On Dec 5th, a Neurex meeting will address the pathophysiology of Multiple Sclerosis (MS), an autoimmune disorder generally thought to begin with an immune dysregulation. However, this concept has been disputed and the intriguing question of whether inflammatory demyelination is primary or secondary in the disease process will be one of those raised during a controversy debate held the next day. Research on MS is strongly represented in Basel. The Neurology Department of the Hospital, led by Prof. Kappos, the Clinical Neuroimmunology group led by Profs. Derfuss & Lindberg, as well as the Neuroscience group led by Prof. Schoeren-Wiemers investigate both the clinical and fundamental aspects of the pathophysiology of MS. MS research is also strongly represented in Strasbourg and Freiburg, and we are most grateful to the scientists from these groups who will participate in these events. Interestingly, with the recent demonstration of a possible involvement of the gut microbiome in triggering immune processes, the compartmentalization of science is further challenged. Beyond the obvious implications for the study of autoimmune disorders, such data encourage our network to further build horizontal bridges between disciplines. This might be among the coming aims of our transborder collaborative actions and strengthen the already fruitful interactions of our network. ■P.P.
**Summer 2013: 2 professors in neurobiology appointed at the Biozentrum Basel**

Professor Sonja Hofer and Professor Thomas Mrsic-Flogel recently (August 2013) joined the neurobiology research groups at the Biozentrum, Basel. Professor Sonja Hofer studies how neuronal circuits develop and change during learning. Professor Thomas Mrsic-Flogel’s work focuses on processing of visual information and the synaptic organization of circuits in visual cortex. A detailed report of their research interests will be published in the next Neurex newsletter (Spring 2014). In the meantime, we are pleased to welcome them in Neurex!  ■ P.P.

**Introduction to Computational Neuroscience**

Next, CNIB organizes a weekly lecture series “Introduction to Computational Neuroscience” at the FMI Basel. From September 16th - December 9th, 2013, outstanding researchers from all over Europe present key topics in computational and theoretical neuroscience. The course is eligible for 2 ECTS at the University of Basel (VV-No. 35768-01). Another lecture Series will begin in March 2014. For more information visit the CNIB web-page: www.fmi.ch/courses/Comp.Neuroscience/ ■ A.W.

**Support**

CNIB is supported by the FMI, Neurex and the Young Swiss Society for Neuroscience.

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**Report 03**

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**Spreading Computational Neuroscience in Basel**

The last decade has seen an unprecedented growth of experimental methods for investigating the anatomical, functional and molecular properties of large neuronal ensembles. The vast size, dimensionality and complexity of the data require sophisticated data analysis methods as well as a theoretical framework to help interpret and drive experiments. Computational neuroscience, a young but thriving discipline, addresses these challenges by developing suitable analysis tools, models and theories. At this highly interdisciplinary interface, experimentalists and theoreticians need a common language to generate fruitful collaborations and share knowledge. In May 2013, a group of young scientists from the Friedrich Miescher Institute for Biomedical Research (FMI) founded the Computational Neuroscience Initiative Basel (CNIB). The mission statement of CNIB is to:

- foster dialogue and collaboration between experimental and computational neuroscientists
- provide training in computational neuroscience for experimental neuroscientists

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**1st Swiss Computational Neuroscience Summer School**

From August 19th-24th CNIB hosted the 1st Swiss Computational Neuroscience Summer School of the FMI in Basel. 25 participants at the graduate and post-doc level were selected from applicants from all across Europe. With the aim to introduce experimental neuroscientists to computational neuroscience, the course focused on mathematical concepts of dynamical systems, neural coding, information theory and signal processing and their application to neuroscience. The faculty included speakers from Hebrew University in Jerusalem, from ETH Zurich and from FMI Basel. “The summer school has definitively broadened my understanding in mathematical theories”, says Dhanasak Dhanasobhon (University of Strasbourg).

Every day, the students were challenged with extensive hands-on exercises, in which they had to write their own programs for data analysis and modeling. This was tough, but the students learned quickly. “The progress was amazing”, says Dynamical Systems and Neural Coding teacher Yael Bitterman from the Hebrew University. Obviously, the students had fun – and not only at the evening socials. “During the hands-on sessions, I solved problems that I had no idea how to deal with beforehand. I really enjoyed this process”, says Xiao-Hua Huang, a post-doc at the FMI. ■ A.W.
In September 2013, 19 students have arrived in Strasbourg (France) from all over the world to follow the internationally renowned Joint Master in Neuroscience (JMN). Students of 12 different nationalities, speaking 15 languages altogether, will be trained in English to obtain a Master degree in Neuroscience.

Since 2006, the University of Strasbourg, together with its partners of Basel (Switzerland) and Freiburg-i.Br. (Germany) offers a complete training in Neuroscience, each partner city adding expertise in its own research domains, respectively Cellular and Integrative Neuroscience, Neurogenomics and Computational Neurosciences.

Students will be part of a two-year training which combines high level academic courses with extensive laboratory practice. They will share their time between lectures/practicals in the three partner cities and research work in the Neuroscience institutes of the upper Rhine valley. Since its birth in 2006, the JMN beneficiaries from the support of NEUREX, through its highly developed Neuroscience network, its scientific workshops and meetings and its financial assistance.

JMN students successfully continue their path in Neuroscience once graduated. 13 students of the 2011-2013 promotion have obtained their Master degree, and 9 of them have begun a Doctorate in the three months following their graduation. Since 2006, 80% of JMN students have continued in PhD, and 11% have found work.

In October 2013, the JMN programme has been awarded an IDEX grant (Initiative of Excellence). IDEX are funds attributed by the French Government to 8 Universities in France (including the University of Strasbourg) in order to promote the development of multidisciplinary poles of excellence in higher education and scientific research. The JMN programme is one of the projects the University of Strasbourg has chosen to reward and encourage. More information about the Joint Master in Neuroscience on http://neuromaster.u-strasbg.fr/JMN01homepage.html. 

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The Joint Master in Neuroscience 2013-2015 class

We remind you that you may:
- consult a list of job offers or
- post your own offer on our website. Detailed information available at http://www.neurex.org/jobinternship-market/jobs/
Multiple sclerosis (MS) is a demyelinating disease of the central nervous system (CNS) that causes neurological disability in young adults and affects worldwide about 2.5 million people. The most common form, relapsing remitting MS (RRMS), is characterized by intermittent attacks and subsequent partial improvement of neurological symptoms, with stable symptoms in between attacks, and comprises 85% of all patients at the onset of disease. However, up to 85% to 90% of untreated patients with RRMS develop secondary progressive MS (SPMS) characterized by continuous, irreversible neurological decline unassociated with relapses. A less common clinical phenotype, primary progressive MS (PPMS), encompasses 10% to 15% of the population with MS. It tends to occur in a population that is older than that with RRMS. In PPMS, