lssue May 2014

# Neurex Newsletter <sup>n°28</sup>



# Edito

A training event on hallucinations was recently organized by Neurex which brought together clinicians –mostly neurologists and psychiatrists– and researchers. Most of the clinicians were private practitioners, taking care of patients in their everyday medical practice, but –for most of them– not involved in research. The multifaceted aspect of their work, including a busy agenda and remoteness from universities, clearly represents an obstacle to the permanent training they might expect for an optimal practice of their profession.

Following a review on the various kinds of hallucinations, recent hypotheses on the pathophysiological mechanisms underlying this phenomenon were detailed. The statement made by a "voice hearer" –while reminding the difficulties of diagnosis in psychiatry, draw attention on the possibilities of cognitive therapy & social tricks. Thanks to a survey, the usefulness and benefits of such an event were assessed in the medical community. 83% of practitioners mentioned that they plan to re-invest in their clinical practice the knowledge acquired on that day. A real reward for our network: supporting scientific research has long been a strong involvement. Will Neurex participate in applying as early as possible the benefits of research to society? We really hope so and thank all of you who help us in making this a realistic aim!



# Freiburg

Strasbourg

# Basel

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# Matilde Cordero-Erausquin, INCI, CNRS UPR 3212\_Strasbourg



From left to right: Maria Carmen Medrano (postdoctoral fellow), Dhanasak Dhanasobhon (PhD student) and Matilde Cordero-Erausquin.

Matilde Cordero-Erausquin is a CNRS investigator at the Institute of Cellular and Integrative Neurosciences (INCI, CNRS UPR 3212) in Strasbourg. After completing her studies at the École Normale Supérieure, Matilde Cordero-Erausquin joined Pr. Changeux's lab at the Pasteur Institute in Paris for her PhD that she defended in 2003. She then moved to Canada to perform a first postdoc with Pr. De Koninck at Laval University (Québec) and a second one with Pr. Ribeiro-da-Silva at McGill University (Montréal).

Dr Cordero-Erausauin joined the INCI in 2007. She is a 2013 USIAS fellow and an ENINET Young Investigator. She and her group are interested in the study of the cholinergic modulation of nociceptive pathways, in particular in the spinal cord.

Matilde Cordero-Erausquin has organized a 2-days meeting entitled «Cholinergic tone: Where from? What for? Physiological modes of cholinergic signalling» that will be held on the 19<sup>th</sup> and 20<sup>th</sup> of May (see thereafter)

# Cholinergic tone: Where from? What for? **Physiological** modes of cholinergic signalling

Acetvlcholine (ACh) has been the first neurotransmitter identified in History, and it has been so in the peripheral nervous system. There, it is the main actor of synaptic transmission, released by the motoneuron to induce muscle constriction, or released by the sympathetic system onto its ganglionic targets. In the central nervous system, ACh is rather considered as a neuromodulator, acting on attention, arousal or motor learning. ACh is also a modulator of nociceptive (pain-related) processing, and this aspect represents the basis of Matilde Cordero-Erausquin's research activity.



ACh levels, in particular in the spinal cord, critically control nociceptive behavior. For example, an increase in the level of spinal ACh induces analgesia both in rodents and humans, a property exploited in the clinic for anesthesia coadjuvants or oral analgesics. On the other hand, locally decreasing the level of ACh or blocking cholinergic signaling exacerbates nociceptive responses (hyperalgesia) and/or induces a nociceptive behavior following an innocuous stimulation (allodynia). This suggests that cholinergic receptors are "tonically active" in the spinal cord, and that their activity controls nociceptive responses. However the source of ACh at this level was until recently controversial and its mode of action remains elusive.

Using ChAT::EGFP transgenic mice, Dr Cordero-Erausquin has demonstrated that a sparse population of cholinergic interneurons located in the laminae III-IV of the mouse spinal dorsal horn is the main source of ACh at this level (Mesnage et al., J. Comp. Neurol., 2011). Although a similar population was thought to be absent from the spinal cord of primates, her group recently demonstrated its existence in the dorsal horn of macaque monkeys (Pawlowski et al., J. Neurosci., 2013). Its connectivity suggests that they are likely to modulate incoming somatosensory information and therefore be the source of the ACh involved in the analgesic effects of epidural acetylcholinesterase inhibitors used in the clinic. The similarities observed between primates and rodents validate the interest of a mouse model, and Dr Cordero-Erausquin's research endeavor continues with the goal of understanding how such a sparse neuronal population achieves a major control of nociception. Her group is investigating this using a combination of in vitro and in vivo electrophysiology, optogenetics and transynaptic labeling.

gic tone" affecting nociceptive responses.



< Transverse section of a ChAT::GFP mouse spinal cord where cholinergic neurons express the green fluorescent protein GFP. The large and dense neurons on the ventral side are motoneurons. The more sparse population of cholinergic neurons present in the dorsal horns of the cord is the one involved in nociceptive processing.

- Amongst the questions tackled by her group is the characterization of the so-called "choliner-
- Whether cholinergic neurons in the dorsal horn of the spinal cord are spontaneously active, or continuously activated by the network, or phasically active but the released ACh is acting on a longer time scale due to volume transmission,

remains to be identified. These are general issues in the field of cholinergic signaling, that will be addressed in the Neurex workshop that is organizing on May 19th-20th in Strasbourg.

A workshop entitled "Cholinergic tone: where from, what for?" will take place on the 19th and 20th of May in Strasbourg. This event aims at discussing the physiological modes of cholinergic signaling. It will question the existence of a "cholinergic tone". In particular, its possible origin will be discussed by the description of the firing and signaling mode of cholinergic neurons, and its possible roles by the description of behaviors that are modulated ACh levels. Recording and morphological data on cholinergic synapses will be presented. Finally, the relative importance of elements controlling ACh levels will be discussed. The workshop will combine lectures and debates on deliberately provocative issues to address several controversial issues in the field of cholinergic signaling.

# NEUREX MEETING

# Cholinergic tone: where from, what for? Physiological modes of cholinergic signaling

# 05 19th & 20th 2014 PROGRAM Monday May 19th Location: Collège Doctoral européen

46 Boulevard de la Victoire Strasbourg

Nonda	y May 19 <sup>th</sup>
9.30 - 09.50	Registration and welcome Callee
9.50 - 10.00 ESSION 1	Welcome Address CHOLINERGIC SYNAPSES
0.00-10.30	Philippe Ascher, Poris, France
0.00 10.00	High sensitivity and low sensitivity nicotinic receptors at synapses
0.30-11.00	Michael Beierlein, Houskon, Toxos, US Cholinergic synaptic signaling in the thalamic reticular nucleus
1.00-11.30	Véronique Bernard, Paris, France Subcellular comparimentalization and intraneuronal trafficking of muscarinic receptors
1.30-14.30	Lunch break & poster session
ESSION 2	CHOLINERGIC NEURONS: FIRING AND RELEASE MODES
4.30-15.00	Jan Michael Schulz, Basel, Switzerland Exciting silences: sensory control of cholinergic signaling in the striatum
5.00-15.30	Martin Sarter, Ann Arbor, Michigan, US Deterministic versus neuromodulatory, phasic versus tonic functions of forebrain cholinergia systems
5.30-16.00	Debate 1: What is the physiological release mode of acetylcholine?
luesda	y May 20th
ESSION 3	NICOTINIC RECEPTORS: ACTIVATION BY ENDOGENOUS ACH, MODULATION BY NICOTINE
9.30-10.00	Huib Mansvelder, Amsterdam, Netherland Cholinergic control of prefrontal cortical circuits consequences for plasticity and behavior
0.00-10.30	Jean-Marie Tournier, Reims, France Nicotinic receptors in the airway epithelium
0.30-11.00	Coffee break
1.00-11.30	Uwe Maskas, Paris, France Acetylcholine as a master modulator of the dapaminergic system
1.30-12.00	Wolfgang Kummer, Giessen, Germany Pre-neuronal acetylcholine: nicotinic signaling from epithelia to sensory neurons
2.00-12.30	Debate 2: Can alpha 7 be involved in endogenous signaling?
2.30-14.00	Lunch break
ESSION 4	CONTROLING ACH LEVELS
4.00-14.30	Eria Krejai, Paris, France Cholinesterases are organized in molecular machines specialized to destroy acetylcholine
4.30-15.00	Marco Predo, London, Ontario, Canada Regulation of cholinergic activity, behavior and transcriptional activity by the vestoular acetytcholine transporter
5.00-15.30	Coffee brack
5.30-16.00	Jochen Klein, Frankfurl, Germany Do clinically used AChE inhibitors actually increase ACh levels in the brain ?
6.00-16.30	Debate 3: Does the extracellular concentration of ACh actually matter?

