to measure actin-GFP turnover in dendritic filopodia and spines. The actin recovery is faster in immature dendritic filopodia than in spines, indicating a more dynamic actin network. We expressed either wild type N-cadherin to strengthen N-cadherin adhesions, or a non-adhesive N-cadherin mutant acting as a competitor for catenin scaffolding molecules. Fluorescence recovery was faster in dendritic spines expressing the N-cadherin mutant, consistent with the concept that actin is stabilized through a linkage with N-cadherin adhesions. We have also built computer simulations describing the motion of single actin molecules in model dendritic structures, and are adjusting kinetic parameters to fit the model to experimental data.

In parallel, we developed computer simulations describing the motion of single actin and N-cadherin molecules in adhesive and non adhesive area within growth cones, based on diffusion and kinetic parameters obtained from our previous spt-PALM experiments using mEOS2-tagged molecules. These simulations will be compared to FRAP experiments to be performed on GFP-tagged N-cadherin, α-catenin, and actin, accumulated at N-cadherin coated micropatterns. Interestingly, enrichments and slowing events calculated from these simulations are comparable with the ones observed experimentally.

Working plan to continue:

Related to the project on dendritic filopodia/spines, we plan to perform optical tweezers experiments with beads coated with N-cadherin, in neurons expressing N-cadherin mutants.

To understand the precise role of α-catenin in the mechanical coupling between N-cadherin and actin in growth cones, I would like to examine the effect of siRNA against this protein on the actin flow. I would like to see if knocking down α-catenin would rescue normal actin flow on N-cadherin adhesions area.

Publications in preparation:

Garcia M, Argento A, Leduc C, Sibarita JB, Thoumine O.
Individual slip bonds between flowing actin and the N-cadherin/catenin complex in growth cones.
To be submitted to Science.

Chazeau A*, Garcia M*, Czöndör K*, Argento A, Perrais P, Levet F, Giannone G, Thoumine O.
A mechanical coupling between N-cadherin adhesions and F-actin flow stabilizes dendritic spines.
To be submitted to Mol Biol Cell(*) equally contributing first authors.

Alterations in neocortical circuits are a crucial feature of cognitive defects in Fragile X Syndrome

Matthias Haberl, supervision Andreas Frick, NCM
LabEx BRAIN support:12 months

Objectives of the project:

Fragile X syndrome (FraX) is the most common inherited cause of mental retardation and autism in humans and leads to deficits of learning and memory and a high prevalence of autistic behavior, seizures, hypersensitivity to sensory stimuli and alterations in the processing of sensory information. We are investigating the structural and functional alterations that occur in the neocortical wiring of the Fmr1KO2 mouse model.

Main results:

We found large-scale connectivity changes in the *Fmr1*KO2 mice. We found deficits on the structural level and a functional decoupling of several cortical areas using diffusion-tensor-imaging (DTI) and functional magnet-resonance-imaging (fMRI) measurements. The structural deficits are on a fine-scale composed of an altered short- and long-range connectivity. To study the deficits on a cellular level we developed a novel anterograde (i.e. infecting cells at the cell body) tracer using a modified rabies virus (SADΔG(chimera glycoprotein)). This tracer permits sparse labeling of neurons and the visualization of all morphological details such as dendritic spines or axonal boutons (Haberl et al., 2014). We are using a combination of retrograde (Wickersham et al., 2007 Nat Meth) and the novel anterograde (Haberl et al., 2014) rabies virus tracing to map the cellular components of the structural wiring deficits. Alterations in the anatomical wiring provide a potential mechanism for the devastating effects on sensory processing in FraX and help to identify promising rescue strategies.

Working plan to continue:

Our study will provide us with the framework to test novel therapeutic agents in their capability to reverse changes in the anatomical wiring in FRAX, which might be essential to reverse cognitive deficits. Recently one small molecule demonstrated the potential to reverse aspects of the reported spine defects (Dolan et al., PNAS 2013). We will test its capability to restore the normal connectivity of the input map in *Fmr1*KO mice.

Additional grant obtained:

EuroBioImaging study using functional magnet-resonance-imaging (fMRI) and diffusion tensor imaging (DTI) research on the large scale connectivity in fragile X mice

Published publications:

*Ginger, M., *Haberl, M., Conzelmann, K.K., Schwarz, M.K., Frick, A. (2012) 'Revealing the secrets of neuronal circuits with recombinant rabies virus technology.' Front Neural Circuits. 2013;7:2.

*Haberl, M.G., *Viana da Silva, S., Guest, J.M., Ginger, M., Ghanem, A., Mulle, C., Oberlaender, M., Conzelmann, K.K., Frick, A. *'Anterograde tracing using a novel envelope-switched ΔG rabies virus variant. Brain Structure and Function (In Press)* DOI: 10.1007/s00429-014-0730-z.
*Equal contributions

Publications in preparation:

Haberl, M., Zerbi, V., Veltien, A., Ginger, M., Heerschap, A. and Frick, A. '*Structural and functional connectivity deficits in neocortical circuits of Fragile X mice*'

Viana da Silva, S., Haberl, M., Labrousse, V., Gorlewicz, A., Blanchet, C., Frick, A., Mulle, C., '*Synapse Specific Morphofunctional Alterations in a Mouse Model of Alzheimer's Disease in CA3 pyramidal cells*'.

Communications:

"A novel anterograde rabies virus vector for high-resolution large-scale reconstruction of 3D neuron morphology" Haberl, M., Viana da Silva, S., Guest, J.M., Ginger, M., Ghanem, A., Mulle, C., Oberlaender, M., Conzelmann, K.K., Frick, A. Nov. 7th 2013, The Networked Brain Cell Conference San Diego (USA); Poster Presentation

"*New developments to study neuronal circuits using RabV based viral tracing"* Haberl, M.; Viana da Silva, S.; Ginger, M.; Mulle, C.; Conzelmann, K.-K.; Frick A. Oct. 17th 2012, SfN Meeting New Orleans, Novel Microscopic Methods; Nanosymposium Talk

"*Pathophysiology of hippocampal CA3 area in Alzheimer's disease*." Viana da Silva, S.; Haberl, M.; Blanchet, C.; Mulle, C. Oct. 17th 2012, SfN Meeting New Orleans (USA), Poster Presentation

"*Studying Neuronal Circuits Using Rabies Virus Based Tracing*" Haberl, M.; Ginger, M.; Frick, A. July 15th, 2012, FENS Meeting Barcelona, Poster Presentation "*Connectivity-changes of cortical circuits as crucial feature of cognitive defects in Fragile X Syndrome*", Barcelona (Spain) Haberl, M.; Ginger, M.; Frick, A. 13th July 2012 ENC Annual Meeting Barcelona, Talk

"*Measuring Neocortical Connectivity in Fragile X Syndrome*", 3rd European Synapse Meeting, Balatonfüred, (Hungary), Oct. 13-15th 2011, Poster Presentation "*Neocortical circuitry in Fragile X Syndrome*", Annual Meeting Symbad ITN PhD Training, Balatonfüred, (Hungary), Oct. 11th 2011, Talk

"*Changes in neocortical connectivity as a feature of fragile X syndrome*", Haberl, M.; Ginger, M.; Frick, A. May 25-26th 2011, 'Computations in Neocortical Circuits, What does the Cortex Do', Janelia Farm HHMI Research Campus Conference (VA, USA), Poster Presentation "*Neocortical circuitry in a model of mental retardation*", Haberl, M.; Ginger, M.; Frick, A. Young Scientist Symposium, Bordeaux (France); 20th May 2011, Talk

"*Alterations in the neuronal connectivity of neocortical circuits as crucial feature of cognitive defects in Fragile X Syndrome*" Haberl, M.; Ginger, M.; Frick, A. March 23rd 2011, ENC Network Kick-Off Meeting, Göttingen (Germany), Talk

Activity-dependent regulation of AMPA-type glutamate receptors trafficking by auxiliary proteins interaction with PSD-95

Anne-Sophie Hafner, supervision Daniel Choquet, IINS

LabEx BRAIN support: 12 months

Objectives of the project:

The difference between TARP γ-2 (stg) and γ-8 might come from differences in their primary structures. Although they share 59% identity and 74% homology, γ-8 possesses unique insertions that make its intracellular C-terminus domain 76 amino-acids longer than γ-2. The objective of the project is to determine the impact of TARP C-terminus domain length on the properties of AMPAR complexes.

Main results (10 lines max):

Artificially increasing γ-2 (stg) cytoplasmic C-tail length increases AMPAR mediated synaptic transmission.

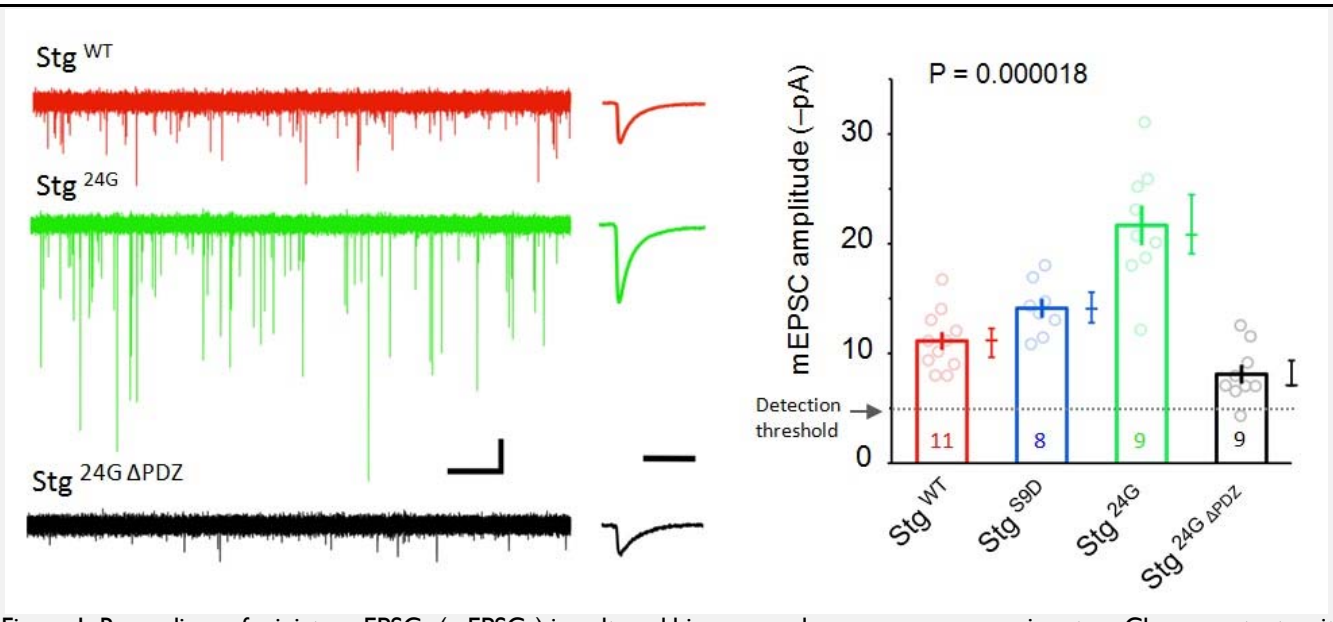


Figure 1: Recordings of miniature EPSCs (mEPSCs) in cultured hippocampal neurons co-expressing stg-mCherry mutants with PSD-95::eGFP. Left. Example 20 second recoding traces in cells expressing wild-type stg and stg extended C-tail mutant (24G) either with or without its PDZ binding domain. Horizontal scale bar is 2 second; Vertical scale bar 10 pA. Middle. Expanded view of mean mEPSCs. Horizontal scale bar is 10 ms; vertical scale is the same as the left panel. Right. The 24G mutant of stg potentiates EPSC amplitude by ~2-fold through a mechanism requiring its C-terminal PDZ domain.

Working plan to continue:

Investigate the impact of γ-8 binding its nexwly discovered interactor calcineurin A on the stabilization of γ-8 containing AMPAR complexes at the synapses during LTP.

Publications in preparation:

"Extension of the stargazin (γ-2) cytoplasmic domain tunes AMPA receptor mediated transmission" submission at Neuron

Communications:

Poster "Extension of the stargazin (γ-2) cytoplasmic tail controls synaptic transmission" at the Biophysical Society Annual Meeting 2014 in San Francisco

Neuromodulation by ATP P2X receptors of excitatory synapses

Johan-Till Pougnet, supervision Eric Boue-Grabot, IMN

LabEx BRAIN support:7 months

Objectives of the project:

Ionotropic AMPA receptors (AMPAR) activated by glutamate are the main actors of the fast excitatory synaptic transmission in the brain. They also play a crucial role in synaptic plasticity that are widely recognized to be the basis cognitive functions. The objective of this study is to demonstrate that P2X receptors modulate AMPAR trafficking and consequently post-synaptic efficacy in hippocampus.

Main results:

We show in cultured hippocampal neurons that activation of postsynaptic P2X receptors by exogenous ATP or glial release of endogenous ATP decreases the amplitude of miniature excitatory postsynaptic currents and AMPA-evoked currents. Using a combination of electrophysiology, surface or internalization assays and real time imaging, we demonstrate that the calcium influx through the ATP-gated channels triggers AMPAR internalization through clathrin-mediated dynamin-dependent endocytosis leading to reduced surface AMPAR and therefore, altered AMPA-mediated current. We also identified by pharmacological approaches that P2X-mediated alteration of surface AMPAR trafficking is dependent on CamKII kinase or phosphatase actvities. This work was submitted for publication to Neuron and revised version should be resubmitted to Neuron at the end of March.

Working plan to continue:

We are currently performing additionnal electrophysiological experiments in brain slices to provide a more physiological support and high resolution imaging (collabwith E. hozy IINS) of native AMPAR to demonstrate that P2X-mediated AMPAR internalization occcurs at synaptic level. We will further identify residues/motifs within AMPAR subunit sequences that are involved in P2X-mediated internalization using mutational or subunit domain swapping approaches and recombinant electrophysiology to evaluate impact of these residues on P2X-mediated AMPAR inhibition.

Publications in preparation:

Pougnet JT, Toulmé E, Martinez A, and Boué-Grabot E. ATP P2X receptors down-regulate AMPA receptor trafficking and postsynaptic efficacy in hippocampal neurons. **Neuron** (in resubmission)

Analysis of synaptic plasticity in CA3 pyramidal cells in vivo

Stefano Zucca, supervision Christophe Mulle, IINS

LabEx BRAIN support:12 months

Objectives of the project:

My project aims at deciphering how granule cells control the activity of CA3 pyramidal cells in the intact hippocampal network. For this I combined electrophysiological recordings *in vivo* (extracellular and whole-cell patch clamp) and optogenetics.

Main results:

In the first part of my project I explored new optogenetic tools to control the activity of granule cells with pulses of light. Optogenetic stimulation, which relies on the activation of the light-gated ion channel channelrhodopsin-2 (ChR2) by blue light reliably induced action potentials over a wide range of frequencies of stimulation. Optical stimulation can be used to trigger short term plasticity at mossy fiber-CA3 synapses in vitro. In the second part I refined optogenetic stimulation methodology in vivo for non-invasive characterization of synaptic functioning of the mf-CA3 synapses. I found that 1) frequency facilitation of fEPSPs occur in vivo at mf-CA3 synapses and 2) the period of synaptic facilitation is correlated with an increase of gamma activity supporting the key role of gamma oscillations in regulating the flow of information among anatomically coupled networks.

Working plan to continue:

Use silicon probes to record from CA3 region extracellular units and local field potential before during and after light stimulation, to assess how granule cells firing affect downstream neurons in the CA3 area (ongoing experiments).

Perform whole cell patch clamp recordings from CA3 neurons in vivo upon light stimulation of granule cells, using different stimulation frequencies, to investigate transmission and plasticity *in vivo*

Publications in preparation:

Zucca S, Griguoli M, Mulle C. Analysis of synaptic function of CA3 microcircuits in vivo using optogenetic tools.

Griguoli M, Zucca S, Mulle C. Cholinergic modulation of neuronal oscillation and hippocampal CA3 circuits using *in vivo* recordings and optogenetics.

III- Facilities

Biochemistry

Head of the facility: Nathalie Sans (NCM) and Matthieu Sainlos (IINS)
Technical head: Clemence Rabin
Location: Institut Francois Magendie, 1rst floor, Room 100

Main activity of the core facility:

1) Service

a) main equipment

The Platform offers to its users a great panel of powerful equipment in terms of centrifugation, analytical techniques and protein purification.

- Production and purification equipments (in use more than 400 hrs per semester)
  - Micropulser (Biorad) for electroporation
  - Incubator-shaker Innova 42R (temperature from 4 to 80°C)
  - Cell disrupter and homogenizer POLYTRON and FastPrep 24
  - Aktä Purifier 10 refrigerated at 4°C for protein purification using liquid chromatography.

- Centrifuges and ultracentrifuges (in use more than 400 hrs /semester)
  - Centrifuge Allegra X-30 with SX4400 rotor
  - Centrifuge Avanti J25 with J25.50 and JS13.1 rotor
  - Ultracentrifuge Optima LE80K dedicated to viral preparations (rotors: SW40Ti, SW32Ti)
  - Ultracentrifuge Optima L100XP (rotors: 50Ti, 70Ti, 80Ti et NVT90, SW60Ti)
  - Ultracentrifuge Optima TL100 (rotor: TLA100.3, TLS55 et TLA120.2)

- Analytical equipment (in use more than 700 hrs per semester)
  - Spectrophotometer DU640B (Beckman Coulter)
  - 1D and 2D protein electrophoresis equipment (Biorad)
  - Microplate Reader Plate Reader Model 680 (Biorad) for ELISA
  - Microplate reader POLARStar Omega (BMG Labtech) used for 5 different measurements: UV absorption, fluorescence intensity, fluorescence time of life, luminescence.
  - Imager G:Box iChemi (Syngene) and ChemiDoc (Biorad) for chemiluminescence and fluorescence

b) Service offer

Our expertise ranges from molecular biology work to production and purification of the recombinant protein. We are specialised in protein production for downstream applications. The platform provides advice and assistance by providing training around the different equipment present on the platform including first use, security rules and help with optimization of protocols and advices. To this end, a full-time engineer is present on the platform.

Differents services:

- Provide powerful equipment with training associated
- Optimization of protocols and research literature in order to improve the techniques proposed by the platform
- Help with the implementation of analytical and biochemical methods needed to do protein purification, characterization of protein/protein interactions, analysis of enzymatic activity, …
- Help for results interpretation
- Diffusion and valorization of the developed methods by oral presentation, report …
- Training in the principles and implementation techniques of experimental biochemistry, user coaching
- Evaluation of the ressource needed for experiments

- Development of privileged partnership with other platforms present in site (Lasercapture (NCM), Proteomic (PGF), etc…
- Implementation of health and safety rules

Since the end of 2013, the Platform offers services in production and purification of native or recombinant proteins and antibodies:

- Protein quantitation (mixed and complex samples)
- Protein characterization using electrophoresis analysis
- Production in bacteria and protein extraction
- Purification with liquid chromatography: Affinity (HisTag, GST, protein A, StrepTag),size exclusion chromatography or ion exchange chromatography
- Elisa

c) Training activities

The Platform forms users on the different instruments (Imagers, Microplate reader, centrifuges and ultracentrifuges)

Personnel list:

1) Permanent (Name, function, %time in the facility)

Nathalie Sans, CR1 INSERM, 5%
Matthieu Sainlos, CR1 CNRS, 5%

2) Non permanent LabEx funded (Name, function, %time in the facility)

Clemence Rabin, IE, UB, 100%

3) Non permanent other funding (Name, function, %time in the facility)

-

Expenses (total in k€):

		2012	2013
Running cost		27604	25167,32
Human ressources	Permanent (k€)		
	Non permanent (k€)		25000
Equipment		87085	73023

Incomes (total in k€)

	2012		2013	
	organism	amount (€)	organism	amount (k€)
Service provision	NCM INSERM U862	4 500,00 €	NCM INSERM U862	3 978,25 €
	IINS CNRS	3 350,00 €	IINS CNRS	1 278,50 €
	IMN CNRS	500,00 €	IMN CNRS	152,25 €
	NutriNeuro	500,00 €	NutriNeuro	761,50 €
Subventions	LABEX	105 000,00 €	LABEX	105 000,00 €
Research contract				
public permanent grant				

Users:

Name of the PI	Laboratory	Affiliation	Prestation	Nb of prestation	Year
Abrous	NCM	LabEx	Centrifuge	25,5h	2012
Cota	NCM	LabEx	Analysis	3,5h	2012
Frick	NCM	LabEx	Analysis	1h	2012
Frick	NCM	LabEx	Centrifuge	13,75h	2012
Marsicano	NCM	LabEx	Analysis	113,50h	2012
Marsicano	NCM	LabEx	Centrifuge	96,75h	2012
Montcouquiol/Sans	NCM	LabEx	Analysis	3h	2012
Montcouquiol/Sans	NCM	LabEx	Centrifuge	177,75h	2012
Montcouquiol/Sans	NCM	LabEx	Microplate reader	8h	2012
Choquet	IINS	LabEx	Analysis	127,75h	2012
Choquet	IINS	LabEx	Microplate reader	28,5h	2012
Groc	IINS	LabEx	Analysis	21,50h	2012
Humeau	IINS	LabEx	Analysis	6h	2012
Mulle	IINS	LabEx	Analysis	11,5h	2012
Thoumine	IINS	LabEx	Analysis	1,25h	2012
Bezard	IMN	LabEx	Analysis	25,75h	2012
Layé	NutriNeuro	Bordeaux Neurocampus outside LabEx	Analysis	93,75h	2012
Layé	NutriNeuro	Bordeaux Neurocampus outside LabEx	Centrifuge	6,5h	2012
Pallet	NutriNeuro	Bordeaux Neurocampus outside LabEx	Analysis	45,25h	2012

The following pricing is applied:

- Package analytical analysis 150€/year: Imager Syngene, microplate reader Biorad, electrophoresis equipment, cell homogenizer POLYTRON and spectrophotometer DU640B.
- Package microplate reader POLARStar Omega (BMG Labtech) 100€/year
- Package centrifuges 350€/year: all the centrifuges and ultracentrifuges of the Platform
- Package MilliQ water 400€/year

Hours of utilization are then billed at 3€/hours.

Reductions are applied:

- Hours < 5: no package
- 50< hours <100: reduction of 25% on the package
- 100< hours: reduction of 50% on the package

The package analytical techniques and centrifuges decreased since the last 2 years. These 2 packages have been reduced thanks to the augmentation of the Platform utilization which can pay most of the maintenance contracts.

Name of the PI	Laboratory	affiliation	prestation	nb of prestation	year
Abrous	NCM	LabEx	Analysis	10h	2013
Abrous	NCM	LabEx	Centrifuge	74,25h	2013
Cota	NCM	LabEx	Analysis	4,25h	2013
Cota	NCM	LabEx	microplate reader	2h	2013
Frick	NCM	LabEx	Centrifuge	42,5h	2013
Frick	NCM	LabEx	Analysis	5,5h	2013
Marighetto	NCM	LabEx	Analysis	2h	2013
Marsicano	NCM	LabEx	Analysis	274,75h	2013
Marsicano	NCM	LabEx	Centrifuge	129,75h	2013
Montcouquiol/Sans	NCM	LabEx	Centrifuge	153,5h	2013
Montcouquiol/Sans	NCM	LabEx	microplate reader	9h	2013
Montcouquiol/Sans	NCM	LabEx	incubator	27h	2013
Montcouquiol/Sans	NCM	LabEx	FPLC	50h	2013
Choquet	IINS	LAbEx	Analysis	120,75h	2013
Choquet	IINS	LAbEx	microplate reader	37h	2013
Choquet	IINS	LAbEx	FPLC	19h	2013
Groc	IINS	LabEx	Analysis	60,75h	2013
Groc	IINS	LabEx	Centrifuge	1h	2013
Groc	IINS	LabEx	microplate reader	4h	2013
Humeau	IINS	LabEx	Analysis	54h	2013
Humeau	IINS	LabEx	Centrifuge	18,75h	
Humeau	IINS	LabEx	Incubator	722,25h	2013
Landry	IINS	LabEx	Analysis	8,5h	2013
Mulle	IINS	LabEx	Analysis	35,75h	2013
Mulle	IINS	LabEx	Centrifuge	7,5h	2013
Thoumine	IINS	LabEx	Analysis	18,25h	2013
Cell Biology		LabEx	microplate reader	8,5h	2013
Bezard	IMN	LabEx	Analysis	109,50h	2013
Bezard	IMN	LabEx	Centrifuge	4h	2013
Layé	NutriNeuro	Bordeaux Neurocampus outside LabEx	Analysis	85,75h	2013
Layé	NutriNeuro	Bordeaux Neurocampus outside LabEx	Centrifuge	37,5h	2013
Pallet	NutriNeuro	Bordeaux Neurocampus outside LabEx	Analysis	71h	2013

<u>LabEx support expenses in 2012:</u>
Equipment:
LabEx support: 90 000€
Name of the equipment:
- Aktä Purifier 10 (GE Healthcare): FPLC system for protein or antibody purification
- Incubator shaker Innova 42R (New Brunswick)
- Microplate reader POLARStar Omega (BMG Labtech)
- Bench centrifuge Allegra X30 (Beckman Coulter)

Co-financers: none in 2012
Running costs (total labEx support expenses): 15 840€
Human Resources: (total LabEx support expenses): -
List of recruitments (name, function, nb of month): none

<u>LabEx support expenses in 2013:</u>
Equipment:
LabEx support: 70 000€
Name of the equipment:
- P960 pump and 50mL superloop for Aktä Purifier (GE Healthcare)
- LVis Plate (BMG Labtech) for the POLARStar Omega
- Cell disrupter/homogenizer FASTPREP 24 (MP Biomedicals)
- Bench Ultracentrifuge Optima MAX XP (Beckman Coulter)
- Infrared-based biomolecular quantitation system, Direct Detect (Merck Millipore)
- Imager ChemiDoc MP and electrophoresis equipment (Biorad)

Co-financers: none in 2013
Running costs (total labEx support expenses): 10 000€
Human Resources: (total LabEx support expenses): 25 000€
List of recruitments (name, function, nb of month): Clémence Rabin, engineer, 4 months

Genotyping

Head of the facility: Gonzales Delphine
Technical head: Delphine Gonzales
Location: Neurocentre Magendie, 146 Rue Léo Saignat, 33077 Bordeaux

Service offer:

The genotyping platform, located in Neurocentre Magendie, offers a variety of technics and methods adapted to different projects of transgenic mouse genotyping. The platform has equipment and space that are entirely dedicated to this function.

The services offered by the platform are:
-Development and validation of genotyping protocols (Primer design),
-Genomic DNA extractions (NaOH, FTA, Isopropanol, Column silica),
-Specific PCR for target transgene (simplex , multiplex),
-Universal PCR for common transgene (GFP, neomycin, Cre, LacZ)
-Capillary Electrophoresis analysis (automatic capillary)
-Interpretation and result reports (by email , or on the animal database: ANISE)

Equipment:
- 5 blocks of Biorad thermocycler (3x96 and 2x48)
- Liquid handling automat epMotion 5070
- Capillary electrophoresis automat Caliper LabChip GX

The hired staff is fully dedicated to this platform providing expertise, repeatability, and personnalized service.

Price list:

Price List :	2012			2013		
	academic	Labex	private	academic	Labex	private
Genotyping (including DNA Extraction, 1 PCR reaction)	5,80 €	3,90 €	9,45 €	4,00 €	3,00 €	5,60 €
PCR reaction supplementaire	2,10 €	1,40 €	3,15 €	1,90 €	1,40 €	2,70 €
Development protocol	52,50 €	35,00 €	84,00 €	30,00 €	22,50 €	42,00 €

Note that Labex prices are 33% less than academic ones

NB: Labex subventions have generated a 24% increase in the platform activity in 2012, allowing better negotiation of consumables and amortization of equipment. As a consequence, plateform prices were decrease by 30% in 2013.

Personnel list (permanent and non permanent):
1/Permanent: Gonzales Delphine IE 50%
Lordan Claire, 100%
Helene Doat, 100% (from September to December)
2/Non Permanent Laplagne Guillaume, 100%
Isabelle Seynat (100% for 2months)

Outcomes (total in €):

		2012	2013
Running cost		36 700 €	37 200 €
Human ressources	Permanent (€)	47 585 €	59 900 €
	Non permanent (€)	28 510 €	34 200 €
Equipment		19 500 €	

Incomes (total in €)

	2012		2013	
	organism	**amount (€)**	**organism**	**amount (€)**
Service provision	Bergonie	2350	Bergonie	4872
	IINS	0	IINS	19976
	IMN	11917	IMN	9098
	INCIA	6823	INCIA	4486
	Inserm 1026	1020	Inserm 1026	2228
	Inserm 1029	1044	Inserm 1029	452
			Private	375
	TOTAL	**23154**	TOTAL	**41487**
Subventions	Labex	**35195**	Labex	**35195**
	NCM	**49515**	NCM	**36205**
Research contract				
public permanent grant				

Users:

Name of the PI	Laboratory	affiliation	prestation	nb of prestation	year
Iggo Richard	Bergonie	outside Bordeaux Neurocampus	Genotyping	304	2012
Iggo Richard	Bergonie	outside Bordeaux Neurocampus	réaction PCR	130	2012
Landry Marc	IINS	LabEx	Genotyping	34	2012
BAUFRETON Jérôme	IMN	LabEx	Genotyping	1048	2012
BAUFRETON Jérôme	IMN	LabEx	réaction PCR	129	2012
BEZARD Erwan	IMN	LabEx	Genotyping	1259	2012
BEZARD Erwan	IMN	LabEx	réaction PCR	42	2012
Boue-Grabot Eric	IMN	LabEx	Genotyping	570	2012
Boue-Grabot Eric	IMN	LabEx	réaction PCR	227	2012
Barriere Greg	INCIA	LabEx	Genotyping	261	2012
Barriere Greg	INCIA	LabEx	réaction PCR	185	2012
Bertrand Sandrine	INCIA	LabEx	Genotyping	24	2012
Bertrand Sandrine	INCIA	LabEx	réaction PCR	515	2012
CHO Yoon	INCIA	LabEx	Genotyping	2090	2012
CHO Yoon	INCIA	LabEx	réaction PCR	37	2012
PIETROPAOLO Susanna	INCIA	LabEx	Genotyping	1474	2012
RIPOCHE Jean	Inserm U1026	outside Bordeaux Neurocampus	Genotyping	64	2012
Cathy Quemener	Inserm U1029	outside Bordeaux Neurocampus	Genotyping	90	2012
SOULET Fabienne	Inserm U1029	outside Bordeaux Neurocampus	Genotyping	72	2012
Abrous	Magendie	LabEx	Genotyping	467	2012
Cota Daniela	Magendie	LabEx	Genotyping	2021	2012
Frick Andreas	Magendie	LabEx	Genotyping	1868	2012
Herry Cyril	Magendie	LabEx	Genotyping	97	2012
LeMasson Gwendal	Magendie	LabEx	Genotyping	3130	2012
Marighetto Aline	Magendie	LabEx	Genotyping	367	2012
Marsicano Giovanni	Magendie	LabEx	Genotyping	8922	2012
Montcouquiol Mireille	Magendie	LabEx	Genotyping	4458	2012
Oliet Stéphane	Magendie	LabEx	Genotyping	132	2012
Piazza Pier-Vincenzo	Magendie	LabEx	Genotyping	1218	2012
TOTAL			Genotyping	29970	
			réaction PCR	1265	

Name of the PI	Laboratory	affiliation	prestation	nb of prestation	year
Iggo Richard	Bergonie	outside Bordeaux Neurocampus	Genotyping	696	2013
Iggo Richard	Bergonie	outside Bordeaux Neurocampus	réaction PCR	1099	2013
Choquet Daniel	IINS	LabEx	Genotyping	538	2013
Choquet Daniel	IINS	LabEx	réaction PCR	534	2013
Humeau Yann	IINS	LabEx	Genotyping	1261	2013
Humeau Yann	IINS	LabEx	réaction PCR	480	2013
Landry Marc	IINS	LabEx	Genotyping	813	2013
Mulle Christophe	IINS	LabEx	Genotyping	3248	2013
Mulle Christophe	IINS	LabEx	réaction PCR	537	2013
Bessede Alban	Immunosol	private	Genotyping	67	2013
BAUFRETON Jérôme	IMN	LabEx	Genotyping	945	2013
BAUFRETON Jérôme	IMN	LabEx	réaction PCR	11	2013
BEZARD Erwan	IMN	LabEx	Genotyping	677	2013
Boue-Grabot Eric	IMN	LabEx	Genotyping	1254	2013
Boue-Grabot Eric	IMN	LabEx	réaction PCR	141	2013
Nicole Olivier	IMN	LabEx	Genotyping	86	2013
Barriere Greg	INCIA	LabEx	Genotyping	89	2013
Bertrand Sandrine	INCIA	LabEx	Genotyping	29	2013
Bertrand Sandrine	INCIA	LabEx	réaction PCR	446	2013
Branchereau Pascal	INCIA	LabEx	Genotyping	101	2013
CHO Yoon	INCIA	LabEx	Genotyping	210	2013
CHO Yoon	INCIA	LabEx	réaction PCR	1329	2013
PIETROPAOLO Susanna	INCIA	LabEx	Genotyping	238	2013
RIPOCHE Jean	Inserm U1026	outside Bordeaux Neurocampus	Genotyping	557	2013
Cathy Quemener	Inserm U1029	outside Bordeaux Neurocampus	Genotyping	51	2013
SOULET Fabienne	Inserm U1029	outside Bordeaux Neurocampus	Genotyping	62	2013
Abrous	Magendie	LabEx	Genotyping	1931	2013
Abrous	Magendie	LabEx	réaction PCR	40	2013
Cota Daniela	Magendie	LabEx	Genotyping	2016	2013
Cota Daniela	Magendie	LabEx	réaction PCR	15	2013
Frick Andreas	Magendie	LabEx	Genotyping	2103	2013
Frick Andreas	Magendie	LabEx	réaction PCR	22	2013
Herry Cyril	Magendie	LabEx	Genotyping	643	2013
LeMasson Gwendal	Magendie	LabEx	Genotyping	1790	2013
Marsicano Giovanni	Magendie	LabEx	Genotyping	8788	2013
Marsicano Giovanni	Magendie	LabEx	réaction PCR	9	2013
Montcouquiol Mireille	Magendie	LabEx	Genotyping	4553	2013
Oliet Stephane	Magendie	LabEx	Genotyping	148	2013
Piazza Pier-Vincenzo	Magendie	LabEx	Genotyping	1079	2013
TOTAL			Genotyping	33973	
			réaction PCR	4663	

LabEx support expenses in 2012:

Equipment:

LabEx support: 15000€

Name of the equipment: liquid handling automat EpMotion 5070 (Eppendorf): 17 000€

Co-financers: Neurocentre Magendie

Human Resources: (total LabEx support expenses): 20195€

List of recruitments (name, function, nb of month)

Amandine Martinet (20195€) 8,5 month

LabEx support expenses in 2013:

Running costs (total labEx support expenses): 12585€

Human Resources: (total LabEx support expenses): 22610€

List of recruitments (name, function, nb of month)

Guillaume Laplagne (22610€) 10 month

Laser Microdissection

Head of the facility: Marlène Maitre

Technical head: Marlène Maitre

Location: Neurocentre Magendie Inserm U862, 146 rue Leo Saignat 33077 Bordeaux cedex

Service offer:

Technic description:

Laser Microdissection System allows to isolate and to collect homogeneous populations of cells from tissues or cell cultures containing heterogeneous populations of cells thanks to visual microscopic inspection.

This technique is necessary to study accurate and targeted cells populations visible at a microscopic scale and located in a heterogeneous tissue.

The platform is equipped with a PALM laser microdissecteur (by Zeiss) automated laser microdissector coupled with fluorescence.

The Laser Capture Microdissection (LCM) system works thanks to a solid state UV laser that guarantees an accurate cutting (thickness of cutting: 1 µm) without damaging the tissue.

It's possible to cut:

-Tissue as cerebral structures (dental gyrus of the hippocampus, substantia nigra…)

- Cells (neurons, astrocytes...)

-Chromosomes

The LCM process does not alter neither the chemistry nor the morphology of the cells or tissues of the sample.

Furthermore, with this process, there is no contact between the sample and the collector, thus reducing the risk of contamination for molecular analysis.

For this reason, LCM is well adapted for DNA, RNA and/or protein analysis. With PALM automated robot, several areas can be microdissected and collected into the collector that will be used for the extraction of biomolecules.

Service offer:

The platform can process tissus samples to RNA.

Equipment:

The laboratory is dedicated to the preparation and processing of samples for laser microdissection.

A second laboratory allows the processing of RNA from the microdissection.

The platform provides:

- A cryostat (Leica)
- Material for conducting stains and immunostaining.
- A laser for microdissection (version 4.6 Zeiss) coupled with fluorescence (DAPI , GFP , Rhodamine) and equipped with 5X , 20X , 40X , 63X , 100X and 150X magnification.
- Sufficient material for the extraction of nucleic acids
- Material for measuring the quality and quantity of the RNA samples

The platform offers the following services:

1. Training for the laser microdissection system
2. Unrestricted access to the platform with the provision of equipment (only after training). In this case the user can independently use the hardware platform and access the expertise of the platform.
3. Platform managed laser microdissection project.

The sample is fully treated by the platform personnel:

- Development and validation of the project
- Sample preparation for laser microdissection: cutting, staining
- Microdissection of tissus or cells (fluorescent or not)
- RNA extraction (microquantity)
- Quantitative and qualitative analysis of samples
- Preparation of a report detailing the work carried cut and the results obtained

4 . Provision of consumables needed for all services offered by the platform

Price list:

Offer	Academic price	Labex/SFR price	Private price
*1 hour LCM free use**	25	16,75	35
*1 hour LCM service***	40	26,80	56
Laser microdissection training	154	103,18	215,60
RNA extraction/sample	11,60	7,77	16,24
Dnase treatment/sample	2,50	1,68	3,50
RNA Quality Pico Agilent ship - 11 samples	32	21,44	44,80
RNA quantity fluorimeter/10 sample	9,60	9,43	13,44
RNA quantity Spectrometer/10 sample	2,30	1,54	3,22
MembraneSlide NF 1.0 PEN piece	3,30	2,21	4,62
MembraneSlide NF 1.0 PET piece	4,30	2,88	6,02
MembraneSlide NF 0.17 PEN piece	5,54	3,71	7,76
Tube AdhesiveCap 500 piece	3	2,01	4,20
Tube AdhesiveTouch 500 piece	3,15	2,11	4,41
Petrish Dish	25	16,75	35
MembraneRing 50	17	11,39	23,80

Personnel list (permanent and non permanent):

Marlène Maitre, ingeneer non permanent 100%-Tehnical platform manager

Hélène Doat, technician, permanent, 50%- Technical assistance.

Hélène Doat followed samples on the laser microdissection platform and the transcriptome platform. Some samples after laser microdissection are used in q-PCR.

Hélène Doat supersede Guillaume Laplagne (non permanent technician) in 2013.

Outcomes (total in €):

		2012	2013
Running cost		31 000 €	21 000 €
Human ressources	Permanent (€)		
	Non permanent (€)	38 000 €	55 500 €
Equipment		15 000 €	5 000 €

Incomes (total in €)

	organism	amount (€)	organism	amount (€)
Service provision	U1029	2200	U1029	891
	IINS	4 871	CHU Bordeaux	439
	NCM	7 000	U1026	186
			Private	573
			IINS	879
			NCM	14 587
	Total	**14 071**	**Total**	**17 555**
Subventions	Labex	44 000	Labex	44 000
	NCM	25 000	NCM	32 500
Research contract				

Users:

Name of the PI	Laboratory	affiliation	prestation	b of prestatio	year
2012					
Bikfalvi	U1029	outside Bordeaux Neurocampus	Laser microdissection (hour)	3	2012
	U1029	outside Bordeaux Neurocampus	Extraction	132	2012
	U1029	outside Bordeaux Neurocampus	Agilent pico ship	18	2012
Groc	IINS	LabEx	Laser microdissection (hour)	34	2012
	IINS	LabEx	Extraction	1	2012
Choquet	IINS	LabEx	Laser microdissection (hour)	28	2012
Landry	IINS	LabEx	Laser microdissection (hour)	11	2012
	IINS	LabEx	Extraction	10	2012
Humeau	IINS	LabEx	Laser microdissection (hour)	30	2012
	IINS	LabEx	Extraction	20	2012
	IINS	LabEx	Agilent pico ship	3	2012
Cota	NCM	LabEx	Laser microdissection (hour)	30	2012
	NCM	LabEx	Extraction	30	2012
	NCM	LabEx	Agilent pico ship	3	2012
Piazza	NCM	LabEx	Laser microdissection (hour)	50	2012
Montcouquiol	NCM	LabEx	Laser microdissection (hour)	15	2012
2013					
Bikfalvi	U1029	outside Bordeaux Neurocampus	Laser microdissection (hour)	34	2013
Merlio	CHU Bordeaux	outside Bordeaux Neurocampus	Laser microdissection (hour)	11	2013
Groc	IINS	LabEx	Laser microdissection (hour)	20	2013
	IINS	LabEx	Extraction	22	2013
	IINS	LabEx	Agilent pico ship	3	2013
Choquet	IINS	LabEx	Laser microdissection (hour)	5	2013
Landry	IINS	LabEx	Laser microdissection (hour)	3	2013
Amédée	U1026	LabEx	Laser microdissection (hour)	2	2013
	U1026	LabEx	Extraction	7	2013
	U1026	LabEx	Agilent pico ship	2	2013
Thales avionics	Privé	private	Laser microdissection (hour)	13	2013
Abrous	NCM	LabEx	Laser microdissection (hour)	74	2013
	NCM	LabEx	Extraction	10	2013
	NCM	LabEx	Agilent pico ship	1	2013
Marighetto	NCM	LabEx	Laser microdissection (hour)	104	2013
	NCM	LabEx	Extraction	173	2013
	NCM	LabEx	Agilent pico ship	15	2013
Marsicano	NCM	LabEx	Laser microdissection (hour)	36	2013
	NCM	LabEx	Extraction	36	2013
	NCM	LabEx	Agilent pico ship	4	2013
Montcouquiol	NCM	LabEx	Laser microdissection (hour)	50	2013
Piazza	NCM	LabEx	Laser microdissection (hour)	30	2013

Notes:

In this table the consumables associated with laser microdissection are not referenced (because their amounts don't reflect the use of platform).

<u>LabEx support expenses in 2012:</u>

Equipment:
LabEx support: 15 000€
Name of the equipment:
New camera AxioCam ICc1 by Zeiss
Aim: To perform our images,(high resolution)
Price: 2 312€ HT
Upgrade logiciel by Zeiss
Aim: New function and version pro of the system
Price: 6 547€ HT
LCD-Pen Display PL-720 17"by Zeiss
Aim: To draw quickly and easier the cell and chromosomes with this screen

Price: 1 553€ HT
Laser slide calibration by Zeiss
Aim: To calibrate the laser itself
Price: 844€ HT

Co-financers
Running costs (total labEx support expenses):2 205€
Human Resources: (total LabEx support expenses): 2 6811€
List of recruitments (name, function, nb of month): Marlène Maitre, 9 month

LabEx support expenses in 2013:
Equipment:
LabEx support: 5 000€
Name of the equipment:
This support is used with transcriptome platform to buy a 5000g centrifuge for plates (Qiagen)

Co-financers
Running costs (total labEx support expenses): 3 068€
Human Resources: (total LabEx support expenses): 35 948€
List of recruitments (name, function, nb of month): 35 948€ Marlène Maitre, 12 month

Transcriptome

Head of the facility: Piervi Piazza
Technical head: Thierry Leste Lasserre
Location: Neurocentre Magendie U862 146 rue Leo Saignat 33077 Bordeaux cedex

Service offer:

Transcriptomic platform aims to bring materials and comprehensive expertise in gene expression studies, RNA Extraction and Gene expression analysis by Real-Time PCR

- Extraction of total RNA
- Quantification of total RNA
- Quality control of total RNA
- Synthesis + quality control of cDNA
- Design + validation of primers
- Selection of appropriate controls for qPCR
- Quantitative PCR (qPCR) with the following chemistries: SYBR-green dye (Molecular Probes) and Taqman probes (Applied Biosystems).

Different protocols (from RNA to the qPCR reaction) are designed for small (microdissected brain structures) or large materials. Practical training is provided for the new platform users.

High throughput gene expression:
the LightCycler 480 (Roche) and Twister II (Caliper) integration system provides throughput screening in real-time PCR analysis.
Platform provides an intuitive software for Gene Expression Analysis (GEASE). It's a comprehensive web data-base allowing.
http://cbib1.cbib.u-bordeaux2.fr/outils/Base/index.phtml
GEASE allows us to:

- Trace the samples (total RNA, cDNA, qPCR samples…)
- Analyse qPCR results + microarray results
- Access a bank of primers (with more than 3000 pairs)

Price list:

Labex price = cost price

2013	Academic price	Labex price	Price private institute
Extraction of total RNA	8,4	5,7	11,35
Extraction of total RNA + Qiagen column	14,7	9,85	19,85
Agilent ship	31,5	21,1	42,6
synthesis of cDNA	5,7	3,8	7,7
cDNA plate	4,3	2,9	5,8
Aliquotage plate	24,15	16,2	32,6
96 wells qPCR plate Roche	49,5	33	66,8
384 wells qPCR plate Roche	162,25	108,8	219
96 wells qPCR plate Fermentas	51	34	68,8
384 wells qPCR plate Fermentas	167,1	112,1	225,6
Traitment of sample with DNAse	2,5	1,65	2,9
A pair of primers	13,65	9,15	18,4
Affymetrix ship	see estimate	see estimate	see estimate
Fedex sending	see estimate	see estimate	see estimate
Dry ice 10kg	see estimate	see estimate	see estimate
Additional consumable	see estimate	see estimate	see estimate
Utilisation GEASE/year	525	351	1387
Utilisation GEASE/month	44	30	116
Price per hour	42	28	63

Personnel list (permanent and non permanent):

Thierry Leste Lasserre, engineer Inserm, 100%
Hélène Doat, technician Inserm, 50%

Outcomes (total in €):

		2012	2013
Running cost		80 283 €	80 000
Human ressources	Permanent (€)	79690,5	79690,5
	Non permanent (€)		
Equipment		47 000 €	22 500 €

Incomes (total in k€)

	2012		2013	
	organism	amount (€)	organism	amount (€)
Service provision	CBMN	367,25	CBMN	138,35
	IINS	110,15	IINS	455,33
	U869	5958,7	U869	339
	U1053	390,45	U1053	28,35
	IMN	1828,25	IMN	1960,96
	Bergonié	994,8	Bioadvance	201
	U1029	96	Imagene	88,2
	U862	49790	UMR1065	85,05
			U862 Abrous	921,22
			U862 Cota	10684,65
			U862 Le Masson	1038,48
			U862 Marighetto	2390,54
			U862 Marsicano	757,77
			U862 Montcouquiol	368,64
			U862 Oliet	18232,4
			U862 Piazza	9642,48
			U862 transcriptome+ génotypage+microdissection	12891,89
Subventions				
Research contract				
public permanent grant				

Users:

Name of the PI	Laboratory	affiliation	prestation	nb of prestation	year
Isabelle Soubeyran	Bergonié	outside Bordeaux Neurocampus	A pair of primers	2	2012
		outside Bordeaux Neurocampus	Agilent ship	2	2012
		outside Bordeaux Neurocampus	Aliquotage plate	2	2012
		outside Bordeaux Neurocampus	synthesis of cDNA	12	2012
		outside Bordeaux Neurocampus	Price per hour	5	2012
		outside Bordeaux Neurocampus	96 wells qPCR plate Roche	12	2012
Daniel Choquet	IINS	LabEx	A pair of primers	1	2012
		LabEx	synthesis of cDNA	10	2012
		LabEx	96 wells qPCR plate Roche	2	2012
Jean Louis Mergny	U869	outside Bordeaux Neurocampus	96 wells qPCR plate Fermentas	25	2012
		outside Bordeaux Neurocampus	96 wells qPCR plate Roche	118	2012
		outside Bordeaux Neurocampus	Agilent ship	18	2012
		outside Bordeaux Neurocampus	synthesis of cDNA	121	2012
		outside Bordeaux Neurocampus	Traitment of sample with DNAse	1	2012
Andreas Bikfalvi	U1029	outside Bordeaux Neurocampus	Aliquotage plate	1	2012
		outside Bordeaux Neurocampus	96 wells qPCR plate Roche	2	2012
Jochen Lang	CBMN	outside Bordeaux Neurocampus	Traitment of sample with DNAse	3	2012
		outside Bordeaux Neurocampus	synthesis of cDNA	3	2012
		outside Bordeaux Neurocampus	Agilent ship	1	2012
		outside Bordeaux Neurocampus	96 wells qPCR plate Roche	1	2012
Jean Rosenbaum	U1053	outside Bordeaux Neurocampus	Price per hour	6	2012
		outside Bordeaux Neurocampus	Agilent ship	3	2012
		outside Bordeaux Neurocampus	Utilisation GEASE/month	1	2012
		outside Bordeaux Neurocampus	96 wells qPCR plate Roche	6	2012
		outside Bordeaux Neurocampus	Aliquotage plate	1	2012

Erwan Bezard	IMN	LabEx	A pair of primers	13	2012
		LabEx	96 wells qPCR plate Roche	9	2012
		LabEx	Extraction of total RNA	31	2012
		LabEx	synthesis of cDNA	30	2012
		LabEx	Agilent ship	1	2012
		LabEx	Traitment of sample with DNAse	26	2012
		LabEx	384 wells qPCR plate Roche	1	2012
		LabEx	Aliquotage plate	1	2012
		LabEx	Utilisation GEASE/year	1	2012
Neurocentre Magendie	U862	LabEx	Agilent ship	124	2012
		LabEx	96 wells qPCR plate Roche	1149	2012
		LabEx	synthesis of cDNA	960	2012
		LabEx	Aliquotage plate	74	2012
		LabEx	Extraction of total RNA	600	2012
		LabEx	Traitment of sample with DNAse	600	2012

Name of the PI	Laboratory	affiliation	prestation	nb of prestation	year
Erwan Bezard	IMN	LabEx	Extraction of total RNA	46	2013
		LabEx	Agilent ship	8	2013
		LabEx	synthesis of cDNA	57	2013
		LabEx	Aliquotage plate	1	2013
		LabEx	96 wells qPCR plate Roche	21	2013
		LabEx	384 wells qPCR plate Roche	1	2013
		LabEx	Traitment of sample with DNAse	46	2013
		LabEx	Utilisation GEASE/year	1	2013
Daniel Choquet	IINS	LabEx	cDNA plate	2	2013
		LabEx	Agilent ship	1	2013
		LabEx	synthesis of cDNA	25	2013
		LabEx	96 wells qPCR plate Roche	2	2013
		LabEx	384 wells qPCR plate Roche	2	2013
Daniel Da Silva	Bioadvance	private	Price per hour	3	2013
		private	synthesis of cDNA	3	2013
Jean Louis Mergny	U869	outside Bordeaux Neurocampus	Agilent ship	11	2013
		outside Bordeaux Neurocampus	synthesis of cDNA	2	2013
Jean Rosenbaum	U1053	outside Bordeaux Neurocampus	Agilent ship	1	2013
Denis Thiéry	UMR1065	outside Bordeaux Neurocampus	Agilent ship	3	2013
Jochen Lang	CBMN	outside Bordeaux Neurocampus	A pair of primers	3	2013
		outside Bordeaux Neurocampus	synthesis of cDNA	2	2013
		outside Bordeaux Neurocampus	Traitment of sample with DNAse	2	2013
		outside Bordeaux Neurocampus	96 wells qPCR plate Roche	1	2013
		outside Bordeaux Neurocampus	Agilent ship	1	2013
Imagene	Imagene	private	Agilent ship	2	2013

Stephane Oliet	U862	LabEx	Extraction of total RNA	251	2013
		LabEx	Traitment of sample with DNAse	251	2013
		LabEx	synthesis of cDNA	374	2013
		LabEx	cDNA plate	3	2013
		LabEx	Agilent ship	10	2013
		LabEx	A pair of primers	40	2013
		LabEx	Aliquotage plate	33	2013
		LabEx	96 wells qPCR plate Roche	197	2013
		LabEx	384 wells qPCR plate Roche	20	2013
		LabEx	96 wells qPCR plate Fermentas	64	2013
		LabEx	384 wells qPCR plate Fermentas	9	2013
Daniela Cota	U862	LabEx	A pair of primers	8	2013
		LabEx	Extraction of total RNA	212	2013
		LabEx	Aliquotage plate	21	2013
		LabEx	Agilent ship	24	2013
		LabEx	96 wells qPCR plate Roche	181	2013
		LabEx	synthesis of cDNA	263	2013
		LabEx	Traitment of sample with DNAse	250	2013
		LabEx	cDNA plate	1	2013

Name of the PI	Laboratory	affiliation	prestation	nb of prestation	year
Génotypage	U862	LabEx	A pair of primers	129	2013
		LabEx	96 wells qPCR plate Roche	4	2013
Le Masson Gwendal	U862	LabEx	Extraction of total RNA	35	2013
		LabEx	Aliquotage plate	1	2013
		LabEx	Agilent ship	6	2013
		LabEx	384 wells qPCR plate Roche	3	2013
		LabEx	96 wells qPCR plate Roche	2	2013
		LabEx	synthesis of cDNA	29	2013
		LabEx	Traitment of sample with DNAse	34	2013
		LabEx	A pair of primers	3	2013
Nora Abrous	U862	LabEx	A pair of primers	2	2013
		LabEx	Agilent ship	3	2013
		LabEx	96 wells qPCR plate Roche	11	2013
		LabEx	synthesis of cDNA	26	2013
		LabEx	Aliquotage plate	1	2013
		LabEx	384 wells qPCR plate Roche	2	2013
		LabEx	Traitment of sample with DNAse	24	2013
		LabEx	cDNA plate	1	2013
Microdissection	U862	LabEx	synthesis of cDNA	49	2013
		LabEx	384 wells qPCR plate Roche	1	2013
Aline Marighetto	U862	LabEx	A pair of primers	1	2013
		LabEx	96 wells qPCR plate Fermentas	4	2013
		LabEx	synthesis of cDNA	211	2013
		LabEx	384 wells qPCR plate Roche	6	2013
		LabEx	96 wells qPCR plate Fermentas	16	2013

Giovanni Marsicano	U862	LabEx	A pair of primers	1	2013
		LabEx	96 wells qPCR plate Roche	5	2013
		LabEx	Extraction of total RNA	2	2013
		LabEx	384 wells qPCR plate Fermentas	2	2013
		LabEx	Agilent ship	1	2013
		LabEx	96 wells qPCR plate Fermentas	3	2013
		LabEx	synthesis of cDNA	37	2013
		LabEx	Traitment of sample with DNAse	1	2013
Mireille Montcouquiol	U862	LabEx	A pair of primers	36	2013
Piervi Piazza	U862	LabEx	A pair of primers	13	2013
		LabEx	Aliquotage plate	16	2013
		LabEx	Agilent ship	16	2013
		LabEx	96 wells qPCR plate Roche	176	2013
		LabEx	Extraction of total RNA	196	2013
		LabEx	synthesis of cDNA	174	2013
		LabEx	Traitment of sample with DNAse	174	2013
Transcriptome	U862	LabEx	A pair of primers	114	2013
		LabEx	Agilent ship	7	2013
		LabEx	384 wells qPCR plate Roche	35	2013
		LabEx	96 wells qPCR plate Roche	77	2013
		LabEx	synthesis of cDNA	354	2013
		LabEx	Traitment of sample with DNAse	357	2013
		LabEx	Extraction of total RNA	38	2013
		LabEx	Aliquotage plate	3	2013
		LabEx	cDNA plate	2	2013
		LabEx	96 wells qPCR plate Fermentas	4	2013

LabEx support expenses in 2012:

Equipment:

LabEx support:25000€

Name of the equipment,

- Congélateur -80°c Fisher Scientific: 12191 euros
- Congélateur -20°c Fisher Scientific: 5680.1 euros
- Nanodrop 3300 Labtech: 7275 euros

Co-financers

Running costs (total labEx support expenses):32283€

Human Resources: (total LabEx support expenses):

List of recruitments (name, function, nb of month)

LabEx support expenses in 2013:

Equipment:

LabEx support:10000€ (Microdissection + Transcriptome)

Name of the equipment: 5000g centrifuge for plates Qiagen

No LabEx support: Tissue Lyser II Qiagen 5000€

Co-financers

Running costs (total labEx support expenses): 23223€

Human Resources: (total LabEx support expenses): 24060€ J Dulong 9 month

List of recruitments (name, function, nb of month)

24060€ J Dulong 9 month

Bordeaux Imaging Center (BIC)

Head of the facility: Daniel Choquet
Technical head: Christel Poujol & Etienne Gontier
Location: Plateforme Génomique Fonctionnelle and Magendie building

Service overview

The Bordeaux Imaging Center (BIC) offers resources in photonic and electronic imaging, mainly in life, health and plant sciences.

It is a core facility identified at the national level as "Infrastructure en Biologie Sante et Agronomie" (IBISA). The BIC is part of the France BioImaging network, and Euro BioImaging network.

The BIC provides a state-of the-art facility in Photonic imaging and Electronic imaging.

For Photonic microscopy: macroscopy, widefield microscopy, scanning confocal microscopy, multiphoton microscopy, spinning-disk microscopy, high resolution microscopy like STED, PALM and STORM techniques, but also FLIM, FCS, and single particles detection

For Electronic microscopy: transmission electron microscopy, and scanning electron microscopy.

The specifics of the BIC that make it a unique core facility in France are:

- Strong skills in imaging at ultra-high resolution (single molecule techniques, multi-photon techniques, STED, PALM and STORM imaging).
- The existence of a team of research and development dedicated to the development and implementation to biology of new imaging technologies.
- A close relationship with a physics laboratory and two companies (Amplitude Systems and Roper Scientific)
- An original positioning by making routinely available dynamic imaging of living samples (FRET / FLIM / FRAP / FCS).
- The ongoing development of correlative microscopy techniques and tomography for electron microscopy
- The advanced techniques for electron microscopy such as the cryo-techniques
- Strong skills in sample preparation for electron microscopy in different biological area (animal/plant) or material area

Resources and Facilities

The BIC can take over part or the whole of a study, from sample preparation, to images acquisition, up to the interpretation of the results.

Any use of equipment of the BIC requires first training by the team and agreement on the usage period. It is advisable to apply in advance to predict the period of training and equipment availability. The user exposes his project to determine the equipment and training required.

Once trained, the user can work independently after registering on the reservation site (see the Bordeaux Imaging Center web site).

Photonic imaging: macroscopy, epifluorescence microscopy, video-microscopy, spininning-disk microscopy, scanning confocal microscopy, multiphoton microscopy, high resolution photonic microscopy like STED microscopy, PALM and STORM, FLIM microscopy, F-techniques like FRAP, FCS and also single particles detection and tracking.

Electronic imaging: transmission electron microscopy (TEM) associated with tomography, scanning electron microscopy (SEM). The service offers various sample preparation techniques, conventional to the advanced techniques of cryo-sample preparation including the high-pressure cryofixation followed by freeze substitution and ultracryomicrotomy.

- ☐ TEM sample preparation and observation
- ☐ SEM sample preparation and observation
- ☐ Cryo-ultrasectioning
- ☐ Pre and post embedding immunostaining
- ☐ Tokuyasu's immunolabeling
- ☐ Correlative light and electron microscopy
- ☐ Fixation by high pressure freezing
- ☐ Freeze-substitution

☐ Electron tomography

Terms

In order to use BIC service, you have to subscribe to the website: http://www.bic.u-bordeaux2.fr/
During the registration, users have to accept the terms of use describing the operating rules of the service.

List of Resources

The BIC maintains customized facilities for photonic and electronic microscopy and samples preparation.

PHOTONIC MICROSCOPY

☐ 1 Macroscope
☐ 4 widefield microscopes
☐ 2 spinning-disk FRAP FLIM microscope
☐ 6 Confocal microscope (2 SP2 Leica, 1 SPE Leica, 2 SP5 Leica, 1 SP8)
☐ 2 Confocal multiphoton microscope (2 SP2 Leica FLIM and electrophy)
☐ 1 Confocal multiphoton STED microscope (SP5 STED Leica)
☐ 1 PALM TIRF microscope (Nikon)
☐ 1 GSDIM microscope (Leica)
☐ 1 Slide scanner

ELECTRON MICROSCOPY

☐ TEM 120kV – Hitachi H7650 equipped for High resolution and high contrast imaging
☐ TEM 120 kV – FEI Tecnai 12 equipped for electron tomography
☐ TEM 100kV - FEI CM10.
☐ SEM – FEI Quanta 200 equipped for High vacuum, low vacuum and environmental vacuum observation and for EDX analysis

FREEZE SAMPLE PREPARATION

☐ High Pressure Freezer for Cryofixation of Biological And Industrial Samples: Leica HPM100
☐ 2 High Pressure Freezer: Leica EMPACT1
☐ 3 Freeze Substitution and Low Temperature Embedding System for Light and Electron Microscopy: Leica AFS2 and 2 Leica AFS1
☐ 1 Cryo-ultramicrotome for perfect sectioning for TEM, SEM, AFM and LM: LEICA UC7/FC7

TISSUE PROCESSING

☐ Automatic Microwave Tissue Processor for Electron Microscopy: Leica AMW
☐ Critical Point Dryer: Polaron CPD 7501
☐ 2 Modular high vacuum coating and glow discharge system: Polaron SC500 and Emitech K950x
☐ 3 microtomes (Microm HM 650V, Microm HM 355 S and Reichert 2040).

ULTRAMICROTOMY

☐ 4 ultramicrotomes (LEICA 1 Ultracut E et 2 UCS, 1 UCT) for perfect sectioning at room temperature equipped with a digital camera

EM SAMPLE PREPARATION LABELLING

☐ Automated immunogold labeling system Leica EM IGL

OTHERS RESOURCES

☐ 2 knife makers
☐ 2 centrifuges
☐ pH meter
☐ 2 precision balances
☐ Sonicator
☐ 3 fume hoods
☐ fridges

CELL AND TISSUE CULTURE RESOURCES

☐ 3 incubator s for Cell Culture

COMMERCIAL SOFTWARE

☐ Digital Micrograph (2D and 3D Electron image acquisition)
☐ AutoQuant (Mediacybernetics)
☐ MetaMorph (Molecular Devices)
☐ Imaris (Bitplane)
☐ SPCI Image (Becker and Hickl)
☐ LI-FLIM Offline (Lambert Instrument)

FREE OR OPEN SOURCE SOFTWARE

☐ ImageJ
☐ ITrack4U
☐ Neuron Studio
☐ R
☐ E-Tomo

Price list:
http://www.bic.u-bordeaux2.fr/

Personnel list:
Daniel Choquet, research director, 25%
Christel Poujol, research engineer, 100%
Philippe Legros, research engineer, 100%
Sébastien Marais, engineer, 100%
Florian Levet, research engineer, 20%
Fabrice Cordelières research engineer, 100%
Magali Mondin, engineer, 100%
Marc Landry, professor, 15%
Etienne Gontier, research engineer, 100%
Melina Petrel, engineer, 100%
Isabelle Svahn , Technician, 100%
Sabrina Lacomme Technician, 100%
Lucie Geay Technician, 100%
Marion Garnero Technician, 50%

Outcomes (total in €):

		2012	2013
Running cost		239200	307303
Human ressources	Permanent (k€)		
	Non permanent (k€)	52200	57412
Equipment		698800	728621

Incomes (total in k€)

	2012		2013	
	organism	amount (k€)	organism	amount (k€)
Service provision		273,9		261,9
Subventions	IBISA	269	FRC	29,8
	FRC	68,5	LabEx BRAIN	85,2
	LabEx BRAIN	95	Regional Council	418,6
	Regional Council	418,6	France Bio Imaging	35,3
public permanent grant	infrastructure (afco)	27	infrastructure (afco)	27,3
	Bordeaux Neurocampus	59	Bordeaux Neurocampus	4,7
	INRA	90	INRA	56
	INSERM	15		
	CNRS	10		

Users:

2012:

Name of the PI	affiliation	prestation	nb
Team Bessoule Moreau	outside Bordeaux Neurocampus	Macroscope	1
Team Bordenave-Chassande	outside Bordeaux Neurocampus	Macroscope	3
Team Daignan-Fornier	outside Bordeaux Neurocampus	Macroscope	2
Team Groc	LabEx	Macroscope	11
Team Marighetto	LabEx	Macroscope	5
Team Mulle	LabEx	Macroscope	3
Team Nagerl	LabEx	Macroscope	7
Team Oliet	LabEx	Macroscope	1
Team Photonique	LabEx	Macroscope	6
Département Chimie de Surface	outside Bordeaux Neurocampus	Epifluorescence microscope	1
Team Bessoule Moreau	outside Bordeaux Neurocampus	Epifluorescence microscope	2
Team Choquet	LabEx	Epifluorescence microscope	1
Team Cota	LabEx	Epifluorescence microscope	6
Team Groc	LabEx	Epifluorescence microscope	8
Team Marighetto	LabEx	Epifluorescence microscope	1
Team Mulle	LabEx	Epifluorescence microscope	3
Team Nagerl	LabEx	Epifluorescence microscope	1
Team Photonique	LabEx	Epifluorescence microscope	21
Team Piazza	LabEx	Epifluorescence microscope	10
Team Bézard	LabEx	Epifluorescence DM 5000 Microscope	1
Team Blanco	outside Bordeaux Neurocampus	Epifluorescence DM 5000 Microscope	7
Team Choquet	LabEx	Epifluorescence DM 5000 Microscope	136
Team Cota	LabEx	Epifluorescence DM 5000 Microscope	3
Team Frick	LabEx	Epifluorescence DM 5000 Microscope	6
Team Groc	LabEx	Epifluorescence DM 5000 Microscope	68
Team Herry	LabEx	Epifluorescence DM 5000 Microscope	28
Team Humeau	LabEx	Epifluorescence DM 5000 Microscope	61
Team Landry	LabEx	Epifluorescence DM 5000 Microscope	3
Team Marighetto	LabEx	Epifluorescence DM 5000 Microscope	14
Team Mulle	LabEx	Epifluorescence DM 5000 Microscope	31

Team Oliet	LabEx	Epifluorescence DM 5000 Microscope	3
Team Photonique	LabEx	Epifluorescence DM 5000 Microscope	23
Team Piazza	LabEx	Epifluorescence DM 5000 Microscope	9
Team Rosenbaum	outside Bordeaux Neurocampus	Epifluorescence DM 5000 Microscope	3
Team Thoumine	LabEx	Epifluorescence DM 5000 Microscope	3
Team Choquet	LabEx	Epifluorescence Zeiss Microscope	7
Team Mulle	LabEx	Epifluorescence Zeiss Microscope	46
Team Photonique	LabEx	Epifluorescence Zeiss Microscope	1
Team Abrous	LabEx	Analysis workstation 1	4
Team Baufreton	Bordeaux Neurocampus outside LabEx	Analysis workstation 1	1
Team Bessoule Moreau	outside Bordeaux Neurocampus	Analysis workstation 1	4
Team Bézard	LabEx	Analysis workstation 1	13
Team Choquet	LabEx	Analysis workstation 1	25
Team Dulon	Bordeaux Neurocampus outside LabEx	Analysis workstation 1	7
Team Frick	LabEx	Analysis workstation 1	4
Team Garret	Bordeaux Neurocampus outside LabEx	Analysis workstation 1	2
Team Groc	LabEx	Analysis workstation 1	1
Team Herry	LabEx	Analysis workstation 1	1
Team Layé	bordeaux Neurocampus outside LabEx	Analysis workstation 1	1
Team Marighetto	LabEx	Analysis workstation 1	20
Team Mulle	LabEx	Analysis workstation 1	2
Team Oliet	LabEx	Analysis workstation 1	2
Team Photonique	LabEx	Analysis workstation 1	23
Team Piazza	LabEx	Analysis workstation 1	5
Team Baufreton	Bordeaux Neurocampus outside LabEx	Analysis workstation 2	11
Team Bessoule Moreau	outside Bordeaux Neurocampus	Analysis workstation 2	1
Team Bézard	LabEx	Analysis workstation 2	1
Team Candresse	outside Bordeaux Neurocampus	Analysis workstation 2	1
Team Choquet	LabEx	Analysis workstation 2	14
Team Dulon	Bordeaux Neurocampus outside LabEx	Analysis workstation 2	13
Team Frick	LabEx	Analysis workstation 2	34
Team Garret	Bordeaux Neurocampus outside LabEx	Analysis workstation 2	5
Team Moore	outside Aquitaine Region	Analysis workstation 2	1
Team Nagerl	LabEx	Analysis workstation 2	11
Team Oda	outside Aquitaine Region	Analysis workstation 2	8
Team Oliet	LabEx	Analysis workstation 2	54
Team Petry	Bordeaux Neurocampus outside LabEx	Analysis workstation 2	1
Team Photonique	LabEx	Analysis workstation 2	22
Team Choquet	LabEx	Analysis workstation PALM	1
Team Garret	Bordeaux Neurocampus outside LabEx	Analysis workstation PALM	6
Team Maurel	outside Aquitaine Region	Analysis workstation PALM	1
Team Montcouquiol	LabEx	Analysis workstation PALM	3
Team Nagerl	LabEx	Analysis workstation PALM	42
Team Photonique	LabEx	Analysis workstation PALM	3
Team Thoumine	LabEx	Analysis workstation PALM	6

Team Blanco	outside Bordeaux Neurocampus	Confocal SP5 (SFR TransBioMed) Microscope	5
Team Megraud	outside Bordeaux Neurocampus	Confocal SP5 (SFR TransBioMed) Microscope	1
Team Oda	outside Aquitaine Region	Confocal SP5 (SFR TransBioMed) Microscope	19
Team Petry	Bordeaux Neurocampus outside LabEx	Confocal SP5 (SFR TransBioMed) Microscope	7
Team Photonique	LabEx	Confocal SP5 (SFR TransBioMed) Microscope	19
Team Robinson	outside Bordeaux Neurocampus	Confocal SP5 (SFR TransBioMed) Microscope	3
Team Rosenbaum	outside Bordeaux Neurocampus	Confocal SP5 (SFR TransBioMed) Microscope	64
Team Wodrich, Kann	outside Bordeaux Neurocampus	Confocal SP5 (SFR TransBioMed) Microscope	149
Team Bessoule Moreau	outside Bordeaux Neurocampus	Confocal SP8 Microscope	3
Team Candresse	outside Bordeaux Neurocampus	Confocal SP8 Microscope	1
Team Canioni	outside Bordeaux Neurocampus	Confocal SP8 Microscope	3
Team Dulon	Bordeaux Neurocampus outside LabEx	Confocal SP8 Microscope	14
Team Frick	LabEx	Confocal SP8 Microscope	1
Team Garret	Bordeaux Neurocampus outside LabEx	Confocal SP8 Microscope	9
Team Humeau	LabEx	Confocal SP8 Microscope	5
Team Lambert	outside Bordeaux Neurocampus	Confocal SP8 Microscope	2
Team LPO	outside Bordeaux Neurocampus	Confocal SP8 Microscope	14
Team Montcouquiol	LabEx	Confocal SP8 Microscope	26
Team Oliet	LabEx	Confocal SP8 Microscope	24
Team Ortega	Bordeaux Neurocampus outside LabEx	Confocal SP8 Microscope	4
Team Photonique	LabEx	Confocal SP8 Microscope	26
Team Abrous	LabEx	Confocal SPE Microscope	97
Team Baufreton	Bordeaux Neurocampus outside LabEx	Confocal SPE Microscope	19
Team Bézard	LabEx	Confocal SPE Microscope	19
Team Choquet	LabEx	Confocal SPE Microscope	3
Team Cota	LabEx	Confocal SPE Microscope	1
Team Dulon	Bordeaux Neurocampus outside LabEx	Confocal SPE Microscope	3
Team Frick	LabEx	Confocal SPE Microscope	4
Team Groc	LabEx	Confocal SPE Microscope	6
Team Herry	LabEx	Confocal SPE Microscope	2
Team Humeau	LabEx	Confocal SPE Microscope	15
Team Lambert	outside Bordeaux Neurocampus	Confocal SPE Microscope	2
Team Landry	LabEx	Confocal SPE Microscope	8
Team Marighetto	LabEx	Confocal SPE Microscope	15
Team Marsicano	LabEx	Confocal SPE Microscope	7
Team Montcouquiol	LabEx	Confocal SPE Microscope	6
Team Mulle	LabEx	Confocal SPE Microscope	6
Team Petit	Bordeaux Neurocampus outside LabEx	Confocal SPE Microscope	2
Team Photonique	LabEx	Confocal SPE Microscope	15
Team Abrous	LabEx	Confocal STED Microscope	2
Team Bessoule Moreau	outside Bordeaux Neurocampus	Confocal STED Microscope	22
Team Candresse	outside Bordeaux Neurocampus	Confocal STED Microscope	8
Team Frick	LabEx	Confocal STED Microscope	33
Team Garret	Bordeaux Neurocampus outside LabEx	Confocal STED Microscope	7
Team Lambert	outside Bordeaux Neurocampus	Confocal STED Microscope	3
Team LPO	outside Bordeaux Neurocampus	Confocal STED Microscope	4
Team Montcouquiol	LabEx	Confocal STED Microscope	3
Team Mulle	LabEx	Confocal STED Microscope	82
Team Nagerl	LabEx	Confocal STED Microscope	98
Team Photonique	LabEx	Confocal STED Microscope	60

