ISSUE OCTOBER 2017

NEUREX NEWSLETTER N° 31

CONTENT

neurex
neuroscience·upper·rhine·network

EDITO

The implementation of a trinational training campus in neuroscience was, as its name implies, the main aim of the Interreg V project "NeuroCampus" (launched in November 2015). Thanks to the strong involvement of scientists and clinicians of the 3 Neurex universities (& companies), the network has harnessed the complementary expertise of our laboratories to create transboarder trainings which enrich the curriculum of our Masters, PhD students and postdoctoral fellows. Lab tours are one example: the second lab tour recently organized illustrated the different scientific approaches of research on sleep disorders performed by the CIRCSom in Strasbourg, the Sleep Research Center in Freiburg and the Chronobiology Center of the University Psychiatry Klinik in Basel. Psychiatry and cognition are in the spotlight during the second part of 2017. We would like to welcome Prof Katharina Domschke, who was recently appointed Medical Director by the Department of Psychiatry & Psychotherapy Freiburg. In November 2017, Prof Tebartz van Elst, from the same Department, will organize a meeting and a controversy debate where the ICD- and DSM-based psychiatric diagnosis of schizophrenia will be discussed. Classification in psychiatry raises several important issues: how a system of classification of psychiatric disorders may lead to a dead-end in terms of therapy, but also how and why it is a determining factor that may hamper the development of promising research models. This important question is also at the heart of the issues raised by Dr Jack Foucher (University of Strasbourg) who founded the Circle of Excellence of Psychosis which provides dedicated e-learning. English versions of the CEP' educational series of lectures will now be available on the Neurex multimedia platform (created in the context of the Neurocampus project). Research on cognition is also at the forefront of the scene at the University of Basel where the teams of Prof Papassotiropoulos & Prof De Quervain (MCN, Molecular & Cognitive Neuroscience Transfaculty Research Platform) recently published in *Nature Communications* and *Nature Human Behaviour* the demonstration of a link between the Immune System, Brain Structure and Memory. Our network is rich of talented neuroscientists and clinicians who offer a solid basis for an attractive international training over a limited geographical area: take profit of it and join our events!

P.P.

REPORT

LAB TOUR 2017

SLEEP & SLEEP DISORDERS: A CORNERSTONE IN THE COMPLEMENTARY EXPERTISE OF OUR 3 NEUREX UNIVERSITIES

The Neurex LAB TOURS aim at illustrating the research approaches used by different laboratories - located on each side of our trinational Neurocampus- to investigate a common topic. After the event on memory in 2016, another tour took place on the 6th and 7th of September 2017. This year, it focused on sleep and sleep disorders.

Sleep (see Box 1, page 7) is a complex physiological function which has been suggested to play many important roles, such as energy restoration, brain repair, memory consolidation, metabolic clearance, or synaptic downscaling to cite a few of them. The alternance of sleep and wakefulness defines a sleep-wake cycle (see Box 2, page 7) which differs in timing across individuals (chronotype).

Sleep disorders include –but are not limited to– insomnias, circadian rhythm sleep disorders, sleep related breathing disorders, hypersomnias, sleep related movement disorders, etc.

Insomnias and circadian rhythm disorders may result in excessive daytime sleepiness and fatigue, a real burden which stronly impacts the quality of life of poor sleepers. There is growing evidence that sleep disorders are observed in parallel or may even precede the occurrence of neuropsychiatric disorders as varied as Alzheimer's disease, Parkinson's disease, autism, depression, schizophrenia, etc. The study of insomnia and circadian rhythm disorders is at the heart of the activities of the respective research centers of Basel, Freiburg and Strasbourg and closely connected to research in psychiatry. It was presented at the 2017 lab tour on sleep & sleep disorders where a detailed presentation & visit of the 3 centers was organized during 2 days-tour in bus.

- 1. The lab tour began in Strasbourg at the **CIRCSom** (International Research Center for ChronoSomnology, University Hospital Strasbourg & INCI).
- 2. It continued the next morning at the **Sleep Center of the Department for Psychiatry & Psychotherapy** in Freiburg,
- 3. and concluded in the afternoon at the **Chronobiology Centre of the UPK** (University Psychiatry Klinik) in Basel.

These three centers address complementary aspects of clinical research on human sleep and sleep disorders, using an incomparable technical and clinical platform unique in Europe[1].
As we shall see below, research at the **CIRCSom Strasbourg** and the **Centre for Chronobiology Basel** is more focused on the circadian regulation of sleep and its disorders while the **Sleep Center at the University of Freiburg** puts more emphasis on insomnia and its therapy.

1 / The lab tour 2017 also includes a video report made at the Chronobiotron (INCI, Strasbourg), a platform which hosts and allows the study of chronobiological rhythms in conventional & transgenic animal. One strength of this platform, unique in Europe, is the hosting of the *Arvicanthis Ansorgei* model, a diurnal rodent – a rather unusual feature, that allows better comparison with humans. For security reasons (among which the possibility of transmission of infectious agents), this facility is not opened to public access. The *multimedia* section of our Neurocampus project (see article "A new website for Neurex" on page 32) took the relay and a movie of the facility was made for educational purpose. Once ready, its release will be announced to all Neurex members.

There is a real need to characterize the regulatory mechanisms for sleep and alertness, and in particular the effects of light: the abundance of artificial light exposure nowadays and the high prevalence of sleep disorders, social jet lag as well as their impact on mood and cognition are a real burden in modern societies.

The circadian regulation of sleep (see Box 2, page 7) and its impact on sleep / vigilance and cognitive function in healthy volunteers and patients suffering from neuropsychiatric disorders is at the heart of the research activities of the Centre for Chronobiology (UPK, University of Basel) and of the CIRCSom (University Hospital & INCI, Strasbourg). In these laboratories, sleep / vigilance and circadian regulation are studied under different well-controlled conditions. These conditions include lighting with different wavelengths (see pictures thereafter), temperature, different light / dark regimes and long / short photoperiods, etc. Sleep is assessed using polysomnographic EEG video recordings, in parallel with the measurement of several different parameters (qualitative analysis of sleep, subjective and objective evaluation of sleepiness and vigilance, biological sampling, hormone measurements, core body temperature, mood and cognition, etc).

ON THE 2ND OF OCTOBER,

the Nobel Price 2017 has been attributed jointly to **Jeffrey C. Hall, Michael Rosbash and Michael W. Young** for their discoveries of **molecular mechanisms controlling the circadian rhythm**.

Their discoveries explain how plants, animals and humans adapt their biological rhythm so that it is synchronized with the Earth's revolutions. Sleep is one of the fundamental physiological processes which displays a strong circadian rhythmicity.

REPORT

LAB TOUR 2017

THE CENTRE FOR CHRONOBIOLOGY

UNIVERSITY PSYCHIATRIC CLINICS IN BASEL

Universität Basel

Fig. 1

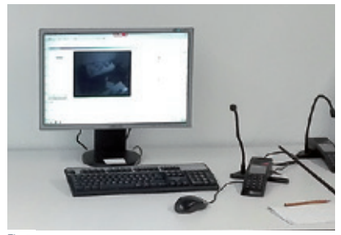


Fig. 2

Fig. 3

Figure 1 / Chronobiology Center, Basel
Dr Ruta Lasauskaite explains how light has a strong impact on brain activity through visual and non visual photoreceptors on the brain. While visual photoreceptors are involved in vision, the role of the nonvisual photoreception is to synchronise periodic functions of living organisms to the environmental light periods. Therefore, a great majority of blind people experience sleep disorders due to the impairment in transmission of ocular light from the retina to their circadian clock.

Figure 2 / Room at the Centre for Chronobiology (UPK, Basel)
equipped for the monitoring of the volunteers under study in a controlled bedroom. The screen of the computer displays the video recording of such a volunteer sleeping in a dark room.

Figure 3 / A look at the ceiling of one of the bedrooms of the Centre for Chronobiology (UPK, Basel): the software has been programed so as to mimick the daylight, including a pattern of movements of clouds in the sky.

The Centre for Chronobiology (UniBasel) focuses on circadian and homeostatic (see Box 2, page 7) regulation of human sleep, alertness, cognitive performance, mood, memory consolidation and thermoregulation, and on the study of these mechanisms in ageing and psychiatric disorders. Its research interests include (but are not limited to) the non-visual effects of light on circadian physiology, sleep and cognition, the cerebral mechanisms underlying the influence of age-related changes in circadian and homeostatic processes on cognition, sleep and cognitive function in older adults, the circadian rhythms and sleep regulation in psychiatric disorders (for example depression, schizophrenia, borderline personality disorder) as well as chronotherapy (e.g. light treatment) in psychiatric disorders.

LAB TOUR 2017

THE SLEEP CENTER

AT THE CLINIC FOR PSYCHIATRY & PSYCHOTHERAPY IN FREIBURG

UNIVERSITÄTS KLINIKUM FREIBURG

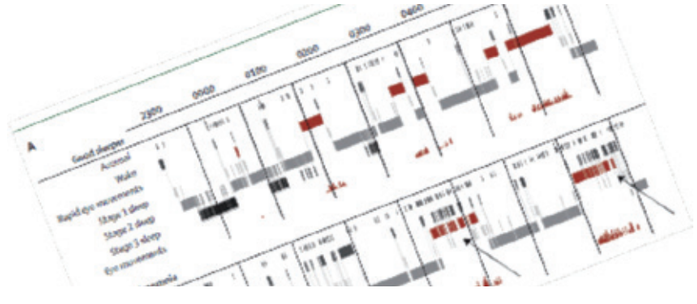
Fig. 4

Fig. 5

Figure 4 / Prof Dieter Riemann
Head of the Sleep Center at the Psychiatry & Psychotherapy Department of the University of freiburg, during a lecture at the lab tour 2017. Prof Riemann explains that insomnia is a typical symptom that accompanies depression, reaching a frequency of 100% in this disorder.

Figure 5 / Dr Elisabeth Hertenstein
(Sleep Center, Freiburg) explains the new developments in the psychotherapy of insomnia. At present, Cognitive Behavioural Therapy of Insomnia is the first-line treatment for chronic insomnia. This treatment comprises advice on sleep– wake behaviour (sleep hygiene), stimulus control and sleep restriction, and relaxation and cognitive techniques. The efficacy of Cognitive Behavioural Therapy has been shown in meta-analyses of randomised controlled trials.

Research at the Sleep Center (University of Freiburg) is focused more particularly on insomnia and its involvement in neuropsychiatric disease. Insomnia is defined by some difficulties falling asleep, difficulty staying asleep, early awakening or poor sleep quality.



Prof Riemann (Research at the Sleep Center (University of Freiburg) is focused more particularly on insomnia and its involvement in neuropsychiatric disease. Insomnia is defined by some difficulties falling asleep, difficulty staying asleep, early awakening or poor sleep quality. Prof Riemann (Figure 4) and his team, studying the polysomnographic EEG of insomnia patients demonstrated in 2012 that "*the polysomnographic sleep of many patients with insomnia is characterised by an increased frequency of brief events such as shifts in sleep stages between NREM and REM sleep and among NREM stages, brief periods of awakening and microarousals (brief and transient changes in EEG frequency suggestive of an awake state), and not by extremely long periods of wakefulness. Thus, although the macrostructure of sleep (cycling between NREM and REM periods) is only mildly affected, the microstructure within both NREM and REM periods strongly shows a disturbance of the switch between sleep and wakefulness... As compared with healthy sleepers, people with insomnia, have the most pronounced differences in the EEG fast frequency range (β power). This type of instability has also been suggested to be relevant for the disruption of REM sleep, which is known to be especially fragmented in insomnia patients, with microarousals.*" (Spiegelhalder, Regen et al. 2012).