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#### Organisateur: Matilde Cordero-Erausquir are info on www.meurex.arg or contact: Pascale.Piquet&



Program Interreg M Upper Rhine "Transcending barders with every project". CRIVES, INSERIA, Université de Sincebourg, Région Alexon, Déportement du Ros-Ahin, Déportement du Houl-Ahin, Communauté Urbaine de Sincebourg, Bernstein Center Reiburg, Universitét Reiburg, Universitét Bosel, Kunton Bosel-Stock, Konton Bosel-Londschoft, Confédération Helvétique.

# Coming Events

# The LSTF (Life Science Training Facility) platform: A platform dedicated to a genome-wide dimension of research







eading technician of the LSTF Molecular Psychology department Group of Prof. Andreas Papassotiropoulos

Director of the LSTF, Basel dean of the Faculty of Psychology Basel





Because multidisciplinarity is inherent to neuroscience, technological platforms have been developed over the last decade, which allow sharing facilities and technologies within a scientific community. In Neurex, the universities of Basel, Freiburg and Strasbourg do not derogate to this rule and offer services through their platforms. In 2013, a Neurex event was dedicated to the presentation of the Strasbourg Chronobiotron, a platform dedicated to the study of biological rhythms. The relevance of the Chronobiotron's animal models for chronobiology was addressed.

In 2014, the neurogenomic platform of the University of Basel will be presented during a one day-event. On the 30th of October 2014, a series of lectures at the LSTF Basel (Life Science Training Facility, led by Prof. Andreas Papassotiropoulos) will take place in the Pharmazentrum. During that day, a double (theoretical & practical) approach will allow participants to familiarize with techniques used in genomewide studies to investigate RNA expression.

Philippe Demougin (Papassotiropoulos' group) will present the different aspects of isolation of total RNA and of micro RNA (protocol design, quality control, etc.). He will discuss this bench work in the context of genome wide studies, and illustrate the rapid evolution of the latter during the last decade. Philippe Demougin has tought neurogenomics during previous Neurex Summer and Winter Schools since 2002 (see neurex newsletter 15). **P.P.** 

# **Contribution of global approaches** to the study of neurodegenerative diseases

The advent of "omic" technologies over the last decade opened new and apparently endless possibilities for researchers in all fields.

Coming Events

# A meeting entitled: **CONTRIBUTION OF** GLOBAL APPROACHES TO THE STUDY OF NEURODEGENERATIVE DISEASES

will take place on the 2<sup>nd</sup> of June, 2014 (Salle Pasteur, University of Strasbourg) The aim of this symposium will be to give a broad overview of these nonsupervised approaches. Since such approaches are not "hypothesis driven", new and unsuspected findings on mechanisms and underlying molecular pathways are expected outcomes of these studies. Various "omics" at the technical level and their application to neuro-degenerative diseases will be reviewed during this meeting. The potential and limits will be discussed.

We would like to express our gratefulness to the organizer Dr Jean-Philippe LOEFFLER (UMR-S, INSERM U1118, University of Strasbourg) as well as to all the scientists who kindly accepted to participate in this event.





# On the 10<sup>th</sup> of April 2014,

a Meet & Match event took place at the BCF, Freiburg. The program of this meeting on neurological implants brought together scientists from the Universities of Basel, Freiburg and Strasbourg with scientists working in private companies. The use of implants in various fields of neurology such as pain treatment or motor disorders was addressed. raising also the issue of ethical considerations. P.P.



Dr Ludovic Collin (Roche, Basel) will present the "Brain Shuttle", a transferrinreceptor based system developed by researchers of Hoffmann La Roche (Basel) for the transport of a variety of molecules across the Blood Brain Barrier. Such events are part of our program of interactions between universities and industry within Neurex.



# Crossing the blood-brain barrier: the Brain Shuttle design

06 12<sup>th</sup> 2014

Centre de neurochimie

Strasbourg

5 Rue Blaise Pascal



NEUREX EVENT

Thursday June 12th 14.30

#### Ludovic COLLIN, PhD Senior Scientist E Hoffmann-La Roche Ltd.

e blood-brain barrier (BBB) prevents the passage ( cules from the bloodsheam to the brain fis chers at the Haffmann-La Roche institute Basel have developed a transferrin receptor-based tem, the Brain Shuttle, to increase the BBB penetion of an AB-specific antibody into the brain of a ouse model for Alzheimer's disease.

On a broader range of application, the Brain Shuttle hight be designed for the transport of a variety of moecules across the BBB, such as therapeutic prowith octors, enzymes and peopletes

eres Revolver et d. 2014 horses

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# On the 12<sup>th</sup> of June 2014.

## News



Sonja HOFER did her PhD at the Max Planck Institute of Neurobiology in Martinsried-Munich, followed by a post doctorate at University College London, where she also started her own research group. In 2013, she came to the Biozentrum as Assistant Professor.

Sonja Hofer's research is focused on understanding how neuronal circuits process visual information and integrate it with other signals to enable animals to interpret the visual world and interact with their environment.

Furthermore, she investigates how these circuits change during learning and new experiences, allowing the brain to store new information and to adapt to changes in the environment.

To study these questions her lab uses a wide range of multi-disciplinary methods: in vivo two-photon imaging of neuronal and synaptic function and structure, extracellular and intracellular electrophysiological recordings, animal behavior and theoretical modelling, together with molecular and genetic approaches to identify different cell types, record and manipulate their function and trace specific pathways.

2 new professors of neurobiology at the Biozentrum Base



Professor Sonja Hofer and Professor Thomas Mrsic-Flogel recently (August 2013) joined the neurobiology research groups at the Biozentrum, Basel.



High resolution map of orientation preference in mouse visual cortex



Image of six simultaneously recorded neurons in a slice of mouse visual cortex



Thalamic axons expressing the genetically-encoded calcium indicator GCaMP5 imaged in visual cortex and example traces of calcium transients from individual axons showing their activity in a behaving mouse.

Thomas MRSIC-FLOGEL received a B.A. degree in Biological Science (1996) and a PhD in Neuroscience (2001) from the University of Oxford. He conducted his postdoctoral research at the Max Planck Institute of Neurobiology in Munich where he applied imaging methods to study the structure and function of the mammalian visual system. In 2007, he took up a lectureship and became a Wellcome Trust Research Fellow at University College London. In 2014, he moved to the Biozentrum at University of Basel as an Associate Professor in Neuroscience.

His research aims to understand how sensory function in the visual system emerges from highly complex synaptic interactions in large neuronal populations. His laboratory approaches this question by (i) recording activity in single neurons and large neuronal ensembles in the intact brain during visual processing and behaviour, (ii) mapping synaptic connections between functionally identified neurons of this circuit, and (iii) using computational models to understand which circuit components are important forms single neuron and network function.





# **The Neurex** Program of Support to publication:

Neurex supports some costs inherent to the publication process: Publication fees, etc. Further details available on the Neurex website.

# Neu<sub>E</sub>Time

NeuroTime EPJD program: **Different name - Same program!** 

# "A rose by any other name would smell as sweet."

# (Romeo and Juliet, Act II, Scene 2, Shakespeare)

Last March, The President of the University of Strasbourg has signed the amendment to the Framework Partnership Agreement that binds the NeuroTime consortium to the European Agency (EACEA) and approved the new affiliation of the programme to the EU's research and innovation funding new scheme Horizon 2020. Our program will hence change its name from NeuroTime Erasmus Mundus to NeuroTime Erasmus+.

## The name is changed, but the original flavor remains.

The operational modalities are maintained and the yearly calendar remains the same. The 3rd Edition of the program will start on Oct. 1st 2014 and a maximum of 9 selected PhD students is expected to join the labs of the consortium.

The call for scientific projects of the 4<sup>th</sup> Edition (starting Oct. 2015) will be launched in June 2014. Instructions for submitting a collaborative project will be sent by email to the supervisors who are part of the NeuroTime consortium.

For more information, visit our website at www.neurotime-erasmus.org or contact Domitille Boudard at dboudard@inci-cnrs.unistra.fr.

**D.B.** 

**Annual ENINET** meeting 2014

The annual ENINET meeting 2014 will take place in Freiburg from Thursday, September 4th to Saturday, September 6th, in collaboration with Neurex. VENUE (to be confirmed): Albert Ludwigs University, Institutes of Pharmacy and Pharmacology, Otto-Krayer-Haus, Albertstraße 25, D-79104 Freiburg

http://www.eni-net.org/news/events/annual-networkmeetings/eninet-annual-meeting-4-6-september-2014-albert-ludwigs-university-freiburggermany/

# Info & News



Prof Dr Silvia Aber Biozentrum & FMI, Basel

Support program for "Welcome/Coming back of researchers": results of the 2<sup>nd</sup> call

Neurex

The objective of the Neurex "Support program for Welcome/Coming back of researchers" is to encourage and support the research work performed by young teams in our academic laboratories.