Team Robinson	outside Bordeaux Neurocampus	Confocal STED Microscope	3
Team Sibarita	LabEx	Confocal STED Microscope	1
Team Thoumine	LabEx	Confocal STED Microscope	3
Team Layé	bordeaux Neurocampus outside LabEx	Multi-photon Electrophysiology Confocal Microscope	11
Team Photonique	LabEx	Multi-photon Electrophysiology Confocal Microscope	1
Team Brisson	outside Bordeaux Neurocampus	Multi-photons FLIM Confocal Microscope	11
Team Choquet	LabEx	Multi-photons FLIM Confocal Microscope	16
Team Photonique	LabEx	Multi-photons FLIM Confocal Microscope	17
Team Bézard	LabEx	Slides Scanner - Nanozoomer	7
Team Garret	Bordeaux Neurocampus outside LabEx	Slides Scanner - Nanozoomer	1
Team Herry	LabEx	Slides Scanner - Nanozoomer	1
Team Humeau	LabEx	Slides Scanner - Nanozoomer	4
Team Maziarz	private	Slides Scanner - Nanozoomer	2
Team Photonique	LabEx	Slides Scanner - Nanozoomer	6
Team Piazza	LabEx	Slides Scanner - Nanozoomer	1
Team Végétal	outside Bordeaux Neurocampus	Slides Scanner - Nanozoomer	1
Team Choquet	LabEx	Spinning-disk DC Microscope	22
Team Photonique	LabEx	Spinning-disk DC Microscope	1
Team Baufreton	Bordeaux Neurocampus outside LabEx	Spinning-disk LIFA Microscope	27
Team Boue-Grabot	Bordeaux Neurocampus outside LabEx	Spinning-disk LIFA Microscope	20
Team Choquet	LabEx	Spinning-disk LIFA Microscope	79
Team Frick	LabEx	Spinning-disk LIFA Microscope	23
Team Groc	LabEx	Spinning-disk LIFA Microscope	42
Team Humeau	LabEx	Spinning-disk LIFA Microscope	2
Team Landry	LabEx	Spinning-disk LIFA Microscope	10
Team Mulle	LabEx	Spinning-disk LIFA Microscope	5
Team Oliet	LabEx	Spinning-disk LIFA Microscope	42
Team Photonique	LabEx	Spinning-disk LIFA Microscope	41
Team Piazza	LabEx	Spinning-disk LIFA Microscope	6
Team Thoumine	LabEx	Spinning-disk LIFA Microscope	10
Team Wodrich, Kann	outside Bordeaux Neurocampus	Spinning-disk LIFA Microscope	20
Team Choquet	LabEx	TIRF - PALM Microscope	48
Team Lambert	outside Bordeaux Neurocampus	TIRF - PALM Microscope	4
Team Maurel	outside Aquitaine Region	TIRF - PALM Microscope	3
Team Mège	outside Aquitaine Region	TIRF - PALM Microscope	4
Team Montcouquiol	LabEx	TIRF - PALM Microscope	22
Team Photonique	LabEx	TIRF - PALM Microscope	35
Team Thoumine	LabEx	TIRF - PALM Microscope	40
Team Barthélémy	outside Bordeaux Neurocampus	Video-spinning-disk Microscope	2
Team Baufreton	Bordeaux Neurocampus outside LabEx	Video-spinning-disk Microscope	1
Team Choquet	LabEx	Video-spinning-disk Microscope	16
Team Frick	LabEx	Video-spinning-disk Microscope	3
Team Landry	LabEx	Video-spinning-disk Microscope	4
Team Montcouquiol	LabEx	Video-spinning-disk Microscope	6
Team Photonique	LabEx	Video-spinning-disk Microscope	18

2013

Name of the PI	prestation	affiliation	nb
Team Abrous	Analysis workstation 1	LabEx	72
Team Arveiler	Analysis workstation 1	outside Bordeaux Neurocampus	9
Team Baufreton	Analysis workstation 1	Bordeaux Neurocampus outside LabEx	1
Team Berger	Analysis workstation 1	outside Bordeaux Neurocampus	26
Team Bessoule Moreau	Analysis workstation 1	outside Bordeaux Neurocampus	14
Team Bézard	Analysis workstation 1	LabEx	1
Team Blanco	Analysis workstation 1	outside Bordeaux Neurocampus	7
Team Cardinal	Analysis workstation 1	outside Bordeaux Neurocampus	1
Team Cattaert	Analysis workstation 1	LabEx	4
Team Choquet	Analysis workstation 1	LabEx	8
Team Davanger	Analysis workstation 1	outside Aquitaine Region	5
Team Dulon	Analysis workstation 1	outside Bordeaux Neurocampus	11
Team Frick	Analysis workstation 1	LabEx	3
Team Garret	Analysis workstation 1	outside Bordeaux Neurocampus	24
Team Groc	Analysis workstation 1	LabEx	5
Team Humeau	Analysis workstation 1	LabEx	4
Team Landry	Analysis workstation 1	LabEx	1
Team Marighetto	Analysis workstation 1	LabEx	14
Team Maziarz	Analysis workstation 1	private	2
Team Montcouquiol	Analysis workstation 1	LabEx	17
Team Mulle	Analysis workstation 1	LabEx	7
Team Nagerl	Analysis workstation 1	LabEx	2
Team Oliet	Analysis workstation 1	LabEx	2
Team Ollat	Analysis workstation 1	outside Bordeaux Neurocampus	2
Team Photonique	Analysis workstation 1	LabEx	29
Team Piazza	Analysis workstation 1	LabEx	10
Team Abrous	Analysis workstation 2	LabEx	11
Team Arveiler	Analysis workstation 2	outside Bordeaux Neurocampus	10
Team Baufreton	Analysis workstation 2	Bordeaux Neurocampus outside LabEx	17
Team Bessoule Moreau	Analysis workstation 2	outside Bordeaux Neurocampus	1
Team Blanco	Analysis workstation 2	outside Bordeaux Neurocampus	6
Team Bontempi	Analysis workstation 2	LabEx	2
Team Cardinal	Analysis workstation 2	outside Bordeaux Neurocampus	1
Team Dulon	Analysis workstation 2	outside Bordeaux Neurocampus	14
Team Garret	Analysis workstation 2	outside Bordeaux Neurocampus	8
Team Groc	Analysis workstation 2	LabEx	4
Team Kind	Analysis workstation 2	outside Aquitaine Region	2
Team Layé	Analysis workstation 2	outside Bordeaux Neurocampus	26
Team Marighetto	Analysis workstation 2	LabEx	6
Team Montcouquiol	Analysis workstation 2	LabEx	7
Team Mulle	Analysis workstation 2	LabEx	9
Team Nagerl	Analysis workstation 2	LabEx	4
Team Oliet	Analysis workstation 2	LabEx	31
Team Photonique	Analysis workstation 2	LabEx	15
Team Piazza	Analysis workstation 2	LabEx	16
Team Rosenbaum	Analysis workstation 2	outside Bordeaux Neurocampus	2
Team Wodrich, Kann	Analysis workstation 2	outside Bordeaux Neurocampus	2
Team Choquet	Analysis workstation PALM	LabEx	9
Team Garret	Analysis workstation PALM	outside Bordeaux Neurocampus	34

Team Kind	Analysis workstation PALM	outside Aquitaine Region	3
Team Maurel	Analysis workstation PALM	outside Aquitaine Region	2
Team Montcouquiol	Analysis workstation PALM	LabEx	4
Team Oliet	Analysis workstation PALM	LabEx	12
Team Photonique	Analysis workstation PALM	LabEx	4
Team Plested	Analysis workstation PALM	outside Aquitaine Region	16
Team Thoumine	Analysis workstation PALM	LabEx	5
Team Wodrich, Kann	Analysis workstation SFR TransBioMed	outside Bordeaux Neurocampus	1
Team Behr	Confocal SP5 (SFR TransBioMed) Microscope	outside Bordeaux Neurocampus	2
Team Bessoule Moreau	Confocal SP5 (SFR TransBioMed) Microscope	outside Bordeaux Neurocampus	8
Team Chevet	Confocal SP5 (SFR TransBioMed) Microscope	outside Bordeaux Neurocampus	2
Team Petry	Confocal SP5 (SFR TransBioMed) Microscope	outside Bordeaux Neurocampus	3
Team Photonique	Confocal SP5 (SFR TransBioMed) Microscope	LabEx	27
Team Rosenbaum	Confocal SP5 (SFR TransBioMed) Microscope	outside Bordeaux Neurocampus	70
Team Ventura, Andréola, Fleury	Confocal SP5 (SFR TransBioMed) Microscope	outside Bordeaux Neurocampus	1
Team Wodrich, Kann	Confocal SP5 (SFR TransBioMed) Microscope	outside Bordeaux Neurocampus	233
Argolight	Confocal SP8 Microscope	private	3
Team Abrous	Confocal SP8 Microscope	LabEx	26
Team Arveiler	Confocal SP8 Microscope	outside Bordeaux Neurocampus	32
Team Baufreton	Confocal SP8 Microscope	Bordeaux Neurocampus outside LabEx	13
Team Bessoule Moreau	Confocal SP8 Microscope	outside Bordeaux Neurocampus	45
Team Bézard	Confocal SP8 Microscope	LabEx	13
Team Bontempi	Confocal SP8 Microscope	LabEx	1
Team Canioni	Confocal SP8 Microscope	outside Bordeaux Neurocampus	16
Team Cardinal	Confocal SP8 Microscope	outside Bordeaux Neurocampus	2
Team Cattaert	Confocal SP8 Microscope	LabEx	2
Team Choquet	Confocal SP8 Microscope	LabEx	2
Team Dulon	Confocal SP8 Microscope	outside Bordeaux Neurocampus	13
Team Electronique	Confocal SP8 Microscope	LabEx	6
Team Frick	Confocal SP8 Microscope	LabEx	10
Team Garret	Confocal SP8 Microscope	outside Bordeaux Neurocampus	19
Team Groc	Confocal SP8 Microscope	LabEx	4
Team Humeau	Confocal SP8 Microscope	LabEx	1
Team Lambert	Confocal SP8 Microscope	outside Bordeaux Neurocampus	5
Team Landry	Confocal SP8 Microscope	LabEx	29
Team Layé	Confocal SP8 Microscope	outside Bordeaux Neurocampus	24
Team LPO	Confocal SP8 Microscope	outside Bordeaux Neurocampus	19
Team Montcouquiol	Confocal SP8 Microscope	LabEx	42
Team Mulle	Confocal SP8 Microscope	LabEx	3
Team Oliet	Confocal SP8 Microscope	LabEx	25
Team Ortega	Confocal SP8 Microscope	outside Bordeaux Neurocampus	11
Team Petry	Confocal SP8 Microscope	outside Bordeaux Neurocampus	7
Team Photonique	Confocal SP8 Microscope	LabEx	36
Team Thoby-Brisson	Confocal SP8 Microscope	LabEx	13
Team Végétal	Confocal SP8 Microscope	outside Bordeaux Neurocampus	2
Team Wodrich, Kann	Confocal SP8 Microscope	outside Bordeaux Neurocampus	5
Team Abrous	Confocal SPE Microscope	LabEx	122
Team Baufreton	Confocal SPE Microscope	Bordeaux Neurocampus outside LabEx	4
Team Bézard	Confocal SPE Microscope	LabEx	2
Team Frick	Confocal SPE Microscope	LabEx	7

Team Groc	Confocal SPE Microscope	LabEx	5
Team Herry	Confocal SPE Microscope	LabEx	6
Team Humeau	Confocal SPE Microscope	LabEx	4
Team Lambert	Confocal SPE Microscope	outside Bordeaux Neurocampus	1
Team Landry	Confocal SPE Microscope	LabEx	32
Team Marighetto	Confocal SPE Microscope	LabEx	21
Team Mulle	Confocal SPE Microscope	LabEx	12
Team Petit	Confocal SPE Microscope	outside Bordeaux Neurocampus	6
Team Photonique	Confocal SPE Microscope	LabEx	17
Team Bessoule Moreau	Confocal STED Microscope	outside Bordeaux Neurocampus	31
Team Canaux Ioniques et Polarité Neuronale	Confocal STED Microscope	outside Aquitaine Region	1
Team Cattaert	Confocal STED Microscope	LabEx	18
Team Choquet	Confocal STED Microscope	LabEx	1
Team Dargent	Confocal STED Microscope	outside Aquitaine Region	2
Team Frick	Confocal STED Microscope	LabEx	15
Team Garret	Confocal STED Microscope	outside Bordeaux Neurocampus	9
Team Genot	Confocal STED Microscope	outside Bordeaux Neurocampus	3
Team Groc-Georges	Confocal STED Microscope	LabEx	3
Team Kind	Confocal STED Microscope	outside Aquitaine Region	24
Team Lambert	Confocal STED Microscope	outside Bordeaux Neurocampus	13
Team Morin	Confocal STED Microscope	outside Bordeaux Neurocampus	18
Team Mulle	Confocal STED Microscope	LabEx	54
Team Nagerl	Confocal STED Microscope	LabEx	15
Team Oliet	Confocal STED Microscope	LabEx	2
Team Photonique	Confocal STED Microscope	LabEx	67
Team Rosenbaum	Confocal STED Microscope	outside Bordeaux Neurocampus	19
Team Thoumine	Confocal STED Microscope	LabEx	2
Team Veyret	Confocal STED Microscope	outside Bordeaux Neurocampus	1
Team Wodrich, Kann	Confocal STED Microscope	outside Bordeaux Neurocampus	2
Team Blanco	Epifluorescence DM 5000 Microscope	outside Bordeaux Neurocampus	1
Team Choquet	Epifluorescence DM 5000 Microscope	LabEx	172
Team Cota	Epifluorescence DM 5000 Microscope	LabEx	1
Team Frick	Epifluorescence DM 5000 Microscope	LabEx	4
Team Groc	Epifluorescence DM 5000 Microscope	LabEx	40
Team Groc-Georges	Epifluorescence DM 5000 Microscope	LabEx	4
Team Herry	Epifluorescence DM 5000 Microscope	LabEx	31
Team Humeau	Epifluorescence DM 5000 Microscope	LabEx	8
Team Layé	Epifluorescence DM 5000 Microscope	outside Bordeaux Neurocampus	42
Team Marighetto	Epifluorescence DM 5000 Microscope	LabEx	2
Team Mulle	Epifluorescence DM 5000 Microscope	LabEx	24
Team Oliet	Epifluorescence DM 5000 Microscope	LabEx	8
Team Photonique	Epifluorescence DM 5000 Microscope	LabEx	25
Team Choquet	Epifluorescence microscope	LabEx	2
Team Cota	Epifluorescence microscope	LabEx	12
Team Frick	Epifluorescence microscope	LabEx	1
Team Landry	Epifluorescence microscope	LabEx	2
Team Photonique	Epifluorescence microscope	LabEx	17
Team Piazza	Epifluorescence microscope	LabEx	4
Team Choquet	Epifluorescence Zeiss Microscope	LabEx	8
Team Mulle	Epifluorescence Zeiss Microscope	LabEx	38

Team Photonique	Epifluorescence Zeiss Microscope	LabEx	1
Team Choquet	GSD Microscope	LabEx	19
Team Dargent	GSD Microscope	outside Aquitaine Region	3
Team Genot	GSD Microscope	outside Bordeaux Neurocampus	2
Team Oda	GSD Microscope	outside Bordeaux Neurocampus	4
Team Photonique	GSD Microscope	LabEx	29
Team Rosenbaum	GSD Microscope	outside Bordeaux Neurocampus	1
Team Thoumine	GSD Microscope	LabEx	4
Team Groc	Macroscope	LabEx	24
Team Montcouquiol	Macroscope	LabEx	1
Team Nagerl	Macroscope	LabEx	3
Team Photonique	Macroscope	LabEx	5
Team Piazza	Macroscope	LabEx	3
Team Thoumine	Macroscope	LabEx	1
Team Veyret	Macroscope	outside Bordeaux Neurocampus	1
Team Brisson	Microscope Confocal Multi-photons FLIM et FCS	outside Bordeaux Neurocampus	39
Team Photonique	Microscope Confocal Multi-photons FLIM et FCS	LabEx	12
Team Bontempi	Multi-photon Electrophysiology Confocal Microscope	LabEx	6
Team Layé	Multi-photon Electrophysiology Confocal Microscope	outside Bordeaux Neurocampus	21
Team Photonique	Multi-photon Electrophysiology Confocal Microscope	LabEx	2
Team Abrous	Slides Scanner - Nanozoomer	LabEx	17
Team Baufreton	Slides Scanner - Nanozoomer	Bordeaux Neurocampus outside LabEx	2
Team Berger	Slides Scanner - Nanozoomer	outside Bordeaux Neurocampus	14
Team Berrada	Slides Scanner - Nanozoomer	private	2
Team Bézard	Slides Scanner - Nanozoomer	LabEx	23
Team Blanco	Slides Scanner - Nanozoomer	outside Bordeaux Neurocampus	2
Team Bontempi	Slides Scanner - Nanozoomer	LabEx	20
Team Cota	Slides Scanner - Nanozoomer	LabEx	1
Team Frick	Slides Scanner - Nanozoomer	LabEx	32
Team Garret	Slides Scanner - Nanozoomer	outside Bordeaux Neurocampus	1
Team Groc	Slides Scanner - Nanozoomer	LabEx	5
Team Groc-Georges	Slides Scanner - Nanozoomer	LabEx	7
Team Herry	Slides Scanner - Nanozoomer	LabEx	23
Team Humeau	Slides Scanner - Nanozoomer	LabEx	16
Team Landry	Slides Scanner - Nanozoomer	LabEx	6
Team Layé	Slides Scanner - Nanozoomer	outside Bordeaux Neurocampus	13
Team Marighetto	Slides Scanner - Nanozoomer	LabEx	4
Team Maziarz	Slides Scanner - Nanozoomer	private	2
Team Montcouquiol	Slides Scanner - Nanozoomer	LabEx	15
Team Mulle	Slides Scanner - Nanozoomer	LabEx	7
Team Photonique	Slides Scanner - Nanozoomer	LabEx	23
Team Piazza	Slides Scanner - Nanozoomer	LabEx	10
Team Sibarita	Slides Scanner - Nanozoomer	LabEx	2
Team Veyret	Slides Scanner - Nanozoomer	outside Bordeaux Neurocampus	1
Team Choquet	Spinning-disk DC Microscope	LabEx	117
Team Photonique	Spinning-disk DC Microscope	LabEx	8
Team Plested	Spinning-disk DC Microscope	outside Aquitaine Region	8
Team Choquet	Spinning-disk LIFA Microscope	LabEx	110
Team Frick	Spinning-disk LIFA Microscope	LabEx	14
Team Groc	Spinning-disk LIFA Microscope	LabEx	31

Team Le Masson	Spinning-disk LIFA Microscope	LabEx	20
Team Mulle	Spinning-disk LIFA Microscope	LabEx	18
Team Oliet	Spinning-disk LIFA Microscope	LabEx	40
Team Photonique	Spinning-disk LIFA Microscope	LabEx	45
Team Wodrich, Kann	Spinning-disk LIFA Microscope	outside Bordeaux Neurocampus	18
Team Choquet	TIRF - PALM Microscope	LabEx	47
Team Davanger	TIRF - PALM Microscope	outside Aquitaine Region	9
Team Humeau	TIRF - PALM Microscope	LabEx	2
Team Maurel	TIRF - PALM Microscope	outside Aquitaine Region	11
Team Montcouquiol	TIRF - PALM Microscope	LabEx	29
Team Photonique	TIRF - PALM Microscope	LabEx	17
Team Plested	TIRF - PALM Microscope	outside Aquitaine Region	9
Team Thoumine	TIRF - PALM Microscope	LabEx	8
Team Arveiler	Video-spinning-disk Microscope	outside Bordeaux Neurocampus	6
Team Baufreton	Video-spinning-disk Microscope	Bordeaux Neurocampus outside LabEx	19
Team Bessoule Moreau	Video-spinning-disk Microscope	outside Bordeaux Neurocampus	1
Team Choquet	Video-spinning-disk Microscope	LabEx	13
Team Electronique	Video-spinning-disk Microscope	LabEx	1
Team Freyburger	Video-spinning-disk Microscope	outside Bordeaux Neurocampus	2
Team Frick	Video-spinning-disk Microscope	LabEx	2
Team Garbay	Video-spinning-disk Microscope	outside Bordeaux Neurocampus	3
Team Groc	Video-spinning-disk Microscope	LabEx	35
Team Lambert	Video-spinning-disk Microscope	outside Bordeaux Neurocampus	3
Team Landry	Video-spinning-disk Microscope	LabEx	8
Team Le Masson	Video-spinning-disk Microscope	LabEx	1
Team Marsicano	Video-spinning-disk Microscope	LabEx	8
Team Montcouquiol	Video-spinning-disk Microscope	LabEx	2
Team Mulle	Video-spinning-disk Microscope	LabEx	7
Team Nagerl	Video-spinning-disk Microscope	LabEx	1
Team Ollat	Video-spinning-disk Microscope	outside Bordeaux Neurocampus	5
Team Ortega	Video-spinning-disk Microscope	outside Bordeaux Neurocampus	1
Team Photonique	Video-spinning-disk Microscope	LabEx	42
Team Plested	Video-spinning-disk Microscope	outside Aquitaine Region	17
Team Rosenbaum	Video-spinning-disk Microscope	outside Bordeaux Neurocampus	19
Team Sagot	Video-spinning-disk Microscope	outside Bordeaux Neurocampus	5
Team Sibarita	Video-spinning-disk Microscope	LabEx	2
Team Thoby-Brisson	Video-spinning-disk Microscope	outside Bordeaux Neurocampus	1
Team Thoumine	Video-spinning-disk Microscope	LabEx	1

Electronic:

Name of the PI	Laboratory	affiliation	prestation
P. GASSER	BIO-EC	outside Bordeaux Neurocampus	PEC + MDE
L. De GABORY	CHU de Bordeaux	outside Bordeaux Neurocampus	PEC + MDE
M. GARRET	INCIA	Bordeaux Neurocampus outside LabEx	PEC
E. GENOT	INSERM U1053	outside Bordeaux Neurocampus	PEC + MDE
B. SALIN	IBGC	outside Bordeaux Neurocampus	MDE
L. GROC	IINS - CNRS UMR 5297	LabEx	PEC + MDE
H. SEZNEC	Centre Etudes Nucléaires de Bordeaux Gradignan (C.E.N.B.G.)	outside Bordeaux Neurocampus	PEC + MDE
M. KANN	Microbiologie Fondamentale et Pathologique (MFP)	outside Bordeaux Neurocampus	PEC + MDE
N. ITURMENDI	LAFFORT R&D chimie et colloïdes	outside Bordeaux Neurocampus	MDE
M. CARIO-ANDRE	Biothérapies des maladies génétiques et du cancer	outside Bordeaux Neurocampus	PEC + MDE
T. OLINGA	Laboratoire IMS	outside Bordeaux Neurocampus	PEC + MDE
E. PAPON	Laboratoire de Chimie des Polymères Organiques (LCPO)	outside Bordeaux Neurocampus	PEC + MDE
M. DUMON	Département Science et Génie Matériaux - SGM- IUT Bx1	outside Bordeaux Neurocampus	PEC + MDE
M. BLANCHARD-DESCE	Institut des Sciences Moléculaires	outside Bordeaux Neurocampus	PEC + MDE
M. CARIO-ANDRE	Biothérapies des maladies génétiques et du cancer	outside Bordeaux Neurocampus	PEC + MDE
M. BLANCHARD-DESCE	Institut des Sciences Moléculaires	outside Bordeaux Neurocampus	PEC + MDE
J. COULON	Société LAFFORT	private	PEC + MDE
J. B. SIBARITA	IINS	LabEx	PEC + MDE
J. COLAT-PARROS	UFR Odontologie	outside Bordeaux Neurocampus	PEC + MDE
H. SEZNEC	Centre Etudes Nucléaires de Bordeaux Gradignan (C.E.N.B.G.)	outside Bordeaux Neurocampus	PEC + MDE
J. ASSERIN	Société COSDERMA	private	PEC + MDE
M. DUMON	LCPO	outside Bordeaux Neurocampus	PEC + MDE
E. GENOT	IECB	outside Bordeaux Neurocampus	PEC + MDE
F. D'Errico	PACEA	outside Bordeaux Neurocampus	PEC + MDE
M. BONHIVERS	UMR 5234	outside Bordeaux Neurocampus	PEC + MDE
N. ITURMENDI	Société LAFFORT	private	PEC + MDE
J. ROSENBAUM	U 1053	outside Bordeaux Neurocampus	PEC + MDE
G. FREYBURGER	Laboratoire d'hématologie	outside Bordeaux Neurocampus	PEC + MDE
S. JAVERZAT	LAMC	outside Bordeaux Neurocampus	PEC + MDE
L. BENALI	Laboratoire de médecine légale du droit de la santé	outside Bordeaux Neurocampus	MDE
T. DULUC	Société ADEMTECH	private	MDE
O. CHASSANDE	U1026	outside Bordeaux Neurocampus	MDE
D. KRAEMER	Société ASTRIUM	private	MDE
M.F. CORIO-COSTET	UMR santé et agroécologie du vignoble	outside Bordeaux Neurocampus	MDE
T. LEBARBE	Ecole Nationale Superieure de Chimie, de Biologie et de Physique - LCPO	outside Bordeaux Neurocampus	MDE
X. ERROTABEHERE	Institut de Mécanique et d'Ingénieurerie de Bordeaux (I2M)	outside Bordeaux Neurocampus	MDE
C. TALLET	CRPP-UPR 8641	outside Bordeaux Neurocampus	MDE
E. GENOT	INSERM U1053	outside Bordeaux Neurocampus	PEC + MDE
C. LE COZ	Ecole Nationale Superieure de Chimie, de Biologie et de Physique - LCPO	outside Bordeaux Neurocampus	MDE
HÖKFELT Thomas	Karolinska Institutet - Department of Neuroscience - Chemical Neurotrans	outside Aquitaine Region	PEC + MDE
P.C. SIVASANKARAN	CRPP-UPR 8641	outside Bordeaux Neurocampus	MDE
P. RICHETTI	CRPP-UPR 8641	outside Bordeaux Neurocampus	MDE
O. CAHUC	Institut de Mécanique et d'Ingénieurerie de Bordeaux (I2M)	outside Bordeaux Neurocampus	MDE
E. PAPON	Ecole Nationale Superieure de Chimie, de Biologie et de Physique - LCPO	outside Bordeaux Neurocampus	MDE
P. RICHETTI	CRPP-UPR 8641 - equipe 1 nanotubes et graphène	outside Bordeaux Neurocampus	MDE
K. PETRY	INSERM U.1049 Neuroinflammation, imagerie et thérapie de la sclérose e	Bordeaux Neurocampus outside LabEx	PEC + MDE
M. DOLS	ISVV	outside Bordeaux Neurocampus	PEC + MDE
P. RICHETTI	CRPP-UPR 8641	outside Bordeaux Neurocampus	MDE
O. CAHUC	Institut de Mécanique et d'Ingénieurerie de Bordeaux (I2M)	outside Bordeaux Neurocampus	MDE
E. PAPON	Ecole Nationale Superieure de Chimie, de Biologie et de Physique - LCPO	outside Bordeaux Neurocampus	MDE
P. RICHETTI	CRPP-UPR 8641 - equipe 1 nanotubes et graphène	outside Bordeaux Neurocampus	MDE
K. PETRY	INSERM U.1049 Neuroinflammation, imagerie et thérapie de la sclérose e	Bordeaux Neurocampus outside LabEx	PEC + MDE
M. DOLS	ISVV	outside Bordeaux Neurocampus	PEC + MDE

Name of the PI	Laboratory	affiliation	prestation
De GABORY Ludovic	CHU de Bordeaux	outside Bordeaux Neurocampus	PEC + MDE
GENOT Elisabeth	INSERM U1053	outside Bordeaux Neurocampus	PEC + MDE
SEZNEC Hervé	Centre Etudes Nucléaires de Bordeaux Gradignan (C.E.N.B.G.)	outside Bordeaux Neurocampus	PEC + MDE
KANN Michaël	Microbiologie Fondamentale et Pathologie (MFP)	outside Bordeaux Neurocampus	PEC + MDE
SALTEL Frédéric	Laboratoire de Physiopathologie du cancer du foie	outside Bordeaux Neurocampus	PEC + MDE
PAPON Eric	Laboratoire de Chimie des Polymères Organiques (LCPO)	outside Bordeaux Neurocampus	MDE
Blanchard-Desce Mirelle	Institut des Sciences Moléculaires	outside Bordeaux Neurocampus	MDE
HIRSCH Lionel	Laboratoire IMS	outside Bordeaux Neurocampus	MDE
MEUNIER Pauline	BIO-EC	outside Bordeaux Neurocampus	PEC + MDE
TATON Daniel	Laboratoire de Chimie des Polymères Organiques (LCPO)	outside Bordeaux Neurocampus	MDE
LECOUSTUMER Philippe	Ecole d'ingénieurs en Environnement, Géoressources et Ingénierie - ENSEGID	outside Bordeaux Neurocampus	PEC + MDE
LECOMMANDOUX Sébastien	Laboratoire de Chimie des Polymères Organiques (LCPO)	outside Bordeaux Neurocampus	MDE
CRAMAIL Henri	Laboratoire de Chimie des Polymères Organiques (LCPO)	outside Bordeaux Neurocampus	MDE
SAGINEAU Jean-Pierre	Centre de recherche Cardio-Thoracique de Bordeaux	outside Bordeaux Neurocampus	PEC + MDE
Bertrand Daignan-Fornier	IBGC	outside Bordeaux Neurocampus	MDE
REZVANI Hamid Reza	U1035 Biothérapie des Maladies Génétiques et Cancers	outside Bordeaux Neurocampus	PEC + MDE
Guido SONNEMANN	Institut des Sciences Moléculaires (ISM)	outside Bordeaux Neurocampus	MDE
Sebastien Lecommandoux	Laboratoire de Chimie des Polymères Organiques (LCPO)	outside Bordeaux Neurocampus	MDE
Massimiliano BELTRAMO	INRA UMR85	outside Aquitaine Region	PEC + MDE
Wilfried BLANC	UMR 7336	outside Bordeaux Neurocampus	PEC + MDE
Muriel Cario André	Laboratoire Biothérapie des Maladies Génétiques et Cancers	outside Bordeaux Neurocampus	PEC + MDE
C.BREHELIN	UMR 5200	outside Bordeaux Neurocampus	MDE
S.CATROS	U 1026	outside Bordeaux Neurocampus	MDE
C.Laplace-Treyture	IRSTEA	outside Bordeaux Neurocampus	MDE
E.GENOT	IECB	outside Bordeaux Neurocampus	PEC + MDE
G.BACHELET	EPOC/Eco bioc	outside Bordeaux Neurocampus	MDE
L.BORDENAVE	Laboratoire Bio ingénierie Tissulaire	outside Bordeaux Neurocampus	PEC + MDE
N.Mesmer-Dudons	EPOC/Eco Bioc	outside Bordeaux Neurocampus	MDE
J.RIPOCHE	Laboratoire Bio ingénierie Tissulaire	outside Bordeaux Neurocampus	PEC + MDE
HÖKFELT Thomas	Karolinska Institutet - Department of Neuroscience - Chemical Neurotransmission Research - Stockholm, SWEDEN	outside Aquitaine Region	PEC + MDE
FLEURY Guillaume	Laboratoire de Chimie des Polymères Organiques (LCPO)	outside Bordeaux Neurocampus	MDE
LANDRY Marc	UMR 5297 Interdisciplinary Institute for NeuroScience	LabEx	PEC + MDE
SOUM Alain	Laboratoire de Chimie des Polymères Organiques (LCPO)	outside Bordeaux Neurocampus	MDE
GENY Laurence	ISVV	outside Bordeaux Neurocampus	PEC + MDE
POULAIN Philippe	CRPP	outside Bordeaux Neurocampus	MDE
REZVANI Hamid Reza	U1035 Biothérapie des Maladies Génétiques et Cancers	outside Bordeaux Neurocampus	PEC + MDE
GENY Laurence	ISVV	outside Bordeaux Neurocampus	PEC + MDE
LAMBERT Olivier	Chimie et Biologie des membranes et nanoobjets, UMR 5248	outside Bordeaux Neurocampus	PEC + MDE
LECOUSTUMEUR philippe	ENSEGID	outside Bordeaux Neurocampus	PEC + MDE
LEPREUX Sébastien - RIPOCHE Jean	U1026 - Bioingénierie tissulaire	outside Bordeaux Neurocampus	PEC + MDE

LabEx support expenses in 2012:
Equipment:
LabEx support: 95000€
Name of the equipment,
Running costs (total labEx support expenses): 53900€

LabEx support expenses in 2013:
Equipment:
LabEx support: 95000€
Name of the equipment,: System of X microanalyse for MET
Running costs (total labEx support expenses):53900€

Movement Analysis

Head of the facility: CAZALETS Jean-René
Technical head: GUILLAUD Etienne
Location: University of Bordeaux, 146 rue Léo Saignat 33076 Bordeaux

Service offer:

The Movement Analysis Unit (PAM) is dedicated to the human gait, posture and movement studies. It is a part of the Aquitaine Institute for Cognitive and Integrative Neuroscience (INCIA) in Bordeaux.

The aim is to provide a full range of advanced technologies for non-invasive studies on humans to basic researchers and clinicians. Users are scientists from neuroscience, kinesiology or robotics as well as clinicians in neurology, physical rehabilitation, ergonomics, … Our space is approved for biomedical studies, and the proximity with biology laboratories allows us to transfer our technology to animal models.

We support annually about 20 basics research projects, with academic as well as private partners, and our team benefits from several grants for its own research.

The vicinity of Bordeaux hospital offers to the clinicians the possibility of high-level gait and abnormal movement analysis. An agreement with the hospital together with a strong partnership with the physical medicine unit leads to the clinical evaluation of about 150 patients per year (cerebral palsy, Parkinson disease, ...). Lastly, the PAM is an exceptional pedagogical support and we currently give lessons to students in science, medicine and physical rehabilitation that can apply immediately the learned tools.

Price list:

Clinical report	240€
One day rent without Engineer	450€
One day rent including Engineer support	830€

Personnel list (permanent and non permanent):

CAZALETS Jean-René (Scientific supervisor, permanent 10%)
GUILLAUD Etienne (Technic supervisor, permanent 80%)
BESTAVEN Emma (Engineer, non permanent, 100%)
DOAT Emilie (Technician, permanent 100%)

Outcomes (total in k€):

		2012	2013
Running cost		3 910	4 232
Human ressources	Permanent (€)	50 059	84 950
	Non permanent (€)	25 061	32 268
Equipment		30 547	9 960

Incomes (total in k€)

	2012		2013	
	organism	**amount (k€)**	**organism**	**amount (k€)**
Service provision				
	Clinical - CHU	12	Clinical - CHU	24
Subventions				
	Région Aquitaine	12	Région Aquitaine	5
	Labex Brain	10	Labex Brain	10
	EPHE	10		
Research contract				
	PHRC D. Lacombe	23	fondaMental (equipt.)	33
	UFR Odontologie	7	CNES	8
	Proteor company	1	Fond. Rech Med.	4
	CNES	4	UFR Odontologie	2
public permanent grant				
	Univ Bdx	1,5	Univ Bdx	1,5
	CNRS	1,5	CNRS	1,5

Users:

Name of the PI	Laboratory	affiliation	prestation	Hours	Year
Pr. Damon Perriere	IMN UMR 5293	LabEx	Parkinsoniens Neurostimulés	177	2013
Dr. Amestoy / Dr. Gallot /Dr Bouvard	Fondation FondaMental	Bordeaux Neurocampus outside LabEx	AUTISME	100	2013
Dr. Gallot	INCIA UMR 5297	Bordeaux Neurocampus outside LabEx	AUTISME	93	2013
Pr. Lacombe	EA	outside Bordeaux Neurocampus	RUBIVAL	72	2013
M. Lapeyre / M. Oudeyer	INRIA / INCIA	outside Bordeaux Neurocampus	NEUROBOT	60	2013
Pr. Dehail	EA 4136	Bordeaux Neurocampus outside LabEx	IMC	54	2013
Dr Ghorayeb	IMN UMR 5294	LabEx	(Vigiprimate)	50	2013
Pr. Burbaud / Pr Guehl	IMN UMR 5293	LabEx	TMS	50	2013
Dr. Halgand	INCIA UMR 5297	Bordeaux Neurocampus outside LabEx	NEUROBOT	45	2013
Dr. DeSèze	EA 4136	Bordeaux Neurocampus outside LabEx	Camptocormie / Scoliose	39	2013
Pr. Guehl	IMN UMR 5293	LabEx	Parkinson / TE / Dystonies	39	2013
Dr. Michelet	IMN UMR 5293	LabEx		35	2013
Dr. Amestoy / Pr. Bouvard	INCIA UMR 5297	Bordeaux Neurocampus outside LabEx	AUTISME / TDAH	30	2013

LabEx support expenses in 2012:

Equipment:

LabEx support: 10k€

Name of the equipment,

Floor walkway Zebris FDM 1.5mx2

The Zebris measuring system for force distribution enables the distribution of static and dynamic forces to be analyzed under the feet and is therefore suitable both for stance and gait analyses.

Co-financers

EPHE 10k€, Région Aquitaine 12k€

LabEx support expenses in 2013:

Equipment:

LabEx support: 10k€

Name of the equipment

Wrist Manipulandum using a 6-df force/torque transducer (JR3, Woodland, CA)

Co-financers: Région Aquitaine 3k€
Human Resources: (total LabEx support expenses):
List of recruitments (name, function, nb of month)

LabEx support expenses in 2013:
Equipment:
LabEx support:
Name of the equipment,
Co-financers
Running costs (total labEx support expenses):
Human Resources: (total LabEx support expenses):
List of recruitments (name, function, nb of month)

NeuroPsychoPharmacology

Head of the facility: Pr. Pierre PHILIP
Technical head: Jacques TAILLARD & Pr. Pierre PHILIP
Project coordinator: Cécile KLOCHENDLER
Location: CHU Bordeaux

Service offer:

Clinical research:
- Design and conduct of biomedical research in healthy volunteers or patients
- Technical or logistic supports for protocol implementation
- Methodological advice
- Secured storage of biological samples
- Programming of scenarios for virtual reality and simulation

Supply of:
- Specific premises and equipment for clinical research:
  - 1 room for pharmacological trials (4 beds) with a nursing station
  - 4 rooms for polysomnography and EEG recorders connected to a control room
  - Behavioural and electrophysiological equipment: activity and physiological parameters recorders
  - Consultation and experimental rooms
  - Virtual reality equipment: Cave Automatic Virtual Environment, Virtual Classroom, Virtual Supermarket (memory and attention test)
  - Driving and flying performance assessment: driving simulators, assessment in real Environment (car), cockpit simulator

❖ specialized staff
- nurse
- clinical research associates
- clinical research technician
- psychologist
- research engineers
- technicians
- researchers
- medical consultant
- administrative staff

2013 Price List:

PATIENT ROOM PER DAY	
< 24 hours	90,00 €
≥ 24 hours	180,00 €
NON MEDICAL STAFF - Costs per hour	
Clinical Research Associate	31,00 €
Clinical Research Technician	31,00 €
Project Mamager	46,00 €
Secretary	31,00 €
MEDICAL STAFF - Costs per hour	
Nurse	42,85 €
Practitionner	66,00 €
Psychologist	34,84 €
Consultation	25,00 €
Neuropsychologist's consultation	34,30 €
FACILITIES	
Consultation or experimental room (half-day)	50 €
SERVICE PROVISIONS AND EQUIPMENTS	
Ambulatory polysomnograph	50 €
Polysomnography	500 €
Actimeter (/month)	50 €
TME	250 €
Driving simulator (/hour)	200 €
Biological samples storage at ultra-low temperature	
1 Box h50mm /year	48,60 €
1 Box h100mm/year	97,20 €
Administrative fee	9%

Free for Bordeaux Neurocampus Members

Personnel list (permanent and non permanent):

Name	Function	Status	%time in the facility	% LabEx funding in 2013
BACARISSE Muriel	Clinical Research Associate	Non permanent	100%	0%
BIBENE Victor	Clinical Research Technician	Non permanent	100%	62,50%
BIOULAC Stéphanie	Physician-researcher	Permanent	30%	0%
BOISEAU Aurélien	Clinical Research Associate	Non permanent	100%	16%
CHAUDRUC Bénédicte	Nurse	Non permanent	80%	0%
CHAUFTON Cyril	Physician-researcher	Non permanent	50%	0%
CHEN Xue	Technician	Non permanent	100%	0%
COUTANTIN Corinne	Administrative assistant	Permanent	10%	0%
IBARRUTHY Florian	Psychologist	Non permanent	100%	0%
KLOCHENDLER Cécile	Project coordinator	Non permanent	100%	0%
OLIVE Jérôme	Research engineer	Non permanent	100%	0%
PHILIP Pierre	Head of & physician-researcher	Permanent	50%	0%
SAGASPE Patricia	Researcher, project manager	Non permanent	100%	25%
SAUTERAUD Alain	Medical consultant	Non permanent	10%	0%
TAILLARD Jacques	Research engineer	Permanent	100%	0%
VALTAT Cédric	Clinical Research Associate	Non permanent	100%	0%

Outcomes (total in k€):

		2012	2013
Running cost			35 000 €
Human ressources	Permanent (k€)		126 970 €
	Non permanent (k€)		515 432 €
Equipment			878 910 €

Incomes (total in k€)

	2012		2013	
	organism	amount (k€)	organism	amount (k€)
Service provision			Nutrineuro (Bordeaux University)	104,7
Subventions	LabEx BRAIN	99,3	LabEx BRAIN	99,3
	CHU Bordeaux	143,4	CHU Bordeaux	182,1
	EquipEx PHENOVIRT	977,2	EquipEx PHENOVIRT	97,6
	Bordeaux University	22	Bordeaux University	22
	CNRS	49,8	CNRS	16,6
Research contract	Industry	5,7	Industry	3
	ANR	267,66	ANR	67,7
			ACVEAH association	26
			CHU Bordeaux	30
public permanent grant	CNRS	67	CNRS	67
	Bordeaux University	70	Bordeaux University	70
	CHU Bordeaux	5	CHU Bordeaux	5

Users:

Name of the PI	Laboratory	affiliation	prestation	nb of prestation	year
Pr Auriacombe	CHU CMRR - IMN	LabEx	supply of experimental and consultation room	3 half-days	2012
Pr Brochet	CHU Neurology Dpt	Bordeaux Neurocampus outside LabEx	use of driving simulator	74 hours	2012
Dr Gross	IMN	LabEx	conception of a virtual reality maze	1	2012
Dr Cota	Neurocentre Magendie	LabEx	half-days of hospitalization	124 half-days	2012
Pr Moore	Clinical Pharmacology	outside Bordeaux Neurocampus	supply of experimental and consultation rooms	420 half-days	2012
Pr Brochet	CHU Neurology Dpt	Bordeaux Neurocampus outside LabEx	supply of experimental and consultation room	82 half-days	2013
Pr Brochet	CHU Neurology Dpt	Bordeaux Neurocampus outside LabEx	use of driving simulator	20 hours	2013
Pr Brochet	CHU Neurology Dpt	Bordeaux Neurocampus outside LabEx	supply of specialized clinical research staff	1 person-month	2013
Pr Sibon	CHU Neurology Dpt	Bordeaux Neurocampus outside LabEx	supply of consultation room	52 half-days	2013
Pr Meissner	IMN	LabEx	biological samples storage	5 boxes-year	2013
Pr Dartigues	IMN	LabEx	supply of rooms	52 half-days	2013
Pr Burbaud	IMN	LabEx	supply of an ambulatory polysomnograph	3 polysomnograph-months	2013
Dr Cota	Neurocentre Magendie	LabEx	half-days of hospitalizations	16 half-days	2013
Dr Cota	Neurocentre Magendie	LabEx	supply of consultation rooms	16 half-days	2013
Dr Cota	Neurocentre Magendie	LabEx	supply of specialized clinical research staff	1 person-month	2013
Pr Layé	UMR INRA 1286	outside Bordeaux Neurocampus	supply of specialized clinical research staff	27 person-months	2013
Pr Zerbib	CHU Gastro-enterology Dpt	outside Bordeaux Neurocampus	supply of actimeters	40 actimeter-months	2013
Pr Bernhard	CHU Urology Dpt	outside Bordeaux Neurocampus	Biological samples storage	230 boxes-year	2013

LabEx support expenses in 2012:

Equipment:

LabEx support: 10k€
Name of the equipment: Ultra-Low temperature freezer
Co-financers: No
Running costs (total labEx support expenses): 39,9 k€
Human Resources: (total LabEx support expenses): 39,2 k€
List of recruitments (name, function, nb of month):
Aurore Capelli, Project Manager, 3 person-months
Victor Bibène, Clinical Research Technician, 3 person-months
Cédric Valtat, Clinical Research Associate, 3 person-months

LabEx support expenses in 2013:

Equipment:
LabEx support: 10 k€
Name of the equipment: 14 actimeters
Co-financers: No
Running costs (total labEx support expenses): 46,4 k€
Human Resources: (total LabEx support expenses): 29,8 k€
List of recruitments (name, function, nb of month):
Victor Bibène, Clinical Research Technician, 5 person-months
Patricia Sagaspe, Project Manager, 2,5 person-months

Primate Experimental Facility

Head of the facility: Christian Gross
Technical head: Tho Hai Nguyen
Location: Institut des Maladies Neurodégénératives
UMR 5293
Université Bordeaux
146 rue Leo Saignat, 33076 Bordeaux cedex

Service offer:
Management of purchase, housing, methodological support and animal supply

The primate animal house was designed so as to house 22 monkeys (Macaca mulatta, Macaca fascicularis) in individual cages, which can be converted into birdcages according to species and their use, thus supporting any kind of experimentation whether it is a behavioural, physiological, genetic or a vigilance study. Management and supply of the experimental rooms and the surgery unit

The surgery unit comprises an operating room enabling any kind of surgeries and a digital radio system providing front and profile images with an enlargement of 1. It is specialised in central nervous system stereotaxy making use of a stereotactic frame combined with a neuronavigation system.

Users can use, under certain conditions:

a lab bench for the preparation of experiments;
three electrophysiological recording stations, equipped with a Faraday cage and a device of work paradigm recording and management;
a room for experimentations with TMS (Transcranial Magnetique Stimulation) also equipped with the Neuronave tracking system and an electophysiological recording station;
a room for behavioural analyses equipped with an observation cage and with a motion analysis device (Vigiprimate);
a big adjustable room (housing a labyrinth of nine identical rooms);
a virtual reality device.

These premises are shared but can be used by a preferred user.

Management and/or common purchase of animal house equipment for research teams

Services offered by a skilled staff who takes into consideration the specific operational imperatives of the platform and the research work

Its objective is also to contribute to the training of the staff working with the animals.

Support to get access to MRI services

Relations with the animal houses of other platforms, with private sector partners (service providers for experimentation) and with the experimentation ethics committee (CREEA50)

The operating of the primate platform is funded by a flat-rate billing i.e a per diem per capita. Users are billed on a quaterly basis. The per diem is reviewed each year according to the last financial period and the forecast of future expenses.

Price list:

laboratories user membership	per diem per capita
Bordeaux Neurocampus Labex users	3.3 €
Others	6.6 €

Personnel list (permanent and non permanent):

- Head of the facility: Christian Gross
- Technical head: Tho Hai Nguyen
- Technician: Hugues Orignac
- Veterinary: Elodie Moureaux

Outcomes (total in k€):

		2012	2013
Running cost		30 k€	31 k€
Human ressources	Permanent (k€)	82 k€	82 k€
	Non permanent (k€)	7 k€	1 k€
Equipment		24 k€	10 k€

Incomes (total in k€)

	2012		2013	
	organism	amount (k€)	organism	amount (k€)
Service provision	Bordeaux Neurocampus Labex users	21,1 k€	Bordeaux Neurocampus Labex users	8,6 k€
Subventions	Labex Brain	40,5 k€	Labex Brain	40,5 k€
Research contract				
public permanent grant				

Users:

Name of the PI	Laboratory	affiliation	prestation	nb of prestation	year
E. Bézard	IMN	LabEx	Housing, methodological support and animal supply, surgery, management of purchase	5 animals	2012
T. Boraud	IMN	LabEx	Housing, methodological support and animal supply, surgery, management of purchase	5 animals	2012
P. Burbaud	IMN	LabEx	Housing, methodological support and animal supply, surgery, management of purchase	10 animals	2012
A. Benazzouz	IMN	LabEx	Housing, methodological support and animal supply, surgery, management of purchase	2 animals	2012
E. Bézard	IMN	LabEx	Housing, methodological support and animal supply, surgery, management of purchase	1 animals	2013
T. Boraud	IMN	LabEx	Housing, methodological support and animal supply, surgery, management of purchase	8 animals	2013
P. Burbaud	IMN	LabEx	Housing, methodological support and animal supply, surgery, management of purchase	10 animals	2013

LabEx support expenses in 2012:
Equipment:
LabEx support: 24 000€
Name of the equipment,
Equipment (23 741€): Primate stereotaxic equipment 6940€, anesthesia system 10736€, surgical table 6065€
Co-financers
Running costs (total labEx support expenses): 14000€

LabEx support expenses in 2013:
Equipment:
LabEx support: 18 K€
Name of the equipment,
Equipement (10098 €):Primate videotracking 5890 €, Primate chair 3022 €, perfusion set 1186 €,
Co-financers
Running costs (total labEx support expenses): 22250 €

Cellular Biology Facility

Head of the facility: Christelle Breillat and Françoise Coussen
Location: Neurocentre magendie et CGFB

Service offer:
a) Main equipment
Levels of confinement: The cell culture facility is divided into 2 culture laboratories with a L2 level of confinement, one of these L2 lab is also in negative pressure relative to intermediate room.

Equipment for cell culture:

These cell culture rooms are equipped with the following:

- 8 laminar flow hoods
- 2 horizontal flow hoods for dissections with stereoscope
- 11 CO2 incubators
- 2 Inverted microscopes for examination of cell growth, 2 of them are equipped with fluorescence
- Refrigerators / Freezers
- Refrigerated centrifuge, Water Bath 37°C
- 2 Amaxa nucleofactors from Lonza
- 2 picospritzers for viral injection in slices

Note: Two laminar flow hoods and two CO2 incubators are dedicated for virus transduction.

Equipment for molecular biology and Biochemistry:

- 2 incubators
- 2 rotative incubators
- 5 Thermocyclers
- 2 Imager E-BOX VX2
- Biochemistry equipment: migration and transfer material

b) Service offer

- Advice
- Primary culture of neurons (rat, mouse)
- Heterologous cells culture (several cells lines)
- Stable cells lines
- Gene transfer (transfection reagent, AMAXA electroporation, AAV and lentivirus transduction)
- Mycoplasma detection
- Building of cDNA
- Protein characterization
- Protein purification and production

c) Training activities:

Knowledge transfer on

- Neuron primary cultures, gene transfer
- Molecular biology (methods and cloning techniques)
- Biochemistry (methods and techniques)

Research and development

The cell culture resource of IINS can help you in setting up your culture systems. It can also provide primary neuronal cultures on a contract basis (specific model for your own application).

The molecular biology and biochemistry resources of IINS can help you in setting up the optimal cloning strategies or protein production systems for your projects of interest.

Price list:

Price/dish (unit):

Private:893€
Academic:223€
Bordeaux Neurocampus:122€
IINS:free

Price/dish (for20):

Private:375
Academic: 94
Bordeaux Neurocampus:50
IINS:free

Epitopes (X4):

Private: 27225€
Academic: 13613€
Bordeaux Neurocampus:7563€

IINS:free

Western Blot:
Private: 690€
Academic: 345€
Bordeaux Neurocampus:192€
IINS:free

Personnel list (permanent and non permanent):

- Emeline Verdier technician, 100%
- Natacha Retailleau, technician, 100%
- Camille Genuer, engineer 50%
- Zeynep Karatas, , technician, 100%
- Isabel Gauthereau, 50%
- Amandine Philippat, 100%
- Pauline Durand, technician, 100%
- Sébastien Benquet, technician, 50%
- Béatrice Tessier, technician, 30%
- Delphine Bouchet, engineer 30%
- Rémi sterling, technician, 10%
- Christelle Breillat, , engineer 20%
- Matthieu Sainlos, researcher, 20%)
- Françoise Coussen, research director, 20%

Outcomes (total in k€):

		2012	2013
Running cost		201	306,6
Human ressources	Permanent (k€)		
	Non permanent (k€)	195	195
Equipment		75,5	130,06

Incomes (total in k€)

	2012		2013	
	organism	amount (k€)	organism	amount (k€)
Service provision		471,5		631,7
Subventions	LabEx	53,13	LabEx	120,5
Research contract	ANR	313,8	ANR	383,4
	European contract	104,6	European contract	127,8
public permanent grant				

Users:

Name of the PI	Laboratory	affiliation	prestation	nb	year
Choquet	IINS	LabEx	culture rat	30	2012
Choquet	IINS	LabEx	BM-Biochimie	75	2012
Groc	IINS	LabEx	culture rat	30	2012
Groc	IINS	LabEx	BM-Biochimie	75	2012
Thoumine	IINS	LabEx	culture rat	30	2012
Thoumine	IINS	LabEx	BM-Biochimie	75	2012
Landry	IINS	LabEx	culture rat	5	2012
Landry	IINS	LabEx	BM-Biochimie	10	2012
Mulle	IINS	LabEx	culture rat	5	2012
Mulle	IINS	LabEx	BM-Biochimie	40	2012
Nagaerl	IINS	LabEx	culture rat	5	2012
Nagaerl	IINS	LabEx	BM-Biochimie	5	2012
Lounis B.	bordeaux I	outside Bordeaux Neurocampus	culture rat	1	2012
Castillo J.	Spain	outside Aquitaine Region	culture rat	1	2012
Meunier	Australia	outside Aquitaine Region	culture rat	1	2012
BIC	bordeaux I	LabEx	culture rat	1	2012
Kazmareck L.	eurobioimaging/Choquet	outside Aquitaine Region	culture rat	1	2012
Heine M.	eurobioimaging/Thoumine	outside Aquitaine Region	culture rat	1	2012
Carvalho A.L.	eurobioimaging/Choquet	outside Aquitaine Region	culture rat	1	2012
Meunier F.	eurobioimaging/Choquet	outside Aquitaine Region	culture rat	1	2012
Cooper D.	eurobioimaging/Choquet	outside Aquitaine Region	culture rat	1	2012
Esteban J.	eurobioimaging/Choquet	outside Aquitaine Region	culture rat	1	2012
Plested A.	eurobioimaging/Choquet	outside Aquitaine Region	culture rat	1	2012
Marian J.	eurobioimaging/groc	outside Aquitaine Region	culture rat	1	2012
Perez-Otano	eurobioimaging/groc		culture rat	1	2012
Choquet	IINS	LabEx	culture rat	50	2013
Choquet	IINS	LabEx	BM-Biochimie	100	2013
Groc	IINS	LabEx	culture rat	50	2013
Groc	IINS	LabEx	BM-Biochimie	100	2013
Thoumine	IINS	LabEx	culture rat	50	2013
Thoumine	IINS	LabEx	BM-Biochimie	100	2013
Landry	IINS	LabEx	culture rat	10	2013
Landry	IINS	LabEx	BM-Biochimie	20	2013
Mulle	IINS	LabEx	culture rat	10	2013
Mulle	IINS	LabEx	BM-Biochimie	50	2013
Nagaerl	IINS	LabEx	culture rat	10	2013
Nagaerl	IINS	LabEx	BM-Biochimie	10	2013
congrès ELMI			culture rat	1	2013
Formation BIC	BIC Bordeaux	LabEx	culture rat	2	2013
ESCUBE	Bordeaux	LabEx	culture rat	1	2013
N. Sans	INSERM U82	LabEx	culture rat	1	2013
N. Macrez	CNRS UMR5293	LabEx	culture rat	1	2013
M. Ortega	académique Bordeaux I	outside Bordeaux Neurocampus	culture rat	1	2013
Davanger	académique Norvège	outside Aquitaine Region	culture rat	1	2013

LabEx support expenses in 2012:

Equipment:

LabEx support:

Name of the equipment,

Co-financers

Running costs (total labEx support expenses):53130€

Human Resources: (total LabEx support expenses):

List of recruitments (name, function, number of month): Emeline Verdier, technicienne, CNRS CDD 10 mois

LabEx support expenses in 2013:

Equipment:

LabEx support: 16392.4€

Name of the equipment, PSM de type II (x2)
Co-financers
Running costs (total labEx support expenses): 54652.6€
Human Resources: (total LabEx support expenses): 49455€
List of recruitments (name, function, nb of month)
Emeline Verdier, technicienne, université CDD 10 mois + CDD 2 mois
Camille Genuer, IE université CDD 1 an
Jessica Gilardin, technicienne université CDD 10 mois

Animal facilities

ANIMAL FACILITIES - MAGENDIE

Head of the facility: Pier Vicenzo Piazza
Technical head: Laumond Sara
Location: INSERM U862, Institut Francois Magendie, 146 rue Leo Saignat, 33000 Bx

Service offer:
Price list:

	NCM	Academic	LabEx	private
breeding rats (Z.P)	37	37	22.2	51.8
breeding mouse (Z.P)	34	34	20.4	47.6
breeding individual cages rats (Z.P)	34	34	20.4	47.6
breeding individual cages mouse (Z.P)	31	31	18.6	43.4
Exp rats	31	31	18.6	43.4
Exp mouse	29.5	29.5	17.7	41.3
Exp individual cage rats	29.5	29.5	17.7	41.3
Exp individual cage mouse	28	28	16.8	39.2

Personnel list:

ALZIEU Philippe – 100% - permanant
AUBAILLY Nathalie – 100% - permanant
BERNARD Jean-Baptiste – 100% - permanant
CHARBONNIER Vanessa – 100% - non permanant
CORAILLER Fiona – 100% - permanant
DELLUC Jean-François- 50% - non permanant
DUBUC Magali – 100% - permanant
DUPUY Cedric – 100% - permanant
DUPUY Lionel - 50% - non permanant
JOURDAIN Jean-Philippe - 50% - non permanant
LAUMOND Sara – 100% - permanant
MONTEUIL Florian – 100% - non permanant
PATA Pauline – 100% - permanant
PERE Benjamin - 50% - non permanant
SOARES Magalie – 100% - permanant

Outcomes (total in k€):

		2012	2013
Running cost/		140883,59	151562,13
Human ressources	Permanent (k€)	198139	164879
	Non permanent (k€)	102919	144216
Equipment		164000	

Incomes (total in k€):

	2012		2013	
	organism	amount (€)	organism	amount (k€)
Service provision/facture	Privé	4440,28	Privé	10404,5
	Nagerl	7684,24	Nagerl	12343,14
	Landry	4817,63	Landry	14589,7
	Mulle/Choquet	442,4	Choquet	558,19
	Groc	440,55	Groc	881,64
			Mulle	11,51
Subventions/argent donné	Labex	149 797	Labex	139 797,00
	Région Aquitaine	164000		
Research contract				
public permanent grant	Inserm	94005	Inserm	155981

Users in 2013:

Name of the PI	Laboratory	affiliation	prestation	nb of prestation
Abrous	U862	LabEx	Exp cage collective rats	45,5
	U862	LabEx	Exp cage indiv rats	794,95
	U862	LabEx	Exp cage collective souris	743,75
	U862	LabEx	Exp cage indiv souris	2776,8
	U862	LabEx	Elevage cage collective rats (Z.P)	369,15
	U862	LabEx	Elevage cage collective souris (Z.P)	612
	U862	LabEx	Elevage cage indiv souris (Z.P)	562,35
Commun	U862	LabEx	Exp cage collective rats	72,95
	U862	LabEx	Exp cage indiv souris	191,95
	U862	LabEx	Elevage cage collective souris (Z.P)	652,3
	U862	LabEx	Elevage cage indiv souris (Z.P)	429,8
	U862	LabEx	Exp cage indiv rats	13
	U862	LabEx	Exp cage collective souris	10
Cota Daniela	U862	LabEx	Elevage cage collective souris (Z.P)	762,85
	U862	LabEx	Elevage cage indiv souris (Z.P)	584,55
	U862	LabEx	Exp cage indiv souris	1177,45
	U862	LabEx	Exp cage collective souris	1,95
	U862	LabEx	Exp cage collective rats	2,5

Frick Andreas	U862	LabEx	Elevage cage collective souris (Z.P)	825,85
	U862	LabEx	Elevage cage indiv souris (Z.P)	355
	U862	LabEx	Exp cage collective souris	64,75
	U862	LabEx	Exp cage indiv souris	341,4
	U862	LabEx	Exp cage indiv rats	8,8
Herry Cyril	U862	LabEx	Elevage cage collective souris (Z.P)	451,8
	U862	LabEx	Elevage cage indiv souris (Z.P)	262,8
	U862	LabEx	Exp cage indiv rats	1,65
	U862	LabEx	Exp cage collective souris	50,35
	U862	LabEx	Exp cage indiv souris	852,1
LeMasson Gwendal	U862	LabEx	Elevage cage collective souris (Z.P)	168,85
	U862	LabEx	Elevage cage indiv souris (Z.P)	120,15
Marighetto Aline	U862	LabEx	Elevage cage collective souris (Z.P)	220,9
	U862	LabEx	Elevage cage indiv souris (Z.P)	272,85
	U862	LabEx	Exp cage collective souris	171,8
	U862	LabEx	Exp cage indiv souris	1783,2
Marsicano Giovanni	U862	LabEx	Exp cage collective souris	366,7
	U862	LabEx	Exp cage indiv souris	1930,45
	U862	LabEx	Elevage cage collective souris (Z.P)	2497,05
	U862	LabEx	Elevage cage indiv souris (Z.P)	972,4
	U862	LabEx	Exp cage indiv rats	1,95

Montcouquiol Mireille	U862	LabEx	Exp cage collective souris	16,05
	U862	LabEx	Exp cage indiv souris	34,7
	U862	LabEx	Elevage cage collective souris (Z.P)	517,1
	U862	LabEx	Elevage cage indiv souris (Z.P)	576,6
	U862	LabEx	Exp cage collective rats	5,8
	U862	LabEx	Exp cage indiv rats	25,05
Piazza Pier-Vincenzo	U862	LabEx	Exp cage collective rats	38,85
	U862	LabEx	Exp cage indiv rats	1459,6
	U862	LabEx	Exp cage collective souris	37,85
	U862	LabEx	Exp cage indiv souris	2732,85
	U862	LabEx	Elevage cage collective souris (Z.P)	634,1
	U862	LabEx	Elevage cage indiv souris (Z.P)	485,8
Stéphane Oliet	U862	LabEx	Elevage cage collective souris (Z.P)	46,15
	U862	LabEx	Elevage cage indiv souris (Z.P)	47,7
	U862	LabEx	Exp cage collective rats	33,5
	U862	LabEx	Exp cage indiv rats	106,85
	U862	LabEx	Exp cage collective souris	87,9
	U862	LabEx	Exp cage indiv souris	11

Choquet Daniel	IINS	LabEx	Exp cage indiv rats	307,09
	IINS	LabEx	Exp cage collective rats	251,1
Fluofarma	Fluofarma		Exp cage indiv rats	117,71
	Fluofarma		Exp cage collective rats	151,9
	Fluofarma		Exp cage collective souris	66,09
	Fluofarma		Exp cage indiv souris	19,6
	Fluofarma		Elevage cage collective rats (Z.P)	10049,2
Groc Laurent	IMN	LabEx	Exp cage collective rats	543,12
	IMN	LabEx	Exp cage indiv rats	116,83
	IMN	LabEx	Exp cage collective souris	213,29
	IMN	LabEx	Exp cage indiv souris	8,4
Landry Marc	IINS	LabEx	Exp cage collective rats	1690,74
	IINS	LabEx	Elevage cage collective souris (Z.P)	5602,86
	IINS	LabEx	Elevage cage indiv souris (Z.P)	5774,37
	IINS	LabEx	Exp cage indiv rats	1310,7
	IINS	LabEx	Exp cage indiv souris	141,12
	IINS	LabEx	Exp cage collective souris	69,91
Mulle Christophe	IINS	LabEx	Exp cage collective souris	11,51
NAGERL Valentin	IINS	LabEx	Elevage cage collective souris (Z.P)	7685,7
	IINS	LabEx	Elevage cage indiv souris (Z.P)	4657,4

<u>LabEx support expanses in 2012:</u>
Equipment: cages, bottles, racks, caps
LabEx support: 0
Name of the equipment, cages, bottles, racks, caps
Co-financers: Région Aquitaine (164k€)
Running costs (total labEx support expenses): 134677€
Human Resources: (total LabEx support expenses): 15120€
List of recruitments (name, function, nb of month)
Belluomo 15120 €

<u>LabEx support expanses in 2013:</u>
Equipment:
LabEx support:

Name of the equipment,
Co-financers
Running costs (total labEx support expenses): 126147€
Human Resources: (total LabEx support expenses): 13650€
List of recruitments (name, function, nb of month)
Monteuil 8400€, Pata 5250 €

ANIMAL FACILITIES- UNIVERSITIES

Head of the facility: Olivier Chassande
Technical head: Sophie North Chassande
Location: University

Service offer:

The rodent experimental facility (mouse and rat) comprises a total of 1 400 m2. It consists of a SPF accommodation zone (400 m2) for the breeding of transgenic colony with a capacity of 2 200 mouse cages. The neighboring experimental area is a conventional accommodation (900 m2 with a capacity of 1 300 mouse cages and 800 rat cages).The protocols conducted are behavioral analysis, surgery, electrophysiology and imaging in anesthetized or vigil animals.

The LabEx BRAIN didn't support directly these animal facilities but allocated funds to the teams according to their use and expenses on the facilities, for a total of 148k€ each year.

Price list:

	Mouse	Rat
Specialized animal facility		
SPF sector 2.73€	-	
Housing cage/week/ SOPF sector	3.78€	-
Animal production	18€	-
Transgenesis	2000€	
A2 Animal facility		
Housing cage/week	3,85€	3.85€
Animal production	18€	-
Conventional animal facility		
Housing cage/week/ with assistance	2,90€	4.05€
Housing cage/week/ without assistance	2.05€	3,35€
Surgery room (/h)	0.8€	0.8€
Special diet/cage	0.1€	0.1€
Injections/prélèvement/pesées	0.05€	0.05€
Mutualised animal facility		
Housing cage/week/ SOPF sector	3.20€ (7€*)	-
Housing cage/week/Immuno-def	5.0€ (7€*)	-
Animal production	12€ (25€*)	-

IV- Support to meetings

4EME COLLOQUE DU CLUB ADHERENCE CELLULAIRE

O. Thoumine, May 24-25 2012
LabEx BRAIN support: 3 000€

Total number of participant: 80
Number of participants from French laboratories: 76
Number of participants from international laboratories: 4
Total number of speaker: 14
Number of speaker from French laboratories: 10
Number of speaker from international laboratories: 4
Obtained grants: SFR/FBN – CRA – SBCF + LabEx Brain

TROUBLES COGNITIFS DE LA SCLEROSE EN PLAQUES ET DES MALADIES INFLAMMATOIRES DU SYSTEME NERVEUX CENTRAL

B. Brochet, May 11-12 2012
LabEx BRAIN support: 1 500€

Total number of participant: 175
Number of participants from French laboratories 85
Number of participants from international laboratories: 90
Total number of speaker: 25
Number of speaker from French laboratories 10
Number of speaker from international laboratories 15
Obtained grants: Labex Brain; conseil regional and pharma companies

NEURON-GLIAL INTERACTIONS: FROM METABOLISM TO ACTIVITY

A.K. Bouzier Sore et S. Oliet, May 252012
LabEx BRAIN support: 800€

Total number of participant: 58
Number of participants from French laboratories: 54
Number of participants from international laboratories: 4
Total number of speaker: 8
Number of speaker from French laboratories: 5
Number of speaker from international laboratories: 3
Obtained grants: LabEx TRAIL, Région Aquitaine, SFR Neuroscience, SFR TECSan.

ADDICTION ET TROUBLE DE L'ATTENTION/HYPERACTIVITE

M. Fatséas, September 13-14 2012
LabEx BRAIN support: 1 500€

Total number of participant: 100
Number of participants from French laboratories: 70
Number of participants from international laboratories: 30
Total number of speaker: 13
Number of speaker from French laboratories: 8
Number of speaker from international laboratories: 5
Obtained grants: 9 000 euros

EUROPEAN NEUROSCIENCE CONFERENCE BY DOCTORAL STUDENTS

M.Haberl, April 11-12 2013

LabEx BRAIN support: 10 000€

Total number of participant: 130
Number of participants from French laboratories: 50
Number of participants from international laboratories: 80
Total number of speaker: 10
Number of speaker from French laboratories: 1
Number of speaker from international laboratories: 9
Obtained grants:
IBRO, Gatsby Foundation, Neuroscience Foundation Bordeaux (SFR), Region Aquitaine, LabEX Brain, IDEX University Bordeaux, Bordeaux Imaging Center, Springer

International Symposium on New Therapeutic Avenues in Parkinson's Disease and Related Disorders

Erwan Bezard, Wassilios Meissner, François Tison; September 4-5 2013
LabEx BRAIN support: 3 000€

Total number of participant: 110
Number of participants from French laboratories: 80
Number of participants from international laboratories: 30
Total number of speaker: 17 (without the chairmen)
Number of speaker from French laboratories: 4
Number of speaker from international laboratories: 13
Obtained grants: 15 (Novartis ; GSK ; TEVA Pharma ; UCB ; Lundbeck; Medtronic ; ANM ; Air Liquide ; Theravance ; Eye Brain ; Lilly ; Conseil régional d'Aquitaine ; SFR Neurosciences ; Labex Brain ; IdEx)

3eme Colloque International Frontieres en NeurophotoniqueFins-2013

Jean-Baptiste Sibarita, Valentin Nägerl, October 1-4 2013
LabEx BRAIN support: 5 000€

Total number of participant: 150
Number of participants from French laboratories: 78
Number of participants from international laboratories: 72
Total number of speaker: 29
Number of speaker from French laboratories: 8
Number of speaker from international laboratories: 21
Obtained grants: FBN – Idex – CRA + LabEx Brain

ELMI microscopie optique

Daniel Choquet ; May 20-24 2013
LabEx BRAIN support: 4 000€

Total number of participant: 419
Number of participants from French laboratories: 258
Number of participants from international laboratories: 161
Total number of speaker: 28
Number of speaker from French laboratories: 7
Number of speaker from international laboratories: 21
Obtained grants: FBI – SFR/FBN – Idex – CRA – GDR2588 + LabEx Brain

Eurogenesis meeting

Nora Abrous; June 24-26 2013
LabEx BRAIN support: 4500€

Total number of participant:125

Number of participants from French laboratories:21
Number of participants from international laboratories: 104
Total number of speaker: 36
Number of speaker from French laboratories: 7
Number of speaker from international laboratories: 29
Obtained grants: ANR pôle Prod'Innov, Neurocentre Magendie, Bordeaux Neuroscience, Marie Curie, Idex, MNS

ESM 2013 4IEME CONGRES EUROPEEN "SYNAPSE"

Christophe Mulle; August 28-30 2013
LabEx BRAIN support: 4500€

Total number of participant: 178
Number of participants from French laboratories: 75
Number of participants from international laboratories: 103
Total number of speaker: 18
Number of speaker from French laboratories: 4
Number of speaker from international laboratories: 14
Obtained grants: Supports from 4 EU consortia: SynSys, Eurospin, SyMBad, Nplast - Idex – CRA - FBN + LabEx Brain

11EME JOURNEE SYNAPSE

Nathalie Sans, Maurice Garret, March 29 2013
LabEx BRAIN support: 750€

Total number of participant: 70
Number of participants from French laboratories: 68
Number of participants from international laboratories: 2
Total number of speaker: 11
Number of speaker from French laboratories: 9
Number of speaker from international laboratories: 2
Obtained grants: 3000 from Bordeaux Neuroscience

RESEAU INSERM DE RECHERCHE SUR LA DOULEUR

Marc Landry,
LabEx BRAIN support: 3000€

Total number of participant:
Number of participants from French laboratories
Number of participants from international laboratories
Total number of speaker:
Number of speaker from French laboratories
Number of speaker from international laboratories
Obtained grants:

SYSTEMS BIOLOGY ON DOPAMINERGIC NEURONS

François Georges
LabEx BRAIN support: 1500€

Total number of participant:
Number of participants from French laboratories
Number of participants from international laboratories
Total number of speaker:
Number of speaker from French laboratories
Number of speaker from international laboratories
Obtained grants:

GDR multielectrode Systems and signall Processing for Neuroscience

Cyril Herry, Thomas Boraud, Pierre Meyrand, Alexander Khun
LabEx BRAIN support: 3000€

Total number of participant: 88
Number of participants from French laboratories: 84
Number of participants from international laboratories: 4
Total number of speaker: 17
Number of speaker from French laboratories: 13
Number of speaker from international laboratories: 4
Obtained grants: Plexon INC, 2000 euros ; Labex Brain: 3000 euros; Neurocentre Magendie: 2500 euros, Multichannel systems: 500 euros, Scilight: 500 euros, Blackrock: 500 euros, Tucker Davis: 500 euros, WPI: 500 euros

Ionotropic Glutamate Receptors and Auxiliary proteins

Anne-Sophie Hafner, Daniel Choquet
LabEx BRAIN support: 1500€

Total number of participant: **40**
Number of participants from French laboratories: **40**
Number of participants from international laboratories: 0
Total number of speaker: **5**
Number of speaker from French laboratories: **2**
Number of speaker from international laboratories: **3**

Journée Bertrand Bloch

Erwan Bezard
LabEx BRAIN support: 1500€

Total number of participant: 90
Number of participants from French laboratories: 85
Number of participants from international laboratories: 5
Total number of speaker: 12
Number of speaker from French laboratories: 9
Number of speaker from international laboratories: 3
Obtained grants: 2; LabEx Brain et SFR Neurosciences

V - Sabbatical stay

Equipe Choquet (IINS) 6k€
Accueil F. Meunier, Associate Professor, Queensland Brain Institute, Australia,
"Timing of molecular events underpinning neurotransmission using super-resolution microscopy".
(20/03/12-20/06/12)

Equipe Ferreira (NutriNeuro) 2k€
Accueil de M. Maroun,Senior Lecturer, Laboratory of Neurobiology of Emotions: , Israel
"Modulation of memory and plasticity by early high-fat diet consumption: bidirectional effects on hippocampus and amygdala"
(20/08/12-30/10/12)

Equipe Simmers (INCIA) 4k€
Accueil KT. Sillar, Professor of Neuroscience, University of St Andrew, UK
"interactions between NO and aminergic pathways in locomotor CPG modulation"
(09/12-01/13)

Equipe Layé (Nutrineuro) 6k€
Accueil G.Luheshi, Professor, Department of Psychiatry, McGill University
"Mechanism of lipid sequestration in microglia of obese rodents: influence on microglia morphology and function"

Equipe Alexandre (IMN) 2,64k€Accueil A. Palacios, Professeur, Universidad de Valparaíso, Centro Interdisciplinario de Neurociencia de ValparaisoKEOPS:beyond the retina:from computational models to outcomes in bioengineering
CORTINA: cortex and retina modeling from an engineering and computational perspective

Annexe 1 Core LabEx Laboratories:

Inserm U862 Research Centre- Pathophysiology of neuronal plasticity

Director: Pier Vincenzo Piazza
Date of initiation: January 2007
Main focus: integrated study of Neurosciences ranging from neurological and behavioural pathologies to the cellular and molecular mechanisms of neural activity. In particular, the specific aim of the Neurocentre Magendie is the understanding of the pathophysiology of neuronal plasticity.
Members:

- Researcher: 25
- Faculty: 17
- post-doc: 17
- student (master +PhD): 26
- ITA: 76

Neurogenesis and pathophysiology

Team leader: Nora Abrous

Main focus: We have studied the physiological significance of hippocampal neurogenesis and its involvement in pathological behaviors. We had shown the existence of a reciprocal relationship between neurogenesis and spatial memory and that neoneurons are involved in the physiopathology of memory.

The prenatal period is sensitive to manipulations of maternal environment. We observed that a prenatal stress causes a hyperactivity of the HPA axis which lows adult neurogenesis and accelerates the occurrence of age-related memory disorders. On the contrary, enriching experiments favor a successful ageing in increasing the production of new neurons. These results reinforce the hypothesis that numerous disorders have their origins in early periods of development.

Main techniques:

5 relevant publications since2011:

Energy balance and obesity

Team leader Daniela Cota

Main focus: Obesity is a major health problem worldwide. Despite the human and economic costs of this disease, efficient anti-obesity therapies are currently lacking. Our studies have so far critically contributed in determining the role of the endogenous cannabinoid system (ECS) and of the mechanistic/mammalian target of rapamycin (mTOR) intracellular pathway in the regulation of energy balance. The goals of our research work currently include: i) to further identify the mechanisms underlying the action of the ECS in energy balance, by studying the system not only in animal models but also in obese humans; ii) to further characterize the mechanisms underlying the action of the mTOR pathway in energy balance and; iii) to study the interplay between the ECS and the mTOR pathway in this context.

Main techniques: We use a multidisciplinary approach, including behavioral, neuro-anatomical and molecular biology analyses. We have an automated system to study feeding patterns (including automated pair-feeding and food choice), home cage activity and energy expenditure in rodents. We also have a quantitative nuclear resonance system and a DEXA system for in vivo body composition analysis and an operant nose-poke apparatus for the microstructural analysis of feeding in mice.

5 relevant publications since2011:

1. Gatta-Cherifi B, Matias I, Vallée M, Tabarin A, Marsicano G, Piazza PV, **Cota D**. Simultaneous postprandial deregulation of the orexigenic endocannabinoid anandamide and the anorexigenic peptide YY in obesity. Int J Obes (Lond). 2012 Jun;36(6):880-5.
2. Cardinal P, Bellocchio L, Clark S, Cannich A, Klugmann M, Lutz B, Marsicano G, **Cota D**. Hypothalamic CB1 cannabinoid receptors regulate energy balance in mice. Endocrinology. 2012 Sep;153(9):4136-43.

3. Bellocchio L, Soria-Gómez E, Quarta C, Metna-Laurent M, Cardinal P, Binder E, Cannich A, Delamarre A, Häring M, Martín-Fontecha M, Vega D, Leste-Lasserre T, Bartsch D, Monory K, Lutz B, Chaouloff F, Pagotto U, Guzman M, **Cota D***, Marsicano G*. Activation of the sympathetic nervous system mediates hypophagic and anxiety-like effects of CB_1 receptor blockade. Proc Natl Acad Sci U S A. 2013 Mar 19;110(12):4786-91. *share senior authorship
4. Binder E, Bermúdez-Silva FJ, André C, Elie M, Romero-Zerbo SY, Leste-Lasserre T, Belluomo I, Duchampt A, Clark S, Aubert A, Mezzullo M, Fanelli F, Pagotto U, Layé S, Mithieux G, **Cota D**. Leucine supplementation protects from insulin resistance by regulating adiposity levels. PLoS One. 2013 Sep 25;8(9):e74705.
5. Bosier B, Bellocchio L, Metna-Laurent M, Soria-Gomez E, Matias I, Hebert-Chatelain E, Cannich A, Maitre M, Leste-Lasserre T, Cardinal P, Mendizabal-Zubiaga J, Canduela MJ, Reguero L, Hermans E, Grandes P, **Cota D***, Marsicano G*. Astroglial CB1 cannabinoid receptors regulate leptin signaling in mouse brain astrocytes. Mol Metab. 2013 Aug 9;2(4):393-404. *share senior authorship

Cortical plasticity

Team leader: Andreas Frick

Main focus: We investigate various aspects of cortical circuit organization and their modulation during development, following activity patterns, or in disease. We have used a number of approaches, including electrophysiological, imaging, anatomical and behavioural methods. More recently, we have developed an improved viral approach to trace monosynaptically connected cells in vivo. Our major findings are as follows: 1) Cortical circuit organisation in the whisker-related barrel cortex changes during development in a cell identity-dependent manner. 2) Dendrites are important players for the overall information storage capacity of a neuron. Dendritic plasticity is a mechanism for metaplasticit, and relies on signalling pathways different from those that induce synaptic plasticity. In addition, dendritic properties vary across the dendritic arbors of neocortical output neurons, setting up zones that possess specific signalling capabilities. Lastly 3) neocortex-dependent behavioural tasks demonstrate cognitive defects in Fmr1 knockout mice (mouse model for Fragile X Syndrome).

Main techniques:

5 relevant publications since 2011:

Neuronal circuits of associative learning

Team leader: Cyril Herry

Main focus: Our research project aims at mapping prefrontal and amygdala circuits controlling fear behavior using a unique innovative cross-level approach combining cutting edge in vivo extracellular and intracellular electrophysiological recording techniques, selective optogenetic manipulations and behavioral approaches. Our scientific objectives are twofold: addressing the anatomical and physiological properties of defined excitatory/inhibitory mPFC circuits controlling fear expression and selectively manipulating these circuits during behavior. The expected results will provide a detailed knowledge of the cellular basis of fear behavior and of behavioral control in general. Moreover, elucidating the neuronal circuits controlling fear behavior should also lead to novel therapeutic strategies for psychiatric disorders involving dysregulation of emotional responses such as post-traumatic stress disorder and related psychiatric conditions.

Main techniques: quantitative analysis of animal behavior ; fear conditioning ; electrophysiology with animal behavior and in anesthetized; memory pharmacology ; optogenetic

5 relevant publications since 2011:

Motor System diseases

Team leader: Gwendal Le Masson

Main focus: Understand and design new therapeutic approaches for Motor Neuron diseases such as Amyotrophic Lateral Sclerosis (ALS) and Spinal Cord Injuries (SCI). We are investigating the consequences of impaired energetic metabolism of the electrical activity of cultured motor neuron and sliced spinal cord using patch and sharp electrodes recordings. Realistic computational models are used to guide the experiments and provide new hypothesis to explore.

We are also investigating Spinal Cord Injury following trauma or spinal trans-section. Using theoretical and electrophysiological approaches, we characterize the post lesion plasticity and trophic factors implicated in spinal cord regeneration in the salamander.

Main techniques: We use a combination of techniques ranging from anatomy, immuno-histo-chemistry, calcium imaging and electrophysiological recordings (extra, intra cellular with sharp or patch on culture and slices, and Multi Electrode Recordings), pharmacology as well as behavioral studies including complex kinematics. We also developed complex computational approaches such as multi-compartmental modeling, electrical and metabolic models and neuro-interface technologies (dynamic clamp and hybrid networking, bio-robotics). Our techniques take full advantage of the Neurocentre Magendie common platform for cellular imagery (confocal, two photons microscopy) and gene profiling.

5 relevant publications since 2011:

Pathophysiology of declarative memory

Team leader: Aline Marighetto

Main focus: Our research activity is aimed at identifying the psychobiological bases of memory degradation occurring in aging and in post-traumatic stress disorder (PTSD). Regarding aging, we have established a model of the preferential declarative memory (DM) degradation in aged mice based on the characteristic flexibility of DM expression and we have translated this model to human subjects. Regarding stress-related memories, we have established the first behavioral model which assesses qualitative features that permit to distinguish between normal/adaptive memory, and maladaptive fear memory characteristic of PTSD. By continuing our integrative approach, linking intracellular markers of activity and plasticity to memory system function, we expect to help developing new therapeutics and prevention strategies of memory alterations in aging and PTSD.

Main techniques:

5 relevant publications since 2011:

Endocannabinoids and Neuroadaptation

Team leader: Giovanni Marsicano

Main focus

The group of Giovanni Marsicano studies the functions of the endocannabinoid system in the brain. By dissecting the roles of G protein coupled cannabinoid receptors (CB1) in different cellular and subcellular localizations, we aim at better understanding the general rules governing behavior.

By using conditional mutagenesis, we have been studying the functions of CB1 receptors in excitatory and inhibitory neurons, in astroglial cells and we recently discovered that brain mitochondrial activity is under the direct control of mitochondrial CB1 receptors.

Thus, we are currently investigating how the negative control of synaptic transmission by presynaptic CB1 receptors regulates the balance between excitation and inhibition in different brain functions, how CB1 receptors participate in the tripartite synapse, and how brain mitochondrial CB1 receptors regulate brain processes and behavior.

Techniques

Conditional mutagenesis, viral gene expression, pharmacogenetics, optogenetics, pharmacology, behavioral analysis (food intake, learning and memory, voluntary physical exercise, affective states, etc.), immunohistochemistry, in situ hybridization, electrophysiology, voltage-sensitive dye imaging, biochemistry (protein analysis and mitochondrial functions), cell biology (neuronal and astroglial cultures).

5 relevant publications since 2011:

Vallée M, Vitiello S, Bellocchio L, Hébert-Chatelain E, Monlezun S, Martin-Garcia E, Kasanetz F, Baillie GL, Panin F, Cathala A, Roullot-Lacarrière V, Fabre S, Hurst DP, Lynch DL, Shore DM, Deroche-Gamonet V, Spampinato U, Revest JM, Maldonado R, Reggio PH, Ross RA, **Marsicano G*** and Piazza PV* (2014) Pregnenolone can Protect the Brain from Cannabis Intoxication. ***Science*** 343(6166):94-8

Soria-Gómez E*, Bellocchio L*, Reguero L, Lepousez G, Martin C, Bendahmane M, Ruehle S, Remmers F, Desprez T, Matias I, Wiesner T, Cannic A, Nissant A, Wadleigh A, Pape HC, Chiarlone AP, Quarta C, Verrier D, Vincent P, Massa F, Lutz B, Guzmán M, Gurden H, Ferreira G, Lledo PM, Grandes P, **Marsicano G** (2014) The endocannabinoid system controls food intake via olfactory processes. ***Nature Neuroscience*** 17(3):407-15

Benard G, Massa F, Puente N, Lourenço L, Bellocchio L, Soria-Gómez E, Matias I, Delamarre A, Metna-Laurent M, Cannich A, Hebert-Chatelain E, Mulle C, Ortega-Gutierrez S, Martín-Fontecha M, Klugmann M, Guggenhuber S, Lutz B, Gertsch J, Chaouloff F, López-Rodríguez ML, Grandes P, Rossignol R and **Marsicano G** (2012) Mitochondrial CB1 receptors regulate neuronal energy metabolism. ***Nature Neuroscience*** 15(4):558-64

Han J#, Kesner P#, Metna-Laurent M#, Duan T, Xu L, Georges F, Koehl M, Abrous DN, Mendizabal-Zubiaga J, Grandes P, Ren W, **Marsicano G*** and Zhang X* (2012). Astroglial CB1 Receptors Mediate Cannabinoid Alterations of Synaptic Plasticity and Working Memory. ***Cell*** 148(5):1039-50

Bellocchio L*, Soria-Gomez E*, Quarta C, Metna-Laurent M, Cardinal P, Binder E, Cannich A, Delamarre A, Häring M, Martín-Fontecha M, Vega D, Leste-Lasserre T, Bartsch D, Monory K, Lutz B, Chaouloff F, Pagotto U, Guzman M*, Cota D* and **Marsicano G*** (2013) Activation of the sympathetic nervous system mediates hypophagic and anxiety-related effects of CB1 receptor blockade, ***Proc Natl Acad Sci U S A*** 110(12):4786-91. Track II-direct submission

Planar polarity and plasticity

Team leader: Mireille Montcouquiol and Nathalie Sans


Main focus: Human mutations of Planar Cell Polarity (PCP) genes have been directly linked to neural tube defects, which is one of the most common birth defects occurring in approximately one in 1,000 births. Recent studies have identified mutations on PCP proteins in autistic patients, or other pathologies like epilepsy or ataxia. Although scarce, data on PCP signalling disruption in mice have revealed sociability defects and memory imbalance, typical of ASD. To the already long list of pathologies associated with PCP signalling defects, recent studies have emphasize a link between PCP and ciliopathies, a link that we partially elucidated recently. Our project relies on specific genetic tools and strong PCP expertise. We have a double expertise in the inner ear -the bona fide model system to study PCP in mammals-, and in the brain, that give us an original and unique perspective to address the role and mechanisms of PCP signalling in the developing and adult nervous system.

Main techniques: cellular biology (cell lines, primary cultures of brain slices and cochlear explants, dissociated cultures); molecular molecular biology; biochemistry; classical histology; fluorescent imaging (classical, confocal, super resolution); social behavior; in utero electroporation.

relevant publications from 2011:

- Ezan J, Lasvaux L, Gezer A, Novakovic A, May-Simera H, Belotti E, Lhoumeau AC, Birnbaumer L, Beer-Hammer S, Borg JP, Le Bivic A, Nürnberg B, Sans N, Montcouquiol M. Primary cilium migration depends on G-protein signalling control of subapical cytoskeleton. **Nat Cell Biol. 2013** Sep;15(9):1107-15.
- Ezan J, Montcouquiol M. Revisiting planar cell polarity in the inner ear. Semin Cell Dev Biol. 2013 May;24(5):499-506. Epub 2013 Apr 3. Review.
- Belotti E, Puvirajesinghe TM, Audebert S, Baudelet E, Camoin L, Pierres M, Lasvaux L, Ferracci G, Montcouquiol M, Borg JP. Molecular characterisation of endogenous Vangl2/Vangl1 heteromeric protein complexes. **PLoS One.** 2012;7(9):e46213.
- Giese AP, Ezan J, Wang L, Lasvaux L, Lembo F, Mazzocco C, Richard E, Reboul J, Borg JP, Kelley MW, Sans N, Brigande J, Montcouquiol M. Gipc1 has a dual role in Vangl2 trafficking and hair bundle integrity in the inner ear. **Development**. 2012 Oct;139(20):3775-85.
- Durand CM, Perroy J, Loll F, Perrais D, Fagni L, Bourgeron T, Montcouquiol M, Sans N. SHANK3 mutations identified in autism lead to modification of dendritic spine morphology via an actin-dependent mechanism. **Mol Psychiatry**. 2012 Jan;17(1):71-84.

Glia-neuron interactions

Team leader: Stéphane Oliet

Main focus: The general aim of our research is to unravel the contribution of astroglial cells to synaptic functions. In the past we have demonstrated the key role played by the astrocytic environment of synapses in controlling the diffusion and concentration of glutamate in the extracellular space. We also shown that through the release of D-serine, an endogenous co-agonist of NMDA receptors, astrocytes were contributing to the regulation of NMDA receptor–dependent processes including long term synaptic plasticity and excitotoxicity.

Presently, we are investigating the morphofunctional plasticity of glia-neuron interactions, the diffusion of key proteins at the surface of astroglial cells and the role of astrocytes in a pathophysiological context such as chronic pain, Alzheimer disease and multiple sclerosis.

Main techniques: In vitro electrophysiology, cellular imaging, immunohistochemistry, nociceptive behavior, cell cultures

5 relevant publications since 2011:

Massa F, Koehl M, Wiesner T, Grosgean N, Revest JM, Piazza PV, Abrous DN and Oliet SHR (2011) Conditional inhibition of adult neurogenesis impairs hippocampal synaptic plasticity. Proceedings of the National Academy of Science USA108(16):6644-6649

Bonfardin VDJ, Theodosis DT, Konnerth A, and Oliet SHR (2012) Kainate receptor-induced retrograde inhibition of glutamatergic transmission in vasopressin neurons. Journal of Neuroscience 32:1301-1310.

Papouin T, Ladépêche L, Ruel J, Sacchi S, Labasque L, Hirawi M, Groc L, Pollegioni L, Mothet JP and Oliet SHR (2012) Synaptic and extrasynaptic NMDA receptors are gated by different co-agonists. Cell 150(3):633-646

Israel JM, Cabelguen JM, Le Masson G, Oliet SH and Ciofi P (2014) Neonatal testosterone suppresses a neuroendocrine pulse generator required for reproduction. Nature Communications 5:3285

Araque* A, Carmignoto* G, Haydon* PG, Oliet* SHR, Robitaille* R and Volterra* A (2014) Gliotransmitters travel in time and space. Neuron 81:728-739 (*Corresponding authors)

Physiopathology of addiction

Team leader: Pier-Vincenzo Piazza

Main focus: An important factor influencing the development of addiction is the peculiar vulnerability shown by certain individuals in developing this pathology. The general aim of our research project is the identification of the pathophysiological basis of the "drug prone" and "addiction prone" phenotypes. Concerning the "drug prone" phenotype we were able to identify the cellular targets and some of the molecular mechanisms through which stress, through the activation of glucocorticoid hormones, increases the sensitivity of the dopaminergic transmission to drugs of abuse. Concerning the "abuse prone" phenotype we were able to show that it is accompanied by a peculiar adaptation to drugs involving the loss of a certain form of synaptic plasticity.

Main techniques: a multidisciplinary approach that included the major methods of behavioral, system and molecular neurosciences

5 relevant publications since 2011:

Interdisciplinary Institute for Neuroscience

Director: Daniel Choquet

Date of initiation: January 2011

Main focus: The IINS unites researchers with diverse areas of expertise, and creates a highly synergistic environment to promote the development of innovative methods and investigation tools, especially those based on molecular biology, physiology, optics, chemistry, physics and computer science. The application of such tools to push the boundaries of the study of molecular events underlying the activity of the brain. This will include studying the

morpho-dynamic and functional properties of the nervous system to understand the complexity of its molecular assemblies and functions at an integrated level.

Members:

- Researcher: 23
- Faculty: 8
- post-doc: 23
- student (master +PhD): 48
- ITA: 49

Dynamic Organization and Function of Synapses

Team leader: Daniel Choquet

Main focus: to study the interplay between the organizational dynamics of the molecular components of glutamatergic synapses and synaptic transmission. By combining the expertise of chemists, biochemists, cell biologists, biophysicists and neurophysiologists, we will develop 3 main research axes:

- Dynamics and physical-chemistry of the macro-molecular complexes of the synapse,
- Nano-scale organization and dynamics of synaptic proteins and membrane trafficking,
- Impact of the dynamic of synapse organization on synaptic physiology.

Results obtained in these three axes will be constantly integrated to provide a global view of glutamatergic synapse physiology, from nano-scale interactions to function.

Main techniques: single particle tracking, super resolution imaging, video microscopy, TIRF microscopy electrophysiology, Patch-clamp, biochemistry, peptide synthesis, molecular biology, cell culture, chemical biology

5 relevant publications since 2011:

- Choquet, D., and Triller, A. (2013). The dynamic synapse. Neuron 80, 691-703.
- Giannone, G., Mondin, M., Grillo-Bosch, D., Tessier, B., Saint-Michel, E., Czondor, K., Sainlos, M., Choquet, D.*, and Thoumine, O.* (2013). Neurexin-1beta Binding to Neuroligin-1 Triggers the Preferential Recruitment of PSD-95 versus Gephyrin through Tyrosine Phosphorylation of Neuroligin-1. Cell Rep 3, 1996-2007.*Co-Last author
- Sainlos, M., Iskenderian-Epps, W.S., Olivier, N.B., Choquet, D., and Imperiali, B. (2013). Caged mono- and divalent ligands for light-assisted disruption of PDZ domain-mediated interactions. JACS 135, 4580-4583.
- Sainlos, M., Tigaret, C., Poujol, C., Olivier, N.B., Bard, L., Breillat, C., Thiolon, K., Choquet*, D., and Imperiali*, B. (2011). Biomimetic divalent ligands for the acute disruption of synaptic AMPAR stabilization. Nat Chem Biol 7, 81-91. *Co-last authors.
- Zhang, H., Etherington, L.A., Hafner, A.S., Belelli, D., Coussen, F., Delagrange, P., Chaouloff, F., Spedding, M., Lambert, J.J., Choquet, D., and Groc, L. (2013). Regulation of AMPA receptor surface trafficking and synaptic plasticity by a cognitive enhancer and antidepressant molecule. Molecular psychiatry 18, 471-484. *Co-last-authors.

Development and Adaptation of Neuronal Circuits

Team leader: Laurent Groc

Main focus: While early intrinsic factors shape initial neuronal contacts, most fine-scale network wiring is driven by environmental factors and experience. A great challenge for our comprehension of brain development is to identify how modulators control the maturation of neuronal connections and brain circuit assemblies. The project of the team is to understand how neurotransmitter systems dialogue in the developing brain in order to shape functional networks. We mostly focus our attention on the molecular physiology of the interplay between NMDA-dependent glutamatergic, monoamine, hormones, and immune signaling in the physiological brain as well as in psychotic disorders.

Main techniques: These fundamental issues will be tackled using a challenging and original set of approaches, e.g. single molecule approach, ensemble measurement, and biochemistry, ex vivo and in vivo electrophysiology, optogenetic, and rodent models of early life challenge (e.g. schizophrenia, stress).

5 relevant publications since 2011:

Dupuis et al., ***EMBO J***, 2014 ; Ladepeche et al., ***PNAS***, 2013 ; Zhang et al., ***Molecular Psychiatry***, 2013 ; Ladepeche et al., ***Semin Cell Dev Biol***, 2013 ; Mikasova et al., ***Brain***, 2012 .

Synapse in Cognition

Team Leader: Yann Humeau

Main focus: to understand the link between synapse and cognition by investigating the consequence of genetically encoded cognitive deficits at the synaptic level. Our recent results show that several mental retardation (MR) mouse models exhibit functional synaptic deficits at long-range projections to the basolateral amygdala, a structure involved in the coding of fear memory. We will examine the role of MR proteins in the process of memory formation by analyzing biochemical, morphological and physiological changes of synapses in mice submitted to fear conditioning. Ex vivo experiments will be completed by an in vitro approach on genetically manipulated cultured neurons, to allow an ideal control of MR-gene expression and the use of imaging of living synaptic contacts at the nanometer scale and single molecule tracking of various synaptic receptors. Finally, we recently installed chronic in vivo imaging of frontal cortex in awake animals submitted to fear conditioning.

Main techniques: optogenetic, fear conditioning, electrophysiology, synaptosome sorting and proteomic, in vivo imaging and electrophysiology

5 relevant publications since 2011:

- Rayachandran, R., Liu, X., BoseDasgupta, S., Mueller, P., Zhang, C.L., Moshous¶, D., Studer, V., Schneider, J., Genoud, C., Fossoud, C., Gambino, F., Khelfaoui, M., Müller, C., Bartholdi, C., Rossez, H., Stiess, M., Houbaert, X., Jaussi, R., Frey, D., Kammerer, R.A., Deupi, X., de Villartay, J.P., Lüthi, A., Humeau, Y*., and Pieters, J*. (2014) Coronin 1 Regulates Cognition and Behavior through Modulation of cAMP/Protein kinase A Signaling. PLoS Biology, 12:e1001820 *(*co-corresponding authors)*.
- Khelfaoui, M., Gambino, F., Houbaert, X., Ragazzon, B., Müller, C., Carta, M., Lanore, F., Srikumar, B.N., Gastrein, P., Lepleux, M., Zhang C.L., Kneib, M., Poulain, B., Reibel-Foisset, S., Vitale, N., Chelly, J., Billuart, P., Lüthi, A., Humeau, Y. (2014) Lack of the presynaptic RhoGAP protein oligophrenin1 leads to cognitive disabilities through dysregulation of the cAMP/PKA signaling pathway Philosophical Transactions B, 369, 20130160
- Biesemann, C., Grønborg, M., Luquet, E., Wichert, S.P., Bernard, V., Bungers, S.R., Cooper, B., Varoqueaux, F., Li, L., Byrne, J.A., Urlaub, H., Jahn, O., Brose, N., Herzog, E. (2014) Proteomic screening of glutamatergic mouse brain synaptosomes isolated by fluorescence activated sorting. The EMBO journal, 33:157-70
- Houbaert, X., Zhang, C.L., Gambino, F., Lepleux, M., Deshors, M., Normand, E., Levet, F., Ramos, M., Billuart, P., Chelly, J., Herzog, E. and Humeau, Y. (2013) Target-specific vulnerability of excitatory synapses leads to deficits in associative memory in a model of intellectual disorder. The Journal of neuroscience. 33, 13805-13819.
- Gambino F, Holtmaat A. (2012) Spike-timing-dependent potentiation of sensory surround in the somatosensory cortex is facilitated by deprivation-mediated disinhibition. Neuron. 75:490-502.

Central Mechanisms of Pain Sensitization

Team leader: Marc Landry

Main focus: Chronic pain relies on maladaptive plasticity that induces neuronal sensitization in dorsal spinal networks. The aim of our project is to shed light on basic mechanisms responsible for cellular and network dysfunctions in the dorsal spinal cord of rodent models of neuropathic pain. We will develop 3 main research axes: i) explore the role of L-type calcium channels-dependent membrane properties in the sensitization of spinal neurons, ii) investigate how GABAB inhibition of calcium-dependent intrinsic properties of dorsal horn neurons is hampered in neuropathic conditions, iii) study the remodeling of electrical coupling and morphological synaptic contacts, whereby deciphering inappropriate post-lesional reshaping of the dorsal horn nociceptive network.