The Sleep Center Freiburg is also interested in the treatment of insomnia, and in particular Cognitive Behavioural Therapy (Figure 5). Insomnia treatments include benzodiazepines, benzodiazepine-receptor agonists, and cognitive behavioural therapy. One facet of CBT is sleep restriction therapy which works for 60% of the patients. CBT has been shown to be equal to pharmacotherapy during acute treatment and more effective for long-term treatment.

REPORT

UNIVERSITÉ DE STRASBOURG

LAB TOUR 2017

THE CIRCSOM

INTERNATIONAL RESEARCH CENTER FOR CHRONOSOMNOLOGY, STRASBOURG

CIRCSom is a joint project between the University Hospital Strasbourg and INCI: it is located within the Sleep Clinic of the Neurology Department and adjacent to the Psychiatry and Child Psychiatry Departments. The CIRCSom is interested in the study of sleep/vigilance and circadian regulation in healthy subjects, but also in patients with neuropsychiatric disorders, from children – i.e with autism spectrum disorder – to older adult patients affected by neurodegeneration (Parkinson disease, Lewy body dementia...). Research at CIRCSom is focused on the role of the direct effects of light on sleep and alertness, their interaction with other sleep regulatory mechanisms, the circadian drive and the sleep homeostatic process. Five bedrooms (including bathrooms) are equipped with a ceiling that gives the possibility to finely adjust spectrum and intensity of light, apply different light/dark regimes and long/short photoperiods (see Figure 6). The ultimate goal is to investigate the functional interactions between sleep/vigilance, circadian rhythm regulation, sleep homeostatic process and the role of light in neuropsychiatric disorders.

Fig. 6

Fig. 7

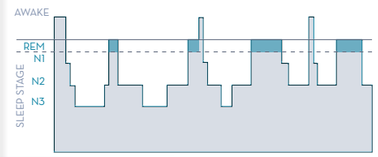
Figure 6 / CIRCSom, Strasbourg
A special ceiling in the bedroom allows for homogenous lighting conditions with control of numerous parameters. For example, a polychromatic white light that can be enriched in cold colors (blue-enriched) or warm colors (red-enriched) white light. Monochromatic lights may also be tested (here, an example with green light), while also controlling a wide range of intensities (from 1 to 20 000 lux at bed level). It is also possible to test long or short photoperiods, straight or square transitions as well as alternating light/dark conditions.

Figure 7 / Prof. Patrice Bourgin at CIRCSom
in a chronobiology bedroom used for the study of sleep and wake mechanisms and their disorders. Such rooms are sound proof and equipped with a sas, that allows monitoring without any visible impact on the volunteer or patient. Blood is regularly sampled using a system that allows to collect it through an opening in the wall (little pane on the left of the door). A video polysomnography is continously recorded and lighting conditions may be adjusted (see Figure 6).

IN CONCLUSION, the study of sleep and sleep disorders is a complex and multifaceted problem, but also a cornerstone in the complementary expertise of our 3 universities. The growing evidence that there is bidirectional relationship between sleep and psychiatric disorders offers the hope that sleep centers will constitute a hope to improve the treatment not only of sleep disorders, but may benefit some psychiatric disorders as well.

BOX 1

SLEEP is featured by marked changes in electroencephalogram (EEG) waves, which, when combined with measurements of the alterations in muscle tone and eye movements characterize different well-defined states. The different stages of sleep occur in a characteristic sequence. The waking state with the eyes open is characterized by high-frequency (15-60 Hz), low-amplitude (~30 µV) beta activity. Relaxed wakefulness (once the eyes are closed and the brain no longer receives visual input) is characterized by a steady and rhythmic pattern of about 10 Hz (alpha-waves). It is followed by a drowsy period (stage N1, transition to light sleep) during which the frequency spectrum of the EEG is shifted toward lower values and the amplitude of the cortical waves slightly increases (theta waves). There is then (stage N2 sleep) a further decrease in the frequency of the EEG waves and an increase in their amplitude, together with intermittent high-frequency spike clusters (10-12 Hz for 1-2 seconds) called sleep spindles. EEG tracings also show a pattern called K-complex during that stage. In the deepest level of sleep (stage N3), low frequency (1-4 Hz) high-amplitude fluctuations -called delta waves- predominate, hence its name Slow Wave Sleep (SWS). The entire sequence from drowsiness to deep stage N3 sleep takes about an hour. These 3 sleep stages are called non-rapid eye movement (non-REM) sleep; its most prominent feature is the SWS (stage N3 sleep, considered to be the deepest stage of sleep). Following a period of SWS, the stages of sleep reverse, reaching a quite different state called Rapid Eye Movement (REM) sleep, during which Electrooculograms (EOG) demonstrate the presence of rapid eye movements, hence its name. In REM sleep, the EEG recordings are remarkably similar to that of the awake state. After about 10 minutes in REM sleep, the brain typically cycles back through the non-REM sleep stages. Slow-wave sleep usually occurs again in the second period of this cycle, but not during the rest of the night. On average, 4 additional periods of REM sleep take place, of increasing duration.



BOX 2

On an evolutionary point of view, human beings are a diurnal species, meaning that their sleep-wake cycle consists of a sleep period during the night and awakeness during the day, in contrast to nocturnal species -such as rats or mice for example- which display an opposite pattern. The sleep-wake cycle is a complex process which has been suggested to result from the interactions between a biological clock (circadian pacemaker) and a sleep homeostatic process that depends on the prior time spent awake. This 2-parameters model applies not only to the sleep-wake cycle, but also to temporal patterns of nearly every neuroendocrine, physiological, and psychological function. Interestingly, the period of the human circadian rhythmicity slightly differs from the natural 24h-period alternance of day and night on earth. When submitted to constant dark conditions, the so-called "free-running" period in humans averages about 24h and 20 minutes, but differs between individuals. In order to maintain an optimal synchronization (entrainment) between the internal clock and the solar day, periodic stimuli called "Zeitgebers" help to maintain an appropriate phase relation. The most important Zeitgeber is light, but food timing and social stimuli are also signiticant cues. The light input sensed by the retina influences the activity of the suprachiasmatic nuclei in the brain, impacting clock genes, and different outputs such as melatonin synthesis, thermoregulation, etc. These factors then interact with the sleep-wake homeostat to permanently adjust sleep propensity and architecture, influencing phenomena as different as mood and performance or hormonal output. Circadian rhythms are important in determining sleeping patterns and can be disturbed by shift work or time zone changes (jet-lag) for example. Phase shifts (phase advance or phase delay) may also affect the sleep-wake cycle architecture and strongly impact the quality of life.

P.P.

Special thanks to:

Prof Christian Cajochen,
Chronobiology Center, University Psychiatry Clinic , Basel

Prof Dieter Riemann,
Department of Psychiatry & Psychotherapy, Freiburg

Prof Patrice Bourgin,
CIRCSom Strasbourg

and their team for kindly welcoming us and for the scientific lectures of the tour.

OBITUARY

OBITUARY FOR PROF. DR. MED. DR. H. C. MICHAEL FROTSCHER

**Prof
Michael Frotscher
(1947-2017)**

On May 27, 2017, Michael Frotscher passed away, suddenly and unexpectedly, at the age of 69. We lost a good friend and great scientist. We will miss his friendly and appreciating personality, his great enthusiasm and his never-ending energy.

Michael Frotscher was an internationally renowned scientist in the fields of Neuroanatomy and Developmental Neuroscience. His scientific success was mirrored by many awards, including the Wolfgang Bargmann-Award of the Anatomical Society (1992), the Gottfried Wilhelm Leibniz-Award of the German Research Foundation (1993), the Max-Planck-Research Award (2000), the Ernst-Jung-Award (2002) and the Hertie-Senior-Research Professorship (2007).

From 1989 until 2011 Michael Frotscher was Director of the Institute of Neuroanatomy and Cell Biology at the University of Freiburg. From 1995 until 2007 he was the Coordinator of the DFG-funded Freiburg CRC 505: "Neuronal Differentiation and Neurotransmission". In 2004, Michael was a founding member of the Freiburg Bernstein Center for Computational Neuroscience (BCCN). In 2011 he moved as Hertie-Senior-Professor to Hamburg, where he headed the Institute of Structural Neurobiology at the Center of Molecular Neurobiology Hamburg (ZMNH), University Clinic Eppendorf. After his departure to Hamburg, Michael served as the Chairman of the Scientific Advisory Board of the Bernstein Center Freiburg (BCF).

Apart from his scientific work, Michael Frotscher was engaged in various societies and did enormous work for the German Research Foundation (DFG). Thus, Michael served as the Founding President of the German Neuroscience Society (NWG), Senator of the German Academy of Sciences Leopoldina, President of the German Anatomical Society, and member of the DFG Senate Committee for CRCs. Over the years, Michael was a strong supporter of the tri-national network for neuroscience Neurex.

Michael was not only a gifted scientist, but also a very talented and highly esteemed university teacher and mentor. His students invariably admired and respected him.

We mourn Michael Frotscher: we will miss his wise advice and inspiring energy.
We wish he would have had more time.

C.H.-A.A.

SCIENTIFIC NEWS

Universität Basel

mcn

UNIVERSITY OF BASEL: LINK DISCOVERED BETWEEN IMMUNE SYSTEM, BRAIN STRUCTURE AND MEMORY

In two independent studies, scientists at the University of Basel have demonstrated that both the structure of the brain and several memory functions are linked to immune system genes. The scientific journals *Nature Communications* and *Nature Human Behaviour* have published the results of the research

The body's immune system performs essential functions, such as defending against bacteria and cancer cells. However, the human brain is separated from immune cells in the bloodstream by the so-called blood-brain barrier. This barrier protects the brain from pathogens and toxins circulating in the blood, while also dividing the immune cells of the human body into those that fulfill their function in the blood and those that work specifically in the brain. Until recently, it was thought that brain function was largely unaffected by the peripheral immune system.
However, in the past few years, evidence has accumulated to indicate that the blood's immune system could in fact have an impact on the brain. Scientists from the University of Basel's Transfaculty Research Platform Molecular and Cognitive Neurosciences (MCN) have now carried out two independent studies that demonstrate that this link between the immune system and brain is more significant than previously believed.

SEARCH FOR REGULATORY PATTERNS

In the first study, the researchers searched for epigenetic profiles, i.e. regulatory patterns, in the blood of 533 young, healthy people. In their genome-wide search, they identified an epigenetic profile that is strongly correlated with the thickness of the cerebral cortex, in particular in a region of the brain that is important for memory functions. This finding was confirmed in an independent examination of a further 596 people. It also showed that it is specifically those genes that are responsible for the regulation of important immune functions in the blood that explain the link between the epigenetic profile and the properties of the brain.

GENE VARIANT INTENSIFIES TRAUMATIC MEMORIES

In the second study, the researchers investigated the genomes of healthy participants who remembered negative images particularly well or particularly poorly. A variant of the TROVE2 gene, whose role in immunological diseases is currently being investigated, was linked to participants' ability to remember a particularly high number of negative images, while their general memory remained unaffected.

This gene variant also led to increased activity in specific regions of the brain that are important for the memory of emotional experiences. The researchers also discovered that the gene is linked to the strength of traumatic memories in people who have experienced traumatic events.

SCIENTIFIC NEWS

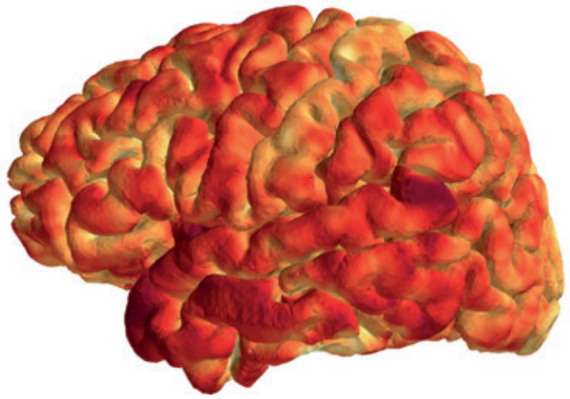


Fig. 1

Figure 1 /
The thickness of the cerebral cortex is correlated with the epigenetic profile of immune-related genes. Photo: MCN

The results of the two studies show that both brain structure and memory are linked to the activity of genes that also perform important immune regulatory functions in the blood. “Although the precise mechanisms behind the links we discovered still need to be clarified, we hope that this will ultimately lead to new treatment possibilities,” says Professor Andreas Papassotiropoulos, co-Director of the University of Basel’s MCN research platform. The immune system can be precisely affected by certain medications, and such medications could also have a positive effect on impaired brain functions.

INNOVATIVE RESEARCH METHODS

These groundbreaking findings were made possible thanks to cutting edge neuroscientific and genetic methods at the University of Basel’s MCN research platform. Under the leadership of Professor Andreas Papassotiropoulos and Professor Dominique de Quervain, the research platform aims to help us better understand human brain functions and to develop new treatments for psychiatric disorders.

A.P.

ORIGINAL SOURCE

Virginie Freytag et al.
A peripheral epigenetic signature of immune system genes is 2 linked to neocortical thickness and memory
Nature Communications (2017),
doi: 10.1038/ncomms15193

Angela Heck et al.
Exome sequencing of healthy phenotypic extremes links TROVE2 to emotional memory and PTSD
Nature Human Behaviour (2017),
doi: 10.1038/s41562-017-0081

FURTHER INFORMATION

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REPORT

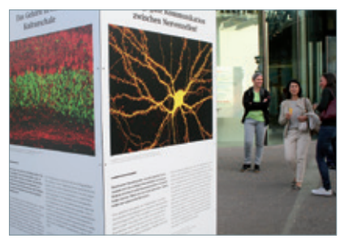
BRAIN RESEARCH FOR ALL

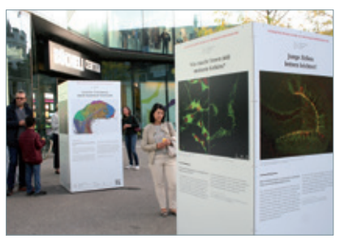
On the **21ST OF SEPTEMBER 2017**, the Neuroscience Network Basel organized a Vernissage for the opening a 10 days-Open Air Exhibition “Brain Research for all”, taking place in Liestal CH. During this period, 2 evenings of public conferences were held (Sept. 21ST & Sept. 25TH) during which researchers and clinicians of the University of Basel gave their scientific input, in particular on brain disorders.

This event was also the occasion to exhibit 15 posters presenting the scientific research of group leaders of the Neuroscience Network Basel (NNB), using beautiful illustrations of their work (see pictures). This event aimed at informing the public on the strong involvement of the University of Basel in neuroscientific fundamental and applied research. Organized by the NNB coordinators Dr Catherine Alioth and Dr Simone Grumbacher, it was a great success and confirmed the growing interest of public for neuroscience.

P.P.

OPEN AIR EXHIBITION SEPT. 21ST- OCT 1ST LIESTAL, CH





REPORT

CONTROVERSY DEBATE / JUNE 1ST, 2017

Amyotrophic Lateral Sclerosis (ALS) is a devastating incurable disease characterized by the degeneration of upper and lower motor neurons controlling skeletal muscles, leading to generalized paralysis and eventually respiratory failure. In about 10% of the patients, the disease is attributed to a familial form; disease-causing gene mutations have been identified in 80% of these patients. Mutations have been reported as causative in 5 to 10% of the remaining 90% of patients who display the sporadic form of the disease. ALS overlaps extensively with FrontoTemporal Dementia (FTD), the second most common form of dementia in people under 65 years of age, especially at the genetic level. Approximately 10% of affected individuals develop FTD.

Over 20 genes have been linked to ALS: historically, the discovery in 1993 of mutations in SOD1 (an enzyme catalysing the detoxification of superoxide) marked the beginning of the era of ALS modelling, with the development of the famous rodent SOD model. This was followed in the following years by the identification of the involvement of several important mutations such as in the TDP-43-encoding gene (TARDBP, TAR DNA-binding protein 43), FUS (FUsed in Sarcoma) and C9*orf*72 (which encodes chromosome 9 open reading frame 72). Many other genetic mutations have also been associated with ALS, even though less frequent. Both FTD and ALS can be caused by many mutations in the same set of genes; the most prevalent of these mutations is the GGGGCC repeat expansion in the first intron of C9*orf*72. Importantly, C9*orf*72, has been reported to underlie 10 - 15% of all ALS (vs 2% of ALS cases for SOD1, 0.9% of cases for TARDBP and 0.7% of cases for FUS mutations).

Unfortunately, the translation of therapeutic strategies conceived from model systems to the clinic has been unsuccessful so far: many of them, even though promising in rodent mutant SOD1 models, subsequently failed in clinical trials among the ALS population. In recent years, however, insights into the pathogenesis of motoneuron degeneration have improved. Thus, it has been suggested that missense mutations in SOD1 do not seem to cause ALS by a loss of dismutase activity, but instead, by a toxic gain-of-function of this protein. Later, TDP-43 was identified as a major constituent of the ubiquitin-positive aggregates found in the motoneurons of ALS patients (and of 50% of cases of FTD not associated with ALS). A mislocalization of TDP-43 and FUS in cytoplasmic protein aggregates and their subsequent nuclear depletion is an important hallmark of ALS. Thus, both the nuclear loss of TDP-43 and FUS function, and their cytoplasmic (& cytotoxic) aggregation are believed to contribute to ALS pathogenesis.

If identifying the potential culprit genes involved in the development of these neurodegenerative diseases is a first very important step, addressing the pathophysiological mechanism of these mutations is the second fundamental aspect. A recent controversy debate was organized by José-Luis Gonzalez de Aguilar and Luc Dupuis (UMR_S Inserm 1118, University of Strasbourg) on the molecular mechanisms of toxicity of C9*orf*72. The UMR_S Inserm 1118, headed by Dr Luc Dupuis, is specialized in the study of Central & Peripheral mechanisms of neurodegeneration.

Controversy Debate available
on our multimedia platform
(https://www.neurex.org/neurocampus)

During this event, the organizers shared their expertise with renowned scientists to address the molecular pathophysiological mechanisms of ALS. We express our gratefulness to the speakers, José-Luis Gonzalez de Aguilar and Luc Dupuis (UMR_S Inserm 1118, University of Strasbourg), Edor Kabashi (Sorbonne Université, Université Pierre et Marie Curie, Université de Paris 06, Unité Mixte 75, INSERM Unité 1127, CNRS UMR 7225, Institut du Cerveau et de la Moelle Épinière, Paris, France), Ludo van den Bosch (VIB-KU Center for Brain & Disease Research, Leuven, Belgium) and Ricardos Tabet (Massachusetts General Hospital, MassGeneral Institute for Neurodegenerative Diseases, Charlestown, USA).

P.P.

NEUROCAMPUS EVENT

OCTOBER 03RD 2017

VENUE

> **PRESTWICK CHEMICAL**
> 220 BOULEVARD GONTHIER D'ANDERNACH
> ILLKIRCH-GRAFFENSTADEN

> **NEUROFIT**
> BIOPARC I, 850 BD SÉBASTIEN BRANT
> ILLKIRCH-GRAFFENSTADEN

INTERACTIONS WITH INDUSTRY: VISIT OF PRESTWICK CHEMICAL & NEUROFIT COMPANIES

Organizers **Pascale Piguet** (Neurex, Basel)
& Jonas Fizet (Neurofit, Illkirch-Graffenstaden)

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NeuroCampus

>>> Program

VISIT OF PRESTWICK CHEMICAL

10.30 am **DR. MARIE-LOUISE JUNG**
(VP Business Development)

DR. DANIELA VERRA
(Business development and Market Intelligence Prestwick chemical)
COMPANY PRESENTATION

11.00 am **DR. CHRISTOPHE MORICE**
(Director of Medicinal Chemistry)
CASE STUDY: DRUG DISCOVERY IN THE CNS

11.30 am **LAB VISIT, IN 2 GROUPS**

12.00 am Lunch Break

VISIT OF NEUROFIT

14.00 pm **DR. EMILE ANDRIAMBELOSON**
(Head of Research)
WELCOME at Neurofit SAS

14.05 pm **DR. JONAS FIZET**
(Business Developer)
COMPANY PRESENTATION

14.30 pm **LAB VISIT, IN 2 GROUPS**
IN-VITRO & IN-VIVO LABORATORIES

REPORT

VISIT OF PRESTWICK CHEMICAL & NEUROFIT

On the **2ND OF OCTOBER 2017**, a visit of the CROs Prestwick Chemical and Neurofit took place in Illkirch-Graffenstaden.

PRESTWICK CHEMICAL, founded in 1999 by Professor C.G. Wermuth, is focused on early drug discovery. During the past decade, Prestwick Chemical has gained international recognition for its input to boost drug discovery process through tailor-made medicinal chemistry services (from hit discovery to lead optimization) and smart chemical screening libraries.

Fig. 1

Founded in 1996, **NEUROFIT** is specialised in the evaluation of treatments for central and peripheral nervous system disorders. The CRO offers a comprehensive list of in vitro and in vivo models covering a wide range of indications, in order to facilitate preclinical drug development by proposing the best models.

Fig. 2

The theoretical and technical know-how presented during that day illustrate distinct and complementary aspects of the 2 CROs in drug development.
We would like to express our gratefulness to Marie-Louise Jung (Prestwick chemicals, VP Business Development), DANIELA Verra (Prestwick chemicals, Business development & Market Intelligence), Christophe Morice (Prestwick chemicals, Director of Medicinal Chemistry), Emile Andriambelososon (Neurofit, Head of Research), Jonas Fizet (Neurofit, Business Developer) and Stéphanie Wagner (Neurofit, Neurobiology Group Leader).

P.P.

Figure 1
Prestwick Chemical,
Illkirch-Graffenstaden.

Figure 2
Neurofit,
Illkirch-Graffenstaden,
Circular Open field used
for behavioural
tests in rodents.
Picture: Neurofit.

NEWS

A NEW BOARD MEMBER FOR NEUREX...

Prof Andrew Straw,
Institute of Biology I & BCF,
A.L. University of Freiburg

We would like to welcome Prof Andrew Straw (Institute of Biology I & BCF, Freiburg) who will join the Neurex scientific board from October 2017.
He will take on the tasks of Prof Marlene Bartos who has been a member of the board for many years. Prof Andrew Straw (https://strawlab.org/) arrived in Freiburg in 2016 (see newsletter 30) and heads a lab at the Institute of Biology I where he and his team study neural circuits and behavior, using a Virtual Reality environment for Freely Moving Animals.

P.P.

FOCUS ON PSYCHIATRY

Fundamental and clinical research in psychiatry is very dynamic and complementary in the 3 Neurex universities of Basel, Freiburg and Strasbourg. The Department of Psychiatry and Psychotherapy in Freiburg has appointed a new Medical Director, while a meeting & controversy debate on schizophrenia will take place next November. The aim of these 2 events is to shed light on a very important issue in the field of psychiatry, namely how the classification of psychiatric diseases affects non only clinical practice, but also fundamental research. This question is also at the heart of the scientific issues raised by the Center of Excellence of Psychosis (Strasbourg), and impacts therapy as well. Zoom on these issues in the pages thereafter...

Prof Katharina Domschke,

A new Medical Director was appointed last December in Freiburg at the Department of Psychiatry & Psychotherapy to replace Prof Mathias Berger who recently retired. Katharina Domschke, MA, MD, PhD, is Full Professor of Psychiatry and Chair of the Department of Psychiatry and Psychotherapy, University of Freiburg, Germany, since December 2016.

Prof. Domschke completed her studies in medicine and psychology at the University of Muenster, Germany, and Trinity College Dublin, Ireland (M.D., 2004), as well as Boston University, Boston, MA, USA (M.A., 2002), and Maastricht University, The Netherlands (Ph.D., 2010). After her board certification as a psychiatrist in 2010 she worked as an attending physician and associate professor at the Department of Psychiatry, University of Muenster, Germany. In January 2012, she was appointed Full Professor of Psychiatry at the University of Wuerzburg, Germany, in October 2013 Executive Senior Physician, and in September 2014 Vice Chair of the Department of Psychiatry, Psychosomatics and Psychotherapy, University of Wuerzburg, Germany.

FOCUS ON PSYCHIATRY

DEPARTMENT OF PSYCHIATRY AND PSYCHOTHERAPY IN FREIBURG: A NEW MEDICAL DIRECTOR APPOINTED

Prof. Domschke's clinical focus is on diagnostics and therapy in adult psychiatry, particularly depression, anxiety disorders, stress-related disorders and obsessive-compulsive disorder.

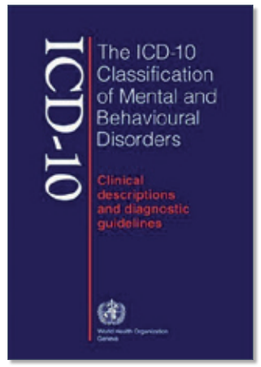
Her research focus is on the identification of multilevel markers for the prediction, prevention and personalized treatment of mental disorders, particularly anxiety disorders and depression. Anxiety disorders and depression are among the most frequent mental disorders worldwide and confer a high socioeconomic burden. Twin studies indicate a considerable heritability of these disorders with contributions from several different genes, which interact with each other as well as with environmental and psychosocial factors in shaping the overall disease risk. Epigenetic mechanisms such as DNA methylation constitute a dynamic link between genes and the environment and have become a central focus in psychiatric research. Therefore, Prof. Domschke's group investigates the role of genetic and epigenetic markers as well as their interactions with environmental factors in the development, prevention and treatment of mental disorders by applying genetic/epigenetic, imaging genetic, pharmaco(epi)genetic and therapy(epi)genetic approaches, as reflected by to date over 170 publications in international journals, one co-edited book, and 16 book chapters.

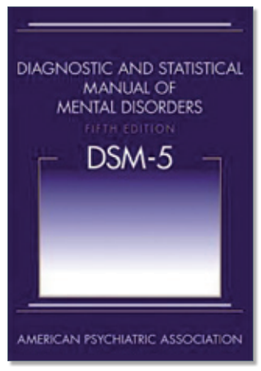
Her work has been recognized by e.g. the Research Award of the World Federation of Societies of Biological Psychiatry (WFSBP), the Fellowship Award of the World Psychiatric Association (WPA), the Travel Award of the International Society of Psychiatric Genetics (ISPG), the Fellowship Award of the European College of Neuropsychopharmacology (ECNP), the Research Award of the German Society of Biological Psychiatry (DGBP), the Research Award of the German Society of Psychiatry, Psychotherapy and Neurology (DGPPN), the Research Award of the German Association of Women in Medicine (DÄB), the Ingrid-zu-Solms Research Award and a Membership in the Young Academy of the National Academy of Sciences Leopoldina. Prof. Domschke has received funding from the EU, the German Research Foundation (DFG) and the German Ministry of Research and Education (BMBF) to the amount of ~€ 4.2 Mio. She is a full member of the American College of Neuropsychopharmacology (ACNP), the European College of Neuropsychopharmacology (ECNP), the Society of Biological Psychiatry (SOBP), the International Society of Psychiatric Genetics (ISPG), the German Society of Biological Psychiatry (DGBP), the German Society of Psychiatry, Psychotherapy and Neurology (DGPPN) and secretary of the German Society of Anxiety Research (GAF).

Prof. Domschke serves on the editorial boards of the International Journal of Neuropsychopharmacology, PLoS ONE, Pharmacopsychiatry, Progress in Neuropsychopharmacology & Biological Psychiatry, World Journal of Biological Psychiatry, International Journal of Methods in Psychiatric Research, Acta Neuropsychiatrica and Frontiers in Molecular Psychiatry and is a regular reviewer for over 50 SCI-listed international journals.

K.D.

COMING EVENTS





FOCUS ON PSYCHIATRY

CLASSIFICATION OF PSYCHIATRIC DISEASE: DIFFICULTIES, PITFALLS AND IMPACT ON CLINICAL DIAGNOSIS, THERAPY & RESEARCH APPROACHES

The international classification tools currently designated as standards in psychiatry, namely the **ICD 10** (International Classification of Diseases, 10th edition) and **DSM 5** (Diagnostic and Statistical Manual of Mental Disorders, 5th edition) have a long evolutional history. The triggering event for developing an International Classification of Diseases was the great exhibition held in London in 1851, where many nations engendered the idea of systematically reviewing subjects that could be candidates for international statistical comparison, leading to the first International List of Causes of Death; the sixth revision (ICD-6), published in 1949, was carried out by the WHO: its scope expanded to explicitly apply to morbidity as well as mortality. ICD-6 contained the first attempt of classification of mental disorders (Moriyama 2011).

With the large-scale involvement of US psychiatrists in the selection and treatment of soldiers during the World War II, the focus was shifted away from mental institutions and traditional clinical perspectives. This led to a need of developing a classification of mental disorders for use specifically in the United States and to standardize confused usage of different documents. This task was attributed to a committee of the APA (American Psychiatry Association) on Nomenclature and Statistics produced the DSM (I), first published in 1952.

In the first versions of ICD (ICD 6 & 7) and DSM (DSM 1 & 2), international nosography in psychiatry was based on etiological principles of psychanalysis, a concept which was later considered to be too vague for the reliability of diagnosis. In order to improve the reproducibility of a classification between observers, but also by the same observer at 2 different moments, Carl Hempel proposed in 1959 to "operationalize" definitions, by equating disorders with the result of an operation (Foucher and Bennouna Greene 2010). For example, with at least a number n of symptoms present for a duration d, and if symptoms x & y are absent, this defines a resulting diagnosis D. A further refinement was proposed by Lewis who was then hoping to obtain a better "scientific" approach by keeping only the descriptive part and removing any theoretical influence. This move aimed at avoiding bias due to a lack of reliability between observers. It however resulted in the exclusion of all the symptoms suspected of a potential low inter-observer reliability, as well as of rare symptoms. Moreover, apparently similar symptoms - despite an obvious distinct cause- were not differentiated anymore. As an example, in the field of psychosis, this led to the broad acceptance of the widely recognized dichotomy between mood disorders and schizophrenia. This overwhelming simplification had some clinical usefulness in terms of reproducibility and practice (helping psychiatrists in the process of decision-making). Unfortunately, one dramatic side-effect, suggested by many clinicians today, is that its use precludes any significant progress in psychiatry research.

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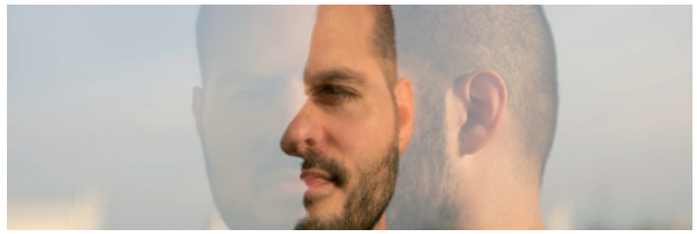
FOCUS ON PSYCHIATRY



Indeed, if a disease is characterized by symptoms, this level of classification is not adapted to validate a scientific model. For example, a headache or a fever are not sufficient to define a disease, they are one of the features of many different diseases. A disease is better defined either by its cause (for example the mutation of the CFTR gene in cystic fibrosis) or by its pathophysiology (for example a loss of motoneurons in ALS). Such hypothetical models may be conceptualized and verified: then, the task of research consists of assessing and refining the model, and suggest adapted treatments. The refinement of the model itself influences in turn the definition of the disease and such cycle of optimization contributes in validating the model. (Foucher and Bennouna Greene 2010). However, for purposes or reproducibility, no change in the classification of the ICD 10 & DSM 5 diagnostic tools in psychiatry is tolerated (be it due to self-censorship or to concerns of not being able to publish). If the definition of the disorder(s) is inappropriate, and if it can't evolve theoretically, how good can be the basis for fundamental research Such a rigid system may well constitute a dead-end in terms of research ?

In the field of psychotic disorders, this problem is at the heart
of a debate that increasingly affects the concept of schizophrenia:
WILL WE STILL CALL IT SCHIZOPHRENIA IN 100 YEARS ?

Why ? Why not ?
Such question will be addressed during a controversy event held on
MONDAY, THE 27TH OF NOVEMBER 2017,
at the Department for Psychiatry & Psychotherapy (University of Freiburg).

This debate will follow a meeting entitled "The beginning & end of schizophrenia: does neuropsychiatry terminate the era of schizophrenia?". During these events, the speakers will discuss and present arguments explaining why and how diagnosis is so important in the field of schizophrenia, not only for clinic, but also for scientific research.
Psychiatric disorders are at the heart of Prof Ludger Tebartz van Elst and Dr Jack Foucher's interests. They detail in the following pages (see page 18 & page 24) their respective approaches and corresponding scientific rationale. This field of psychiatry is another example of common and complementary expertise, a real added-value that is also available to Neurex members using the multimedia platform. There, the interested readers may refer to (beginner & advanced level) lectures of the CEP (Circle of Excellence on Psychosis, see page 24), as well as movies of these 2 events, for further information.

P.P.