Its second call ran until the first guarter of 2014 and in April results in the allocation by the scientific committee of Neurex of 2 grants. The successful candidates are Perrine Inquimbert and Caroline Rouaux, (Strasbourg). Since the beginning of this campaign, 6 grants have been attributed. This will certainly be our last call in the framework of our TriNeuron-Project, but we hope that we will have the opportunity to give you the same kind of support possibilities in a new project on the horizon 2015. Application modalities will then be available timely on our website.

# **Prof Dr Silvig Arber** awarded the Otto Naegeli **Prize 2014**



The Otto Naegeli Prize (200.000 CHF) is awarded to distinguished scientists in the field of medical research. Professor of Neurobiology at the Biozentrum of the University of Basel and Senior Investigator at the FMI (Basel), Silvia Arber is interested in the function and assembly of neuronal circuits controlling motor behavior.

After completing a PhD under the direction or Dr Pico Caroni (FMI), Silvia Arber was a postdoctoral fellow in the lab of Thomas Jessell (Columbia University, New-York). Back to Basel since 2000, Silvia Arber has been awarded with numerous prizes including the National Latzos Prize (2003), the Schellenberg Prize and the Friedrich Miescher Institute Award (2008). P.P.

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#### Bi-annual.

Partners: Program Interreg IV Upper Rhine «Transcending borders with every project», CNRS, INSERM, Université de Strasbourg, Région Alsace, Département du Bas-Rhin, Département du Haut-Rhin, Communauté Urbaine de Strasbourg, Bernstein Center Freiburg, Universität Freiburg, Universität Basel, Kanton Basel-Stadt, Kanton Basel-Landschaft, Contédération Helvétique.



MAY 2014

 19<sup>th</sup>-20<sup>th</sup> - Neurex Meeting
 «Cholinergic tone: where from, what for? Physiological modes of cholinergic signaling»
 Strasbourg, France

Coming events

## **JUNE 2014**

- 2<sup>nd</sup> Neurex Meeting
  «Contribution of global approaches to the study of neurodegenerative diseases»
   Strasbourg, France
- 12<sup>th</sup> Neurex Conference: News & Views from Industry «Crossing the blood-brain barrier: the Brain Shuttle design» Strasbourg, France

#### JULY 2014

 5<sup>th</sup> -9<sup>th</sup> - FENS Meeting
 «9<sup>th</sup> FENS Forum of Neuroscience» Milan, Italy

### SEPTEMBER 2014

 4<sup>th</sup>-9<sup>th</sup> ENINET Meeting, in collaboration with Neurex «Annual ENInet meeting» Freiburg, Germany

## OCTOBER 2014

 30<sup>th</sup> Neurex highlight: platform event
 «Life Science Training Facility Basel: A platform dedicated to a genomewide dimension of research» Basel, Switzerland

#### NOVEMBER 2014

 15<sup>th</sup>-19<sup>th</sup> American Society for Neuroscience's meeting «Annual Meeting» Washington, DC, USA

#### **FALL 2014**

 Neurex Meeting & web conference «Imaging drug effects»
 Basel, Switzerland

## WINTER 2014

 Neurex event «Neurex Annual Meeting» Freiburg, Germany

#### DECEMBER 2014

 1st-2nd - Neurex Meeting
 «Fighting Neuroinflammation: Certainties and illusions & Rebuilding the Myelin: Expectations and hopes»
 Strasbourg, France

This description is not definitive, but lists the events which are ready or in preparation. Please check again on www.neurex.org or in the next newsletter for additional events.

## JANUARY 2015

- 20<sup>th</sup>-22<sup>nd</sup> Erasmus Mundus NeuroTime Meeting Basel, Switzerland
- 23<sup>rd</sup> Neurex-Biozentrum Meeting in the honour of

Prof Heinrich Reichert's retirement «SN development in invertebrates» Basel, Switzerland

## SPRING 2015

- Neurex Meeting «Epigenetics & imaging» Basel, Switzerland
- Neurex Meeting
  «Evolutionary conservation of an atypical molecular cascade»
   Strasbourg, France

## Info & links

#### NEUROSCIENCE FEDERATIONS & LABORATORIES IN THE UPPER RHINE VALLEY

The Neurex network includes the 3 neuroscience federations of Basel (NNB, Neuroscience Network Basel), Freiburg (Neurag) and Strasbourg (Neuropôle) plus additional research units performing research in the NS. For a detailed description of the institutes making up the neuroscience landscape in Neurex, you may download our supplement to newsletter 26 on www.neurex.org.

#### Neuropôle

- http://neurochem.u-strasbg.fr
- NEURAG http://www.neurag.uni-freiburg.de
- NNB

http://www.neuronetwork.unibas.ch

#### NEWSLETTERS

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