Main techniques:

5 relevant publications since 2011:

Physiology of Glutamatergic Synapses

Team Leader: Christophe Mulle

Main focus: The research carried out in the group ambitions to link cell biological mechanisms of protein trafficking to synaptic function and dysfunction. Great efforts are made to implement these questions at an integrated ex vivo or in vivo level in the mouse. The group focuses on two main aims, 1) the mechanisms underlying the specification of synaptic properties in CA3 pyramidal cells and 2) the operation and plasticity of local cortical circuits (mainly CA3) in the context of episodic-like memory encoding, for which we develop methods for interrogation the connectivity and function of local circuits *in vivo*. These studies address control conditions as well as models of cognitive disorders such as Alzheimer's disease.

Main techniques: The studies rely on a combination of approaches ranging from molecular biology and gene-transfer in the brain to synaptic electrophysiology and live imaging. We develop gene-transfer methods in slices and in vivo: (i) single-cell transfection of hippocampal slices for molecular rescue experiments, and (ii) production of lentiviruses and AAV constructs, and in vivo sterotaxic infection in pups and young mice. These methods are fundamental for a number of projects proposed, especially in combination with opto/pharmacogenetic activation of neurons of selected neuronal populations. Confocal imaging setups coupled to electrophysiology serve to couple electrophysiology to glutamate uncaging, Ca2+ imaging and morphological analysis. Image acquisition and analysis is made possible thanks to the central imaging facility (BIC). We also use electrophysiological recordings in vivo (patch-clamp and extracellular recordings), combined with optogenetic stimulation of neurons. Finally we develop transsynaptic rabies virus tracing methods to describe local hippocampal circuits.

relevant publications since 2011:

- Rebola, N., Carta, M., Lanore, F., Blanchet, C., and Mulle, C. (2011). NMDA receptor-dependent metaplasticity at hippocampal mossy fiber synapses. **Nat Neurosci** *14*, 691-693.
- Veran, J., Kumar, J., Pinheiro, P.S., Athané, A., Mayer, M.L., *Perrais, D., and *Mulle, C. (2012). Zinc Potentiates GluK3 Glutamate Receptor Function by Stabilizing the Ligand Binding Domain Dimer Interface. **Neuron** *76*, 565–578. **Equal contribution*
- Carta, M., Opazo, P., Veran, J., Athané, A., Choquet, D., *Coussen, F., and *Mulle, C. (2013). CaMKII-dependent phosphorylation of GluK5 mediates plasticity of kainate receptors. The **EMBO Journal** *32*, 496–510. **Equal contribution*
- Carta M*, Lanore F*, Rebola N*, Szabo Z, Viana Da Silva S, Lourenço J, Verraes A, Nadler A, Schultz C, Blanchet C, Mulle C (2014) Membrane lipids tune synaptic transmission by direct modulation of presynaptic potassium channels. **Neuron**, 81:787–799.
- Vergnano A, Rebola N, Savtchenko L, Casado M, Pinheiro P, Ruzakov D, *Mulle C and *Paoletti P. (2014) Zinc dynamics and function at excitatory synapses. **Neuron** (in press). **Equal contribution.*

Synaptic Plasticity and Superresolution Microscopy

Team leader: Valentin Nägerl

Main focus: The advent of fluorescence microscopy beyond the diffraction limit has opened up huge experimental opportunities to directly image and resolve key physiological signaling events at the level of single synapses in intact brain tissue, a possibility which was considered a pipedream until recently. Our group is invested in harnessing these exciting technological developments to study synapses and their glial partners in their natural habitat and under realistic conditions, aiming to better understand higher brain function and disorders in terms of the underlying synaptic mechanisms.

Main techniques:

- STED microscopy in brain slices and *in vivo*
- Electrophysiology
- Two-photon microscopy: glutamate uncaging, Ca2+ imaging
- Biophysical techniques & modeling
- Viral gene transfer

5 relevant publications since 2011:

- Wijetunge L, Angibaud J, Frick A, Kind P and Nägerl UV STED microscopy reveals nanoscale defects in the developmental trajectory of dendritic spine morphogenesis in a mouse model of FXS. The Journal of Neuroscience (in press)
- Tonnesen J, Katona G, Rozsa B and Nägerl UV. Spine neck plasticity regulates compartmentalization of synapses. Nature Neuroscience DOI 10.1038/nn.3682 (2014)
- Bethge P, Chéreau R, Avignone E, Marsicano G and Nägerl UV. Two-photon excitation STED microscopy in two colors in acute brain slices. Biophysical Journal 104(4): 778-785 (2013)
- Willig KI and Nägerl UV. Stimulated emission depletion (STED) imaging of dendritic spines in living hippocampal slices. Cold Spring Harbor Protocols; May 1; (2012)
- Tonnesen J, Nadrigny F, Willig KI, Wedlich-Söldner R and Nägerl UV. Two-color STED microscopy of living synapses using a single laser beam pair. Biophysical Journal 101(10):2545-52 (2011)

Quantitative Imaging of the Cell

Team leader: Sibarita Jean-Baptiste

Main focus: to develop novel imaging techniques to better understand the living cell activity at high spatial and temporal resolutions, in a high throughput context. Four main research area are investigated: i) Novel instruments for super-resolution microscopy of living samples, ii) Analytical tools for object segmentation, tracking and visualization, iii) High Content Screening Microscopy to quantify the dynamics of active proteins within the living cells, using super-resolution microscopy and iv) Bioengineering for micropatterning and microfluidics to control cell geometry and their local chemical environment.

Main techniques: development of instrumentation and analytical tools for single molecule localization, tracking and quantification, 3D imaging of thick biological specimens, microfluidics and micro photo-patterning, High Content Screening.

relevant publications since 2011:

- Izeddin I, Boulanger J, Racine V, Specht CG, Kechkar A, Nair D, Triller A, Choquet D, Dahan M, Sibarita JB: Wavelet analysis for single molecule localization microscopy. *Opt Express* 2012, 20:2081-2095.
- Morel M, Galas JC, Dahan M, Studer V: Concentration landscape generators for shear free dynamic chemical stimulation. *Lab Chip* 2012, 12:1340-1346.
- Studer V, Bobin J, Chahid M, Mousavi HS, Candes E, Dahan M: Compressive fluorescence microscopy for biological and hyperspectral imaging. *Proc Natl Acad Sci U S A* 2012, 109:E1679-1687.
- Kechkar A, Nair D, Heilemann M, Choquet D, Sibarita JB: Real-time analysis and visualization for single-molecule based super-resolution microscopy. *PLoS One* 2013, 8:e62918.
- Nair D, Hosy E, Petersen JD, Constals A, Giannone G, Choquet D, Sibarita JB: Super-Resolution Imaging Reveals That AMPA Receptors Inside Synapses Are Dynamically Organized in Nanodomains Regulated by PSD95. *J Neurosci* 2013, 33:13204-13224.

Biophysics of Adhesion and Cytoskeleton

Team leaders: Olivier Thoumine and Grégory Giannone

Team leaders: Olivier Thoumine and Grégory Giannone

Main focus: Our aim is to understand the role of adhesion proteins and the actin cytoskeleton in the assembly and turnover of multi-molecular complexes at cell-cell and cell-extracellular matrix contacts. We are developing four specific axes: i) Assembly of macromolecular synaptic complexes triggered by neurexin/neuroligin adhesion, ii) Adhesion and actin dynamics in growth cone steering and dendritic spine shape, iii) Integrin-dependent adhesion and actin dynamics in migrating cells, iv) New imaging methods to probe ligand binding and receptors dynamics in membranes.

Main techniques: we are using a combination of bio-mimetic physico-chemical assays to establish spatially-controlled and molecularly-specific adhesive contacts, and high resolution microscopy imaging to probe in real time the dynamics of these multi-protein complexes.

5 relevant publications since 2011:

- Czöndör K, Garcia M, Argento A, Constals A, Breillat C, Tessier B, Thoumine O. Micropatterned substrates coated with neuronal adhesion proteins for high-content study of synapse formation. **Nat Commun**. Aug 12;4:2252
- Giannone G*, Mondin M*, Grillo-Bosch D, Tessier B, Saint-Michel E, Czöndör K, Sainlos M, Choquet D($), Thoumine O($). Neurexin-1β binding to neuroligin-1 triggers the preferential recruitment of PSD-95 versus gephyrin through tyrosine phosphorylation of neuroligin-1. **Cell Reports**, 27;3(6):1996-2007. (*) co-first authors; ($) co-last authors.
- Rossier O, Octeau V, Sibarita J-B, Leduc C, Tessier B, Nair D, Gatterdam V, Destaing O, Albigès-Rizo C, Tampé R, Cognet L, Choquet D, Lounis B, Giannone G. Integrins β_1 and β_3 exhibit distinct dynamic nanoscale organizations inside focal adhesions. **Nature Cell Biology**. 14:1057-67.
- Czöndör K, Mondin M, Garcia M, Heine M, Frischknecht R, Choquet D, Sibarita JB, Thoumine O. A unified quantitative model of AMPA receptor trafficking at synapses. **Proc Natl Acad Sci USA**. 109(9):3522-7.
- Mondin M, Labrousse V, Hosy E, Heine M, Tessier B, Levet F, Poujol C, Blanchet C, Choquet D, Thoumine O. Neurexin-neuroligin adhesions capture surface-diffusing AMPA receptors through PSD-95 scaffolds. **J Neurosci** 31:13500-15.

Institute of neurodegenerative diseases

Director: Erwan Bezard

Date of initiation: January 2011

Main focus: The IMN aims to encompass fundamental, preclinical and clinical research in the field of neurodegenerative diseases, with the goal of developing therapeutic approaches to neurodegenerative diseases using both vertical and translational approaches. We are fully aware that such an ambitious objective is often claimed by research units but is seldom satisfied. We consider however that our past achievements, obtained under a less favorable and structured environment, give rise to realistic optimism.

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Members:

- Researcher: 12
- Faculty: 10
- post-doc: 3
- student (master +PhD): 22
- ITA: 14

Mnemosyne (Mnemonic Synergy)

Team leader: Frédéric Alexandre

Main focus: At the frontier between integrative and computational neuroscience, we model brain functions at a systemic level. We integrate interactions with the internal and external world and design simulations of robotic and autonomous systems.

This new team, just settling in Bordeaux, had previously an expertise in cortex modeling, visual attention, robotics and hardware implementation.

More recently, we are investigating decision-making (models of the amygdala and basal-ganglia) with application to autonomous behavior.

Main techniques: computer science, mathematics, modeling, robotics, simulation

5 relevant publications since 2011:

M. GUTHRIE, A. LEBLOIS, A. GARENNE, T. BORAUD. Interaction Between Cognitive and Motor Cortico-Basal Ganglia Loops During Decision Making: A Computational Study, in "Journal of Neurophysiology", 109(12):3025-40, March 2013.

K. BORIC, P. ORIO, T. VIÉVILLE, K. WHITLOCK. Quantitative Analysis of Cell Migration Using Optical Flow, in "PLoS ONE", 8(7): e69574 , July 2013.,

A. O. ARDILES, C. C. TAPIA-ROJAS, M. MANDAL, F. ALEXANDRE, A. KIRKWOOD, N. C. INESTROSA, A. G. PALACIOS. Postsynaptic dysfunction is associated with spatial and object recognition memory loss in a natural model of Alzheimer's disease., in "Proceedings of the National Academy of Sciences" (PNAS), August 2012, vol. 109, no 34, p. 13835-40.

G. DETORAKIS, N. P. ROUGIER. A Neural Field Model of the Somatosensory Cortex: Formation, Maintenance and Reorganization of Ordered Topographic Maps, in "PLoS ONE", July 2012, vol. 7, no 7, e40257

J. FIX, N. P. ROUGIER, F. ALEXANDRE. A dynamic neural field approach to the covert and overt deployment of spatial attention, in "Cognitive Computation", 2011, vol. 3, no 1, p. 279-293

Pathophysiology of Parkinson's Syndrome

Team leader: Erwan Bezard

Main focus: Our team aims at understanding the molecular and cellular mechanisms responsible for the motor symptoms in Parkinson's disease, the atypical parkinsonian syndromes (20% of total parkinsonian syndromes) and their modified response to L-dopa. Our goal is to identify therapeutic targets on the basis of pathophysiological investigations in cellular and animal models as well as on human tissus. We then validate those hits as potential clinically-relevant therapeutic targets.

Main techniques: Molecular anatomy ; immunohistochemistry ; microscopies (light, confocal, electron) ; molecular biology; vectorology; animal behaviour; modeling; clinical research

5 relevant publications since 2011:

Charron G, Laux A, Berthet A, Porras G, Canron MH, Barroso-Chinea P, Li Q, Qin C, Nosten-Bertrand M, Giros B, Delalande F, Van Dorsselaer A, Vital A, Goumon Y, Bezard E (2011) Endogenous morphine-like compound immunoreactivity increases in parkinsonism. Brain 134:2321-2338.

Dehay B, Ramirez A, Martinez-Vicente M, Perier C, Canron MH, Doudnikoff E, Vital A, Vila M, Klein C, Bezard E (2012b) Loss of P-type ATPase ATP13A2/PARK9 function induces general lysosomal deficiency and leads to Parkinson disease neurodegeneration. Proc Natl Acad Sci U S A 109:9611-9616.

Engeln M, Fasano S, Ahmed SH, Cador M, Baekelandt V, Bezard E, Fernagut PO (2013) L-dopa gains psychostimulant-like properties after nigral dopaminergic loss. Ann Neurol.

Porras G, Berthet A, Dehay B, Li Q, Ladepeche L, Normand E, Dovero S, Martinez A, Doudnikoff E, Martin-Negrier ML, Chuan Q, Bloch B, Choquet D, Boue-Grabot E, Groc L, Bezard E (2012) PSD-95 expression controls l-DOPA dyskinesia through dopamine D1 receptor trafficking. J Clin Invest 122:3977-3989.

Recasens A, Dehay B, Bove J, Carballo-Carbajal I, Dovero S, Perez A, Fernagut PO, Blesa J, Parent A, Perier C, Farinas I, Obeso JA, Bezard E, Vila M (2013) Lewy body extracts from parkinson's disease brains trigger alpha-synuclein pathology and neurodegeneration in mice and monkeys. Ann Neurol.

Dynamics of neuronal and vascular networks during memory processing

Team leader: Bruno Bontempi

Main focus: Our team aims at elucidating the spatio-temporal evolution of memory traces and of their underlying cerebral support during the processes of encoding, storage and retrieval in normal and pathological conditions. Since brain function integrates several intermingled components such as neuronal and vascular networks, short- and long-term plasticity, molecular, cellular and regional interactions, we have gathered within the same team complementary expertise in behavioral testing procedures, functional brain imaging, confocal calcium imaging of cellular activity, electrophysiological recordings of large cerebral assemblies and molecular techniques. This strategy enabled us to identify early tagging of cortical networks as a crucial mechanisms required for the formation of enduring associative memory. Currently, our research focuses on the functional contributions of NMDA receptors subtypes and vascular networks to the stabilization of remote memories during the course of systems-level memory consolidation.

Main techniques: Behavior and memory testing in rodents ; spatial and nonspatial memory tasks ; intravenous and stereotaxic surgery ; intracranial drug delivery ; in vivo electrophysiology ; in vivo fibered imaging ; molecular biology (PCR, qPCR, viral transfection) ; biochemical approaches (western blotting, IP) ; immunofluorescence and real time fluorescence microscopy.

5 relevant publications since 2011:

Lesburgueres, E., Gobbo, O. L., Alaux-Cantin, S., Hambucken, A., Trifilieff, P., & Bontempi, B. 2011. Early tagging of cortical networks is required for the formation of enduring associative memory. ***Science***, 331(6019): 924-928.

El Gaamouch, F., Buisson, A., Moustie, O., Lemieux, M., Labrecque, S., Bontempi, B., De Koninck, P., & Nicole, O. 2012. Interaction between alphaCaMKII and GluN2B controls ERK-dependent plasticity. ***J Neurosci***, 32(31): 10767-10779.

Molter, C., O'Neill, J., Yamaguchi, Y., Hirase, H., & Leinekugel, X. 2012. Rhythmic modulation of theta oscillations supports encoding of spatial and behavioral information in the rat hippocampus. ***Neuron***, 75(5): 889-903.

Lagadec, S., Rotureau, L., Hemar, A., Macrez, N., Delcasso, S., Jeantet, Y., & Cho, Y. H. 2012. Early temporal short-term memory deficits in double transgenic APP/PS1 mice. ***Neurobiol Aging***, 33(1): 203 e201-211.

Morel, J. L., Dabertrand, F., Porte, Y., Prevot, A., & Macrez, N. 2013. Up-regulation of ryanodine receptor expression increases the calcium-induced calcium release and spontaneous calcium signals in cerebral arteries from hindlimb unloaded rats. ***Pflugers Arch***. Nov 15. [Epub ahead of print].

Institute of Aquitaine Cognitive and Integrative Neuroscience

Director: Jean-René Cazalets

Date of initiation: January 2011

Main focus: we focus on the mechanisms and development of simple motor functions (such as movement or breathing), as well as more complex phenomena (including memory or addiction) in the Central Nervous System. These research themes are examined at several different levels ranging from molecular research to human clinical studies and with approaches spanning molecular biology, biochemistry, cellular and large-scale extracellular electrophysiology, fluorescence imaging, computational and system neuroscience, animal behavior, human brain imaging, psychophysics and clinical investigations.

Members:

- Researcher: 5
- Faculty: 4
-post-doc: 2
- student (master +PhD): 8 (1 PhDstudent, 2 M2, 5 M1)

- ITA: 2

Behavior, development and neural networks

Team leader: Daniel Cattaert

Main focus: Our project aims to analyze the neuronal basis of locomotor network operation and plasticity by combining cellular and integrative neurobiology (electrophysiology, pharmacology, neuroanatomy) and modeling (realistic neuron and network simulations) with two animal models (mouse embryo and crayfish). The 3 themes developed are the analysis of i) long-term plasticity of locomotor networks in two situations: during development (mouse embryo and crayfish molting) and after social interactions (crayfish), ii) the mechanisms underlying the genesis of spontaneous activity in motor networks, at early stages of development in mice, iii) the dynamics of sensory-motor integration during ongoing movements.

Main techniques: Extracellular and intracellular methodologies, patch-clamp, sharp electrodes, dynamic-clamp, neuropharmacology, neuroanatomical and molecular techniques, behavioral analysis, electromyography, neuron and network simulations, neuromechanical simulations.

5 relevant publications since 2011:

Allain, A.E., et al. (2011). Maturation of the GABAergic transmission in normal and pathologic motoneurons. *Neural Plast,* 2011, 905624.

Issa FA, Drummond J, Cattaert D, Edwards DH (2012) Reconfiguration of Neural Networks by Social Status. *J. Neurosci* **32**(16):5638 –5645

Bacque-Cazenave, J., Issa, F.A., Edwards, D.H. & Cattaert, D. (2013). Spatial segregation of excitatory and inhibitory effects of 5-HT on crayfish motoneurons. *J Neurophysiol,* 109, 2793-802.

Martin, E., Cazenave, W., Cattaert, D. & Branchereau, P. (2013). Embryonic alteration of motoneuronal morphology induces hyperexcitability in the mouse model of amyotrophic lateral sclerosis. *Neurobiol Dis,* 54, 116-26.

Fossat, P., Bacqué-Cazenave, J., De Deurwaerdère, P., Delbecque, J.-P. & Cattaert, D. Anxiety-like behavior in crayfish is controlled by serotonin. *Science* (in révision)

Organization and adaptability of motor systems

Team leader: Muriel Thoby-Brisson

Main focus: Our overall research objective is to decipher the neuronal basis of the short- and long-term functional plasticity of motor systems, with the principal experimental goal of trying to relate cellular, synaptic and neural network physiology to particular aspects of adaptive behavior.

Main techniques: extracellular and intracellular electrophysiological methodologies, electrochemistry, dynamic clamp, calcium imaging, neuropharmacology, kinematic and behavioral analyses, electromyography, and neuroanatomical and molecular techniques.

5 relevant publications since 2011:

Sieling, S., Bédécarrats, A., Simmers, J., Prinz, A. & Nargeot, R. (2014) *Current Biology* (sous presse).

Chapuis, C., Autran, S., Fortin, G., Simmers, J. & Thoby-Brisson, M. (2014). Emergence of sigh rhythmogenesis in the embryonic mouse. *J Physiol* (sous presse).

Lambert, F.M., Combes, D., Simmers, J. & Straka, H. (2012). Gaze stabilization by efference copy signaling without sensory feedback during vertebrate locomotion. *Curr Biol,* 22, 1649-58.

Mellen, N.M. & Thoby-Brisson, M. (2012). Respiratory circuits: development, function and models. *Curr Opin Neurobiol*, 22:676-685.

von Uckermann, G., Le Ray, D., Combes, D., Straka, H. & Simmers, J. (2013). Spinal efference copy signaling and gaze stabilization during locomotion in juvenile Xenopus frogs. *J Neurosci,* 33, 4253-64.

Sleep, Attention and Neuropsychiatry

Director: Pierre Philip

Date of initiation:

Main focus: SANPSY's research focuses on establishing links between sleep, sleepiness, fatigue, circadian rhythms, attention and cognitive performance (neuropsychological and experimental tests, real and simulated driving) in healthy subjects (young, middle age and elderly subjects) and patients with sleep or neuropsychiatric disorders (age-related dementia, stroke, multiple sclerosis, head injuries, depression, hyperactivity and attention deficits, addiction).

Members:

- Researcher: 2
- Faculty: 2
- ITA: 9

Sleep, Attention, Attention Deficit Disorder / Hyperactivity Disorder and Aging

Team leader: Pierre Philip

Main focus: Our main objectives are i) to understand the human characteristics accounting for the vulnerability or resistance to fatigue, sleepiness, attention deficit disorders and pathological cognitive decline (in the elderly), ii) to test behavioral, pharmacological and technical countermeasures to restore cognitive performance of healthy subjects or patients, iii) to explore the pathophysiology of sleep disorders and neuropsychiatric diseases.

Main techniques: Real virtuality (1 immersive virtual reality room (CAVE like system), 2 head-mounted mounted display, 2 large displays tactile, full body motion capture); Driving simulators (2 OKTAL and 1 VIGISIM simulators); Flight simulator (THALES); Ambulatory and fixed sleep recordings (36 to 128 channels); Ambulatory nocturnal breathing recordings; Visual and auditory evoked potentials; Behavioural monitors (Actimetry); Vision tracking systems (FaceLab and Continental), Cognitive and neuropsychological tests (Test of visual simple reaction time, Trail Making Test, Tower of London, Stroop, Continuous Performance Task, Wisconsin Card Sorting Test), Physiological parameters recordings (body temperature, heart rate, transcutaneous o2 and Co2, skin conductance).

5 relevant publications since 2011:

Philip P., Chaufton C., Taillard J., Capelli A., Coste O., Léger D., Moore N., Sagaspe P. Modafinil improves real driving performances in hypersomniac patients: A preliminary randomized double-blind placebo-controlled crossover clinical trial. Sleep, 2014, 37 (3): 483-487.

Taillard J., Capelli A., Sagaspe P., Anund A., Akerstedt T., Philip P. In-car nocturnal blue light exposure improves motorway driving: a randomized controlled trial. PLoS One, 2012, 7 (10): e46750.

Philip P., Sagaspe P., Prague M., Tassi P., Capelli A., Bioulac B., Commenges D., Taillard J. Acute Versus Chronic Partial Sleep Deprivation in Middle-Aged People: Differential Effect on Performance and Sleepiness. Sleep, 2012, 35 (7): 997-1002.

Tassi P., Schimchowitsch S., Rohmer O., Elbaz M., Bonnefond A., Sagaspe P., Taillard J., Leger D., Philip P. Effects of acute and chronic sleep deprivation on daytime alertness and cognitive performance of healthy snorers and non-snorers. Sleep Medicine, 2012, 13 (1): 29-35.

Taillard J., Philip P., Claustrat B., Capelli A., Coste O., Chaumet G., Sagaspe P. Time course of neurobehavorial alertness during extended wakefulness in morning- and evening-type healthy sleepers. Chronobiology International, 2011, 28 (6): 520-527.

Annexe 2: Publications

From the beginning of the project (April 2011) until Dec. 2012, a total of 265 papers was published by BRAIN teams. 75 papers in journal with IF>7, **including 28 papers in journals with IF>10**. Most of them are collaborative works, intra-LabEx (10), nationals (138), Europeans (97) or international (84).

In 2013,120 articles were published by LabEx teams. The numbers of papers in journals with 7<IF>10 is 21 and 14 papers in journals with IF>10. **The impact of BRAIN can be observed by the increased number of inter-LabEx collaborations (25 in 2013 vs 10 in 2011-2012).**

2012:

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