NEWS
ZOOM ON

FOCUS ON PSYCHIATRY

PROF TEBARTZ VAN ELST & FREIBURG RESEARCH GROUP FOR DEVELOPMENTAL DISORDERS

**Prof
Ludger
Tebartz van Elst,**
*Department of Psychiatry
& Psychotherapy, Freiburg.*

At the University of Freiburg over the last decade a joint research group in collaboration between child adolescent and adult psychiatry and psychotherapy has been generated. The work of this research group follows the insight that many psychiatric disorders – even though their prominent onset is in adult life – have their roots in the first and second decade of the development of affected people. Prominent examples for this constellation are patients with ADHD, autism, tic disorders but also patients with schizophreniform and personality disorders. The research group headed by Prof. Dr. Ludger Tebartz van Elst follows this insight and tries to disentangle the different causal roots and pathways that might lead to primary neurodevelopmental and personality disorders and sometimes secondary psychiatric syndromes in adult life *(Tebartz van Elst et al. 2013, see bibliography at the end of this article).*

The idea that psychiatric diagnoses like autism, ADHD, depression or schizophrenia do not represent true disease categories but rather are umbrella terms mainly focused on psychopathological syndromes (Tebartz van Elst et al. 2006, Tebartz van Elst 2016, 2017) have led to different clinical but also MRI based and laboratory based research projects trying to disentangle the different causal and pathogenetic roots and pathways that may lead to the psychopathological syndrome (i.e. psychiatric disorder in question) of interest *(Francis et al. 2013, Kanat et al. 2015, Kaller et al. 2014, Maier et al. 2016, Olbrich et al. 2008, Rüsch et al. 2007, 2008, Tebartz van Elst et al. 2005, 2013, 2014a/b).*

The different research endeavors of the Freiburg research groups can be grouped in clinical and technological projects. The clinical projects focus on a psychopathological differentiation of given psychiatric syndromes in that the issue of neurodevelopmental disorders has been developed and elaborated on.

A first main project was the discovery of the relevance of the neurodevelopmental disorder **ADHD** for subsequent secondary psychiatric disorders in the late 1990's (Philipsen et al. 2015). A further main effort into that direction was a creation of an **autism** project looking at the prevalence and relevance in particular of high functioning autism for the subsequent development of psychiatric disorders like depression, anxiety, OCD, personality disorder and psychosis (Tebartz van Elst et al. 2013; https://www.uniklinik-freiburg.de/psych/klinische-schwerpunkte/asperger-autismus.html). Presently the same idea is being realized in generating a focus on the third big group of neurodevelopmental disorders i.e. the **tic disorders**.

A main insight from these clinically focused projects is that in many cases adult depression, anxiety disorders, personality disorder or psychotic disorder developed on the background of clearly recognizable but sometimes also subsyndromal developmental disorders specificity ADHD, autism or tic disorders (Tebartz van Elst 2016). This insight leads to a clinical and psychopathological differentiation of the present psychiatric nosology

where syndromal or subsyndromal neurodevelopmental disorders or personality patterns are recognized as relevant causal entities for subsequent depressive or psychotic reactions, personality abnormalities or anxiety disorders.

Over the last decade a new internal concept of classification of these different neurodevelopmental disorders has evolved in which primary and secondary disorders are being distinguished (i.e. primary vs. secondary ADHD, primary vs. secondary autism, primary vs. secondary psychosis) based on specific etiological and pathogenetic considerations in each case *(Tebartz van Elst 2017).*

In this concept secondary disorder is being diagnosed in case of clearly recognizable or at least probable etiopathogenetic causes for the syndrome of interest. For example a fragile-X syndrome or a 22q11 syndrome might by a secondary genetic cause for autism, ADHD or psychosis. Secondary acquired causes are recognized in form of inflammatory brain disease, epileptic or paraepileptic disorders or metabolic diseases like Niemann pick C disease or acute intermittent porphyria.

On the other hand many patients with autism, ADHD or psychotic disorder do not have any evidence of secondary genesis of their clinical syndrome of interest but still there is a clearly positive family history. This is the typical constellation of a primary disorder with a common, generally multi genetic vulnerability to develop the syndrome of interest like psychosis, autism or ADHD. In this area of primary, multigenetic causation of psychiatric vulnerability there is often a dimensional rather than categorical phenotypical pattern with more or less severely affected phenotypes and common subsyndromal variants in affected families *(Tebartz van Elst 2016, 2017).*

Within this theoretical framework the Freiburg Center for Neurodevelopmental Disorders tries to disentangle the different etiologies and pathogenesis of the different neurodevelopmental syndrome of interest in the context of several clinical and basic science research projects.

1. AUTISM SPECTRUM DISORDER

Since 2004, one subgroup of the research cluster focuses on the neurodevelopmental category of autism spectrum disorder. Over the last 13 years, we recognized that autism is a common basic disorder based on which secondary depression, anxiety, personality or psychotic disorder arises (Ebert et al. 2013; Riedel et al. 2016; Tebartz van Elst 2016). The recognition of high functioning and sometimes subsyndromal autism as the critical background for the subsequent development of other psychiatric syndromes often turns out to be a key concept for the understanding and acceptance of the patients' symptom history. Different neurobiological research projects looking at brain structure, brain connectivity and brain neurochemistry as well as EEG and laboratory studies have

NEWS
ZOOM ON

FOCUS ON PSYCHIATRY
PROF TEBARTZ VAN ELST & FREIBURG RESEARCH GROUP FOR DEVELOPMENTAL DISORDERS

endeavored to identify specific neurobiological features distinguishing autism spectrum disorders from other neurodevelopmental disorders like ADHD and healthy controls *(Riedel et al., Kanat, et al. 2015, Kaller et al. 2014, Maier et al. 2015, Riedel et al. 2014, Tebartz van Elst et al. 2014a/b, Endres et al. 2017).*

2. ADHD IN ADULTHOOD

In a structurally very similar project, the relevance of ADHD in adulthood has been a focus of another subgroup in Freiburg already since 1998. Like in autism, specific group psychotherapy projects had been developed and evaluated along with companying neurobiological research focusing on brain imaging *(Ahrends et al. 2011, Maier et al. 2015, Perlov et al. 2008, 2009, Philipsen et al. 2015, Wilbertz et al. 2012).*

3. SCHIZOPHRENIA AS A LATE ONSET NEURODEVELOPMENTAL DISORDER

Over the last 10 years, it became increasingly clear that there is a yet to be understood link between the different classical neurodevelopmental disorders like autism, ADHD and tic disorders and the group of psychotic disorders still being called schizophrenia. In an attempt to disentangle the different neurobiological causes and pathways behind the different schizophreniform syndromes, another subgroup of the Freiburg Research cluster has focused on the role of immunological processes such as limbic encephalitis or immunological encephalopathy (Hashimoto encephalopathy for example) in causing schizophreniform syndromes. In this context many different studies again focusing on brain imaging but also CSF research has been organized over the last years. Most importantly we were able to illustrate that at least on a single case level there are in fact quite a few patients who until recently would have been diagnosed as suffering from schizophrenia but now turn out to suffer from immunological encephalopathy, which can be treated more causally with immune modulatory interventions like cortisone, plasma exchange, IV-IGG or Rituximap *(Endres et al. 2015a/b, 2017a/b).*

In trying to differentiate the psychopathology and neurobiology of the different psychiatric umbrella diagnoses (depression, schizophrenia, autism, ADHD etc.), the Freiburg research groups concentrate on a few methodological techniques:

1. MOLECULAR BRAIN IMAGING:

In our molecular brain imaging studies, we focused on the neuroanatomy, connectivity and neurochemistry of the brain in groups of patients with autism, schizophrenia, ADHD and borderline personality disorder. A particularly important technological development in this context is the recently developed ability to not only measure the main excitatory neurotransmitter signal glutamate (*Olbrich et al. 2008, Tebartz van Elst et al. 2005, 2014a/b*), but also the main inhibitory neurotransmitter signal, GABA and gluthathione, using MR spectroscopy (MRS) (*Endres et al. 2017*). The advantage of this technology is that it now allows the non invasive assessment of the brains neurochemistry in vivo without employing radiation.

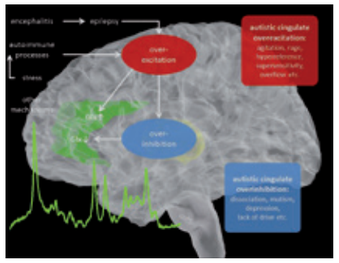
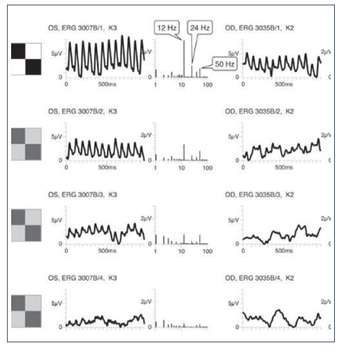
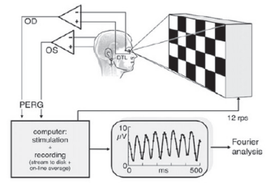


Figure 1
Glutamate signal abnormalities as assessed using magnetic resonance spectroscopy may explain different psychopathological phenomena in the context of autism spectrum disorder *(Tebartz van Elst et al. 2014a/b).*

Figure 2
Illustration of the normalisation of the pattern electroretinogram following therapy in a patient with depressive disorder *(Bubl et al. 2011, 2012)*





2. VISUAL NEUROSCIENCE:

Another technique which has been focused on a lot in another subgroup of the Freiburg research cluster is visual neuroscience. In this context we measure the electroretinogram (ERG) a kind of ECG of the eye in order to obtain objective signals of the neuronal network layer of the retina in different psychiatric disorders like depression, ADHD, autism and schizophreniform disorders. In this context we were able to demonstrate specific objective correlates of patients with depression (reduced contrast gain), ADHD (increased retinal noise) and also schizophrenia. The advantage of measuring the retina electrophysiology is that it allows an objective assessment of the neurophysiology of the retina, which can be regarded as an outpost structure of the brain which might indicate systemic network dysfunction *(Bubl et al. 10, 2012, 2013, 2015a/b, Tebartz van Elst et al. 2015).*

The overarching aim of the different research endeavors of the different research groups headed by Ludger Tebartz van Elst is to clinically and neurobiologically differentiate the present psychiatric diagnostic umbrella terms in form of the given psychiatric ICD diagnoses. By differentiating the psychiatric nosology and pathophysiology we hope to contribute to generating more specific and adequate psychiatric diagnoses and subsequent therapies.

L.T.v.E.

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NEWS
ZOOM ON

FOCUS ON PSYCHIATRY

DR JACK FOUCHER (UNIVERSITY OF STRASBOURG) & RESEARCH ON PSYCHOSIS AT CEP, CEMNIS & AXILUM ROBOTICS

Dr Jack Foucher,
University Hospital Strasbourg, CEP, CEMNIS & Axilum Robotics

Dr Jack Foucher is an associate professor and neuropsychiatrist at the university of Strasbourg. He was first trained in neurology and later in psychiatry, getting specialized in mood and psychotic disorders. Considering the poor pathophysiological foundation of neuropsychiatric disorders, he developed his research along two mainstreams: a fundamental stream of research on naturally funded phenotypes and a practical stream with the development of personalized neuropsychiatric therapies with a special interest in repetitive transcranial magnetic stimulation (rTMS).

On the fundamental side, he turned towards the naturally defined phenotypes proposed by the Wernicke-Kleist-Leonhard School. Those have been elaborated on diachronic observations, based on natural principles such as the longitudinal principle, i.e. one patient is assigned to one phenotype only and the family aggregation principle, i.e. in multiplex families, affected individuals are sharing the same phenotype. Their impressive reliability, predictive and differential validity already made them attractive, but he was further convinced by using them in his clinical practice as an expert in the schizophrenia reference center of Strasbourg. He founded a web site, the CEP, "Cercle d'Excellence sur les Psychoses" (http://www.cercle-d-excellence-psy.org), developed an e-learning based teaching for and organizes symposia with his colleagues to diffuse this powerful clinical tool in France. He also conducted recent anatomical and functional imaging studies supporting the superiority of those phenotypes relative to the classical single schizophrenia concept and proposing pathophysiological basis for some of them.

On the applied side, he first developed reliable imaging and analysis procedures to determine the functional basis of symptoms in a single subject approach. Secondly, he tried to correct these functional abnormalities with rTMS. Although the approach was successful, the manual placement of the coil was too exhausting for being applied in clinical setting. He thus initiated the development of a robotic positioning device, which has now reached the market with the creation of a spin off, Axilum Robotics (see Neurex Newsletter 29). While pursuing the validation of personalized rTMS protocol for psychosis and depression, he more recently opened the CEMNIS, the Noninvasive Neuromodulation Center of Strasbourg, which concretized a decade of applied research in proposing personalized therapies in clinical settings.

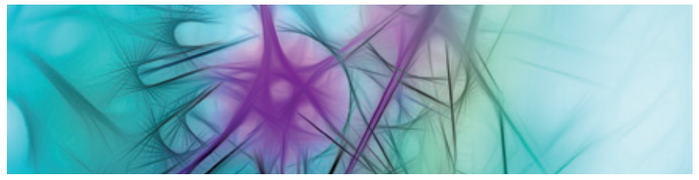
With the CEMNIS, Jack Foucher ambitions to fuse his two streams of research. An example of this is given by the recent development of specific rTMS treatments for two psychotic phenotypes, i.e. periodic catatonia and cataphasia. In case of success, the fundamental distinction between these two phenotypes will not only be validated switching their status towards classical diseases, but this would also pave the way for a new generation of targeted therapies based on their pathophysiological basis.

J.F.

The CEMNIS
(Center of Non Invasive Neuro-Modulation of Strasbourg) is a care unit of Strasbourg university hospital dedicated to the treatment of neuropsychiatric disorders –resistant to conventional therapies– using neuromodulation techniques.

FOCUS ON PSYCHIATRY

THE GUT BRAIN AXIS



The gut brain[1] axis is a complex system that integrates (in a bottom-up and top-down direction) information from the brain, sympathetic, parasympathetic & enteric nervous system (ENS), gut, microbiota (the collection of microorganisms that inhabit the gastrointestinal tract) and immune system. Disturbances of the gut brain axis have been suggested to play a role in a wide range of disorders, including mood disorders, but also neurodegenerative and auto-immune diseases.

Co-morbid gut dysfunctions frequently occur in individuals with Autism Spectrum Disorder (ASD), schizophrenia, anorexia, anxiety, depression, Parkinson's Disease (PD) and Multiple Sclerosis (MS). Distinctive gut microbes have been identified in ASD-affected children and a breakdown of the intestinal barrier (leaky gut) has been shown in IBS, ASD or depression. Enteric microbiota play a role in early programming, but also later response to acute and chronic stress, an important parameter in neuropsychiatric conditions, such as depression, ASD or schizophrenia. Stress is one top-down mechanism that may affect gut microbiota: moreover, stress has been reported to be one of the factors that may be associated to the occurrence of a psychotic episode or development of MS (like in the two-hit hypothesis). Mice devoid of all commensal gut flora have dramatically attenuated susceptibility to Experimental Autoimmune Encephalomyelitis (EAE), a mouse model of human MS. A low-grade inflammatory state which has been suggested to stem from processes related to dysbiosis of the gut microbiome is prevalent in a subset of individuals with schizophrenia and bipolar disorder. In patients with PD, gastrointestinal motility dysfunction often precedes the onset of motor symptoms by many years and Lewy bodies, the typical α–synuclein positive inclusions present in PD brain, have also been found in neurons of the myenteric plexus and dorsal motor nucleus of the vagus, suggesting that the underlying pathological process might involve the autonomic nervous system. In Alzheimer's Disease, epidemiologial studies have reported a link between cognitive decline and infections to Helicobacter Pylori.

The bacterial commensals deeply influence many aspects of host physiology –including nutrient metabolism, resistance to infection and immune system development– through a bi-directional communication network with the brain. This bi-directional system is made up of **neural** pathways, such as the enteric nervous system (ENS), vagus, sympathetic and spinal nerves, and of **humoral** pathways, which include signaling cytokines, hormones, and neuropeptides.

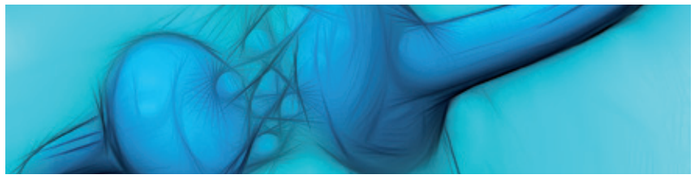
90% of vagal fibres between the gut and brain are afferents to the brain: interestingly, it has been suggested that nerves that interconnect the ENS and CNS could also be conduits for disease spread.

1 / A revised nomenclature has been proposed to use the more inclusive terms "brain-gut-enteric microbiota axis".

NEWS
ZOOM ON

FOCUS ON PSYCHIATRY

THE GUT BRAIN AXIS



Thus, viruses have been shown to be retrogradely transported from the ENS into the brain using peripheral nerves pathways. The neurotropic pathogen varicella zoster virus (VZV) is able to enter into a latent state in enteric and autonomic neurons. VZV reactivation in these neurons is a clandestine cause of gastrointestinal disease, meningitis and stroke. A trans-synaptic cell to cell transfer of pathogens underlies the Braak's hypothesis of PD which states that some pathological process might originate in the gut and spread to the substantia nigra. However, neural pathways also play an important role in restoring homeostasis by regulating immunity and inflammation. Thus, the vagus and splenic nerves – activated by inflammatory peripheral signals – are able to mount an anti-inflammatory reflex response which modulates both the innate and adaptive arms of the immune system. During an infection episode with pathogenic Salmonella, catecholaminergic signaling to the small intestine – indirectly triggered by the activation of vagus afferent neurons – drives an anti-inflammatory program in muscularis macrophages.

Contrary to the traditional view that the brain is immunologically privileged, evidence has accumulated over the last two decades that systemic inflammation can exert a profound influence on the brain, leading to changes in mood, cognition and behaviour, through a number of pathways. The humoral pathway involves the delivery of products of microbiote metabolism (such as short-chain fatty acids (SCFA)), Pathogen-Associated Molecular Patterns (PAMPs) & Damage-Associated Molecular Patterns (DAMPS), or immune molecules directed at them – such as cytokines – from a peripheral (gut, for example) site directly to the brain. Several mechanisms may then contribute to the diffusion of the signal into the brain: an active transport of signalling molecules across the blood-brain barrier (BBB), a volume diffusion into the brain or direct contact with brain parenchymal cells at the choroid plexus (CP) and circumventricular organs that lie outside the BBB. These phenomena transpose the peripheral signal into a central neuroinflammatory response that mirrors the response at the periphery, but may last much longer. Such neuroinflammation has been suggested to play a potential role in the chain of events involved in neurodegenerative disorders. Interestingly, a substantial influence of host microbiota on microglia homeostasis has been reported in an animal model (germ-free mice). Microbiota-derived bacterial fermentation products, the SCFA, have been shown to underlie the modulation of the microglia phenotype.

What are the main pathways which underlie the birectional communication between the gut environment & brain? Why are gastrointestinal-co-morbidities so frequent in some psychiatric and neurological disorders? Are gut dysfunctions an epiphenomenon or are they clearly involved in the aetiopathegenesis of these disorders? How much do these mechanisms prevail and potentially account for the development of these diseases? How might the gut brain axis be targeted to develop potential therapies for the treatment of these diseases?

A **workshop** held on the **23RD OF OCTOBER 2017** in Basel (Museum Kleines Klingental, Unterer Rheinweg 26) will address these questions and summarize the therapeutic perspectives for the treatment of gut-brain related Nervous System disorders. We would like to express our gratefulness to all scientists who kindly agreed to participate in this program and are looking forward to meeting you there !

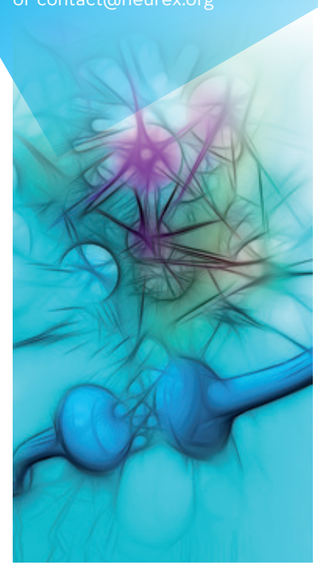
P.P.

NEUREX WORKSHOP

OCTOBER
> 23RD 2017

VENUE / **BASEL**
> Museum Kleines Klingental, Unterer Rheinweg 26

REGISTRATION & MORE INFO /
www.neurex.org
or contact@neurex.org



Project "Trinational NeuroCampus" - Program Interreg V Upper Rhine «Transcending borders with every project», Neurex, CNRS, INSERM, Université de Strasbourg, Région Grand Est, Département du Bas-Rhin, Département du Haut-Rhin, Eurométropole Strasbourg, Hôpitaux Universitaires de Strasbourg, Bernstein Center Freiburg, Klinik für Psychiatrie und Psychotherapie Freiburg, Neurozentrum Freiburg, Universität Freiburg, Universität Basel, Universitäre Psychiatrische Kliniken Basel, Kanton Basel-Stadt, Kanton Basel-Landschaft, Confédération suisse.

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THE GUT BRAIN AXIS & CNS DISORDERS

(RE)-VISITING (PATHO)PHYSIOLOGICAL MECHANISMS

Organizer **Pascale Piguet** (Neurex, Basel)

>>> Monday, October 23RD

08.45 - 09.10 Registration & Welcome Coffee

FIRST SESSION
INVOLVEMENT OF THE MICROBIOTA IN NEUROLOGICAL & PSYCHIATRIC DISORDERS

09.10 - 09.50 **JOHN CRYAN** (Cork, Ireland)
« MICROBIOTA - A KEY PLAYER IN STRESS-RELATED DISORDERS »

09.50 - 10.30 **JAMES ADAMS** (Tempe, Arizona, US)
« EMERGING ROLES OF THE GUT MICROBIOTA IN AUTISM SPECTRUM DISORDER »

10.30 - 11.10 **FILIP SCHEPERJANS** (Helsinki, Finland)
« DO MICROBIOTA PLAY A ROLE IN PARKINSON'S DISEASE ? »

11.10 - 11.40 Coffee break

11.40 - 12.20 **HARTMUT WEKERLE** (Martinsried, Germany)
« TRIGGERING OF AUTOIMMUNE DISEASE BY COMMENSAL GUT BACTERIA : A PATHOGENIC STEP IN THE DEVELOPMENT OF MS ? »

12.20 - 13.00 **GOLAM KHANDAKER** (Cambridge, United Kingdom)
« IMMUNE-TO-BRAIN COMMUNICATION: A ROLE IN SCHIZOPHRENIA ? »

13.00 - 14.30 Lunch break

SECOND SESSION
PATHWAYS INVOLVED IN BIDIRECTIONAL COMMUNICATION IN THE GUT BRAIN AXIS

14.30 - 15.10 **MARCO PRINZ** (Freiburg, Germany)
« HOST MICROBIOTA CONTROL THE FUNCTION OF MICROGLIA IN THE CNS »

15.10 - 15.50 **ROBERT DANTZER** (Houston, Texas, US)
« IMMUNE-TO-BRAIN COMMUNICATION PATHWAYS IN INFLAMMATION-INDUCED SICKNESS BEHAVIOR AND DEPRESSION »

15.50 - 16.30 **ANNE GERSHON** (New-York, New Jersey, US)
« REACTIVATION OF LATENT VIRUSES IN ENTERIC NEURONS & NEUROLOGICAL AND NEUROGASTROLOGICAL DISORDERS: THE EXAMPLE OF VZV »

16.30 - 17.00 Coffee break

17.00 - 17.40 **MICHAEL GERSHON** (New-York, New Jersey, US)
« THE BOWEL AND BEYOND: THE ENTERIC NERVOUS SYSTEM IN NEUROLOGICAL DISORDERS »

17.40 - 18.20 **VALENTIN PAVLOV** (Manhasset, New York, US)
« NEURAL REGULATION OF IMMUNITY: MECHANISMS AND CLINICAL PERSPECTIVES »

COMING EVENTS

BRIDGING PAIN AND DEPRESSION RESEARCH

Mood disorders such as anxiety and depression are recurrent mental illness predicted to become a foremost contributor to the worldwide burden of disease. Among precipitating factors, chronic pain is an important determinant with a prevalence rate around 50% for major depressive disorders . Accordingly, there is an enormous need for fundamental research to progress in the mechanistic understanding of chronic pain and mood disorders comorbidity.

A **meeting** entitled "Bridging Pain And Depression Research" will take place on the **30TH & 31ST OF OCTOBER 2017** in Strasbourg. By gathering outstanding researchers from pain and depression field, this symposium aims at bridging these two research fields.

I. Y.

<<< We would like to express our gratefulness to all scientists who kindly agreed to participate in these programs and are looking forward to meeting you there ! >>>

EARLY SIGNS OF MEMORY DECLINE

A **workshop** entitled"Early Signs of Memory Decline: Object or Place First?" will take place on the **4TH & 5TH OF DECEMBER 2017** in Strasbourg. Co-organized by Dr Chantal Mathis and Dr Céline Héraud, this event is specifically dedicated to the earliest signs of memory impairment in normal aging and Alzheimer's disease. The aim of this workshop is to bring together researchers working on age-related memory decline with specific interests in different types of memory (eg, recognition and spatial memories) in animal models and in humans using a wide range of approaches from behavior to functional imagery.

An open debate is awaited on which form of memory is affected first in normal aging and in pathological aging, and for each condition what are the underlying mechanisms leading to these deficits. In doing so, we hope to increase our knowledge on similarities and differences in initial steps of cognitive decline between the two types of aging. These issues are essential in regard to the development of targeted therapeutic approaches, the identification and validation of early biomarkers specific for each form of cognitive aging and the designing of clinical trials which focus now on the most early stages of Alzheimer's disease.

C.M.

COMING EVENTS

OF GLIA AND MICROGLIA

A broad range of pathological conditions, including brain injury, acute infection, autoimmune disorders, or cancer, is heavily controlled by macroglia and microglia, which makes these cell types a concern of great importance for biomedical research. Macroglia play a major role in the development, function and maintenance of the nervous system. Oligodendrocytes and Schwann glia ensheathe axonal tracts and are crucial for normal impulse conductivity; astrocytes are intimately involved in synaptic transmission, in brain repair and in supporting the blood brain barrier. Microglia, which constitute the resident immune cells of the brain, are derived from a lineage of mesodermal embryonic blood progenitors and migrate into the brain during development. This provides further evidence that, although often regarded as independent, the nervous and the immune systems are intimately intertwined, the connection allowing us to respond and adapt to a continuously changing environment.

Invertebrates also display cells that are commonly called glia and that play similar roles as macroglia during neural function and development, however it is presently not clear at all whether vertebrate and invertebrate cells are truly homologous, i.e., derived from a "macroglial cell" present in a common bilaterian ancestor. Moreover, invertebrate glia accomplish the trophic and protective role of vertebrate macroglia but also the immune role of microglia. In addition, the functional differences observed between invertebrates and vertebrates are accompanied by structural and developmental differences, such as the absence of a compact myelin sheath in invertebrate glia, the glial rather than endothelial nature of the invertebrate blood brain barrier and the lack of a common molecular gliogenic pathway. The latter finding is particularly surprising, given the strong evolutionary conservation of the molecular pathway triggering neuronal differentiation.

These clues point to an intricate network of relationships between glia and blood cells, in terms of development and evolution across different animal taxa. The exact nature of this network is currently unknown, because there exists a large research gap: how similar are glia and blood cells from the molecular and functional standpoints? Furthermore, very little is known about the development of glia and blood cells, and genetic pathways controlling this process, in animal taxa outside the vertebrates and Drosophila. It seems important to get answers to these and many other related questions, and to develop a more complete picture of the shared molecular-genetic pathways active during the development and function of immune and glial cells, in order to improve our capability to manage pathologies affecting the nervous system.

A **meeting** entitled "Of glia and microglia" will take place on the **7TH & 8TH OF DECEMBER 2017** in Strasbourg.

This event is intended to address the existing knowledge gap, by initiating a dialog between scientists at the frontline of research into glia and blood cell biology, in both vertebrate and invertebrate systems. We anticipate that this conference can mark the beginning of a continuing series of similar meetings. The recent finding that microglia arise during vertebrate primitive hematopoiesis and that flies also display primitive and definitive hematopoiesis clearly show that our meeting is particularly timely in addressing the connection and the evolution of the immune and nervous systems. We predict that new insights and hypotheses will ensue when enabling discourse among a critical mass of scientists with an expert knowledge of glial and blood cell biology, working on diverse model organisms.

A.G.

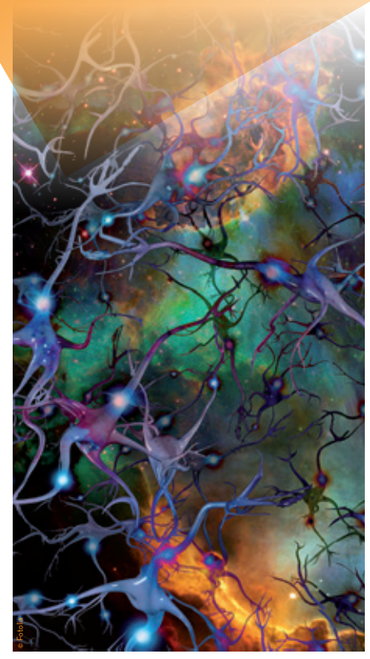
NEUREX MEETING

DECEMBER

› **7TH - 8TH 2017**

VENUE / **STRASBOURG**
› École Doctorale
46, Boulevard de la Victoire

REGISTRATION & MORE INFO
› www.neurex.org
or contact@neurex.org



European Regional Development Fund

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NeuroCampus

OF GLIA AND MICROGLIA

Organizers **Angela Giangrande, Volker Hartenstein & Pascale Piguet**

>>> Thursday, December 7TH

09.40 - 10.00 Introduction
10.00 - 11.00 Keynote lecture: **HELMUT KETTENMANN**
11.00 - 11.30 Coffee break

FIRST SESSION
"MICROGLIA AND BLOOD: ORIGIN AND DEVELOPMENT IN VERTEBRATES AND DROSOPHILA"

11.30 - 12.00 **ELISA GOMEZ PERDIGUERO** (Paris, France)
12.00 - 12.30 **PHILIPPE HERBOMEL** (Paris, France)
12.30 - 13.00 **KATJA BRUECKNER** (San Francisco, CA, USA)
13.00 - 14.30 Lunch break

14.30 - 15.00 **MARCO PRINZ** (Freiburg, Germany)
15.00 - 15.30 **SONIA GAREL** (Paris, France)
15.30 - 16.00 **TAPIO HEINO** (Helsinki, Finland)
16.00 - 16.30 **ANGELA GIANGRANDE** (Strasbourg, France)
16.30 - 17.00 Coffee break

SECOND SESSION
"GLIA: DEVELOPMENT AND FUNCTION"

17.00 - 17.30 **MAGDALENA GOETZ** (Münich, Germany)
17.30 - 18.00 **NATHALIE ROUACH** (Paris, France)
19.00 Dinner

>>> Friday, December 8TH

09.00 - 10.00 Keynote lecture: **DETLEV ARENDT**

SECOND SESSION (Continued)

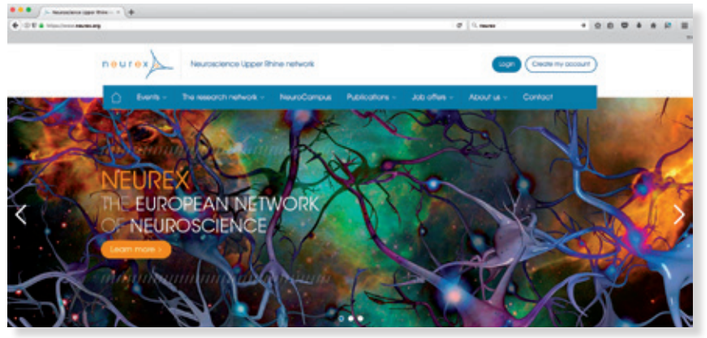
10.00 - 10.30 **WILLIAM STEVE TALBOT** (Stanford, CA, USA)
10.30 - 11.00 **CHRISTIAN KLÄMBT** (Münster, Germany)
11.00 - 11.30 Coffee break
11.30 - 12.00 **BENJAMIN ALTENHEIN** (Mainz, Germany)
12.00 - 12.30 **ESTEE KURANT** (Technion, Israel)
12.30 - 13.00 **ALICIA HIDALGO** (Birmingham, UK)
13.00 - 14.30 Lunch break

THIRD SESSION
"EVOLUTION: GLIA IN INVERTEBRATE PHYLA"

14.30 - 15.00 **DAN HARTLINE** (Manoa, Hawai)
15.00 - 15.30 **MARIOS CHATZIGEORGIOU** (Bergen, Norway)
15.30 - 16.00 **GARCIA- ARRARÁS** (Rio Piedras, Porto Rico)
16.00 - 16.30 Coffee break
16.30 - 17.00 **CHRISTOPHE LEFEBVRE** (Lille, France)
17.00 - 17.30 **VOLKER HARTENSTEIN** (Los Angeles, CA, USA)

REPORT

A NEW WEBSITE FOR NEUREX



Now it's better-looking

At last !

Much more pratical

The positive feedbacks on the new Neurex website witness the fact that our network deserved an embellished showcase, pleasant to the eye and easy to browse through. Launched last July 19th, the website displays the well-known presentation of the **Events to come**, and features several other important novelties.

THE RESEARCH NETWORK

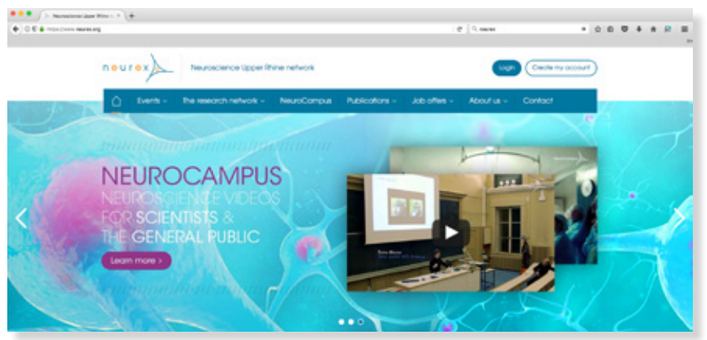
All the laboratories and team leaders of the Neurex network are accessible within a few clicks, sorted by:

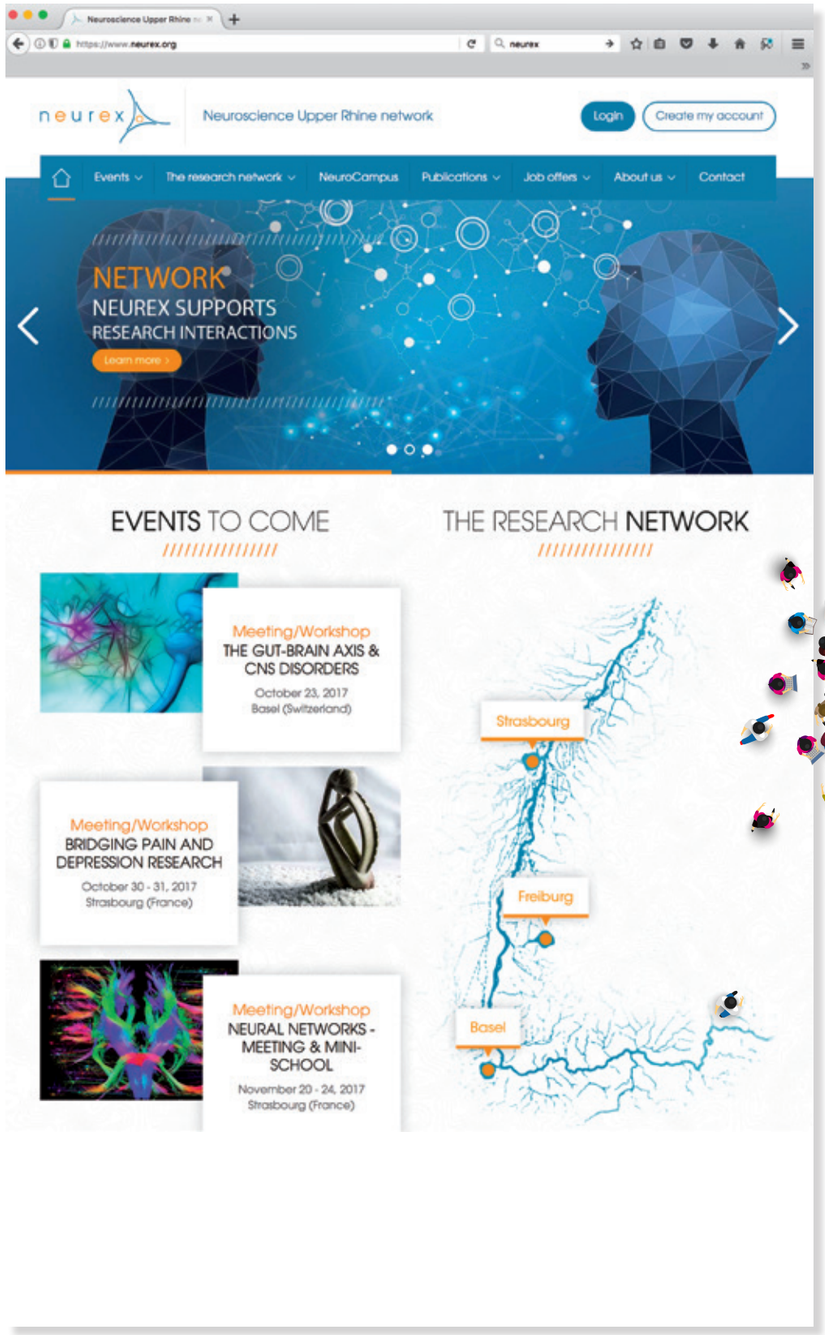
- CITY : all the laboratories of Strasbourg, Freiburg and Basel at a glance
- TOPIC : find the teams working on a specific research thematic, with up to three degrees for the refining of your search

N.B.: if you are not satisfied with the lab/PI pictures displayed, do not hesitate to send us better ones at **contact@neurex.org**.

NEUROCAMPUS

The ongoing Neurex project, NeuroCampus, aims to make accessible to our members the scientific activities happening in the network: conferences, workshops, controversies, lab tours... This requires a **multimedia platform**, which ables us to present all kinds of pedagogical supports (written documents, photos and videos), classified by general thematics.





REPORT

JOB OFFERS

A **job market** section is available for all those who wish to post the description of a position available in our network or beyond.
The offers can be both posted and consulted by any researchers/students within and outside the Neurex network.

Having a Neurex account is the only condition to get access to all our activities and archives.

Alas, the redesign of the website had its drawback: the deletion of all the previous accounts.

Therefore, you must Create your account

de novo, through the appropriate tab on the top right corner.
Legend says it only takes 1 min...

L.N.

REPORT

NEUREX PHD FELLOWSHIPS 2017

During the past decade, Neurex has always worked toward implementation of cross-border collaboration research projects. To help further the development of Neurosciences within the Eucor Eurocampus, the University of Strasbourg supports our network and funded co-tutelle PhD fellowships along its Initiative of Excellence (IdEx) for the period 2017-2020. Early 2017, a call for collaborative projects was launched and Scientific Committee of Neurex selected two of them.

NEURAL PROCESSING OF AMBIGUITY IN PATIENTS WITH AUTISM AND SCHIZOPHRENIA SPECTRUM DISORDERS AND HEALTHY CONTROLS

This project is a collaboration of the following researchers: Dr Anne Giersch (Inserm U1114, University of Strasbourg), PD Dr. Jürgen Kornmeier (Institute for Frontier Areas of Psychology and Mental Health; Department of Psychiatry and Psychotherapy, Medical Center, University of Freiburg) and Prof. Dr. Ludger Tebartz van Elst (Department of Psychiatry and Psychotherapy, Medical Center, University of Freiburg).

ELLEN JOOS, doctoral fellow.
To work on this project, the partner scientists have recruited Ellen Joos, a German citizen with a Master of Biology and experience in EEG techniques, memory and visual perception. The project aims at studying neural correlates of stable and unstable visual perception in normal controls and psychiatric patients.

COMPUTATIONAL MODELING OF THE NEURAL NETWORK DYNAMICS AND SYNAPTIC PLASTICITY IN NON-INVASIVE BRAIN STIMULATION

This project is a collaboration of the following researchers: Ipek Yalcin (INCI, University of Strasbourg), Stefan Rotter (BCF, Faculty of Biology, University of Freiburg) and Claus Normann (Department of Psychiatry, Medical Center, University of Freiburg).

HAN LU, doctoral fellow.
Han Lu, a former student of the Joint Master in Neuroscience, with a Bachelor degree of Psychology from China has been selected by the partners and offered the 3-year fellowship to work on this project.

We wish them both a lot of success with their respective projects!

D.B.

COMING EVENTS

OCTOBER 2017

23RD / NEUREX MEETING
«THE BRAIN-GUT AXIS & CNS DISORDERS»
BASEL, SWITZERLAND

30TH – 31ST / NEUREX MEETING
«BRIDGING PAIN
AND DEPRESSION RESEARCH»
STRASBOURG, FRANCE

NOVEMBER 2017

11TH – 15TH / ANNUAL MEETING
SOCIETY FOR NEUROSCIENCE
WASHINGTON DC, USA

20TH – 22ND / NEUREX-NEURALNET
MINI-SCHOOL
«PYTHON PROGRAMMING,
DATA ANALYSIS AND MODELLING»
STRASBOURG, FRANCE

22TH – 24TH / NEUREX-NEURALNET
MEETING
«ON TECHNICAL AND CONCEPTUAL
ADVANCES FOR THE STUDY
OF NEURAL NETWORKS»
STRASBOURG, FRANCE

27TH / NEUREX MEETING
«THE BEGINNING AND END OF SCHIZOPHRENIA: DOES NEUROPSYCHIATRY TERMINATE THE ERA OF SCHIZOPHRENIA?»
FREIBURG I. BR., GERMANY

27TH / NEUREX CONTROVERSY DEBATE
«WILL WE STILL CALL
SCHIZOPHRENIA IN 100 YEARS?»
FREIBURG I. BR., GERMANY

DECEMBER 2017

4TH – 5TH / NEUREX MEETING
«EARLY SIGNS OF MEMORY DECLINE»
STRASBOURG, FRANCE

6TH / NEUREX WORKSHOP
«NEUROIMMUNOLOGY»
STRASBOURG, FRANCE

7TH – 8TH / NEUREX MEETING
«OF GLIA AND MICROGLIA»
STRASBOURG, FRANCE

FEBRUARY 2018

2ND, NNB MEETING
«BENCH TO BEDSIDE»
BASEL, SWITZERLAND

13TH – 14TH / NEUREX MEETING
«OXYTOCIN THE NEW LOVE POTION?»
STRASBOURG, FRANCE

SPRING-SUMMER 2018 NEUREX MEETINGS

«ARCUATE NUCLEUS»
STRASBOURG, FRANCE

«STEM CELLS»
BASEL, SWITZERLAND

«ARTIFICIAL INTELLIGENCE»
FREIBURG I. BR., GERMANY

«PARKINSON»
BASEL, SWITZERLAND

«COGNITION & THALAMUS»
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.

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 refer to **www.neurex.org** (tab: The research network).

- **NEUROPÔLE**
  http://neuropole.u-strasbg.fr/
- **NEURAG**
  http://www.neurag.uni-freiburg.de
- **NNB**
  http://www.neuronetwork.unibas.ch

NEWSLETTER

- **UNIBASEL**
  http://www.unibas.ch/Section newsletter
- **A.L.UNI FREIBURG**
  http://www.studium.uni-freiburg.de/newsletter
- **UNISTRASBOURG**
  http://www.unistra.fr/index.php?id=1180
- **COMPUTATIONAL NEUROSCIENCE: BERNSTEIN NEWSLETTER**
  http://www.nncn.de/en/news/BernsteinNewsletter-en/Newsletter-en

Neuro Campus

Program Interreg V Upper Rhine «Transcending borders with every project», Neurex, CNRS, INSERM, Université de Strasbourg, Région Grand Est, Département du Bas-Rhin, Département du Haut-Rhin, Eurométropole Strasbourg, Hôpitaux Universitaires de Strasbourg, Bernstein Center Freiburg, Klinik für Psychiatrie und Psychotherapie Freiburg, Neurozentrum Freiburg, Universität Freiburg, Universität Basel, Universitäre Psychiatrische Kliniken Basel, Kanton Basel-Stadt, Kanton Basel-Landschaft, Confédération suisse.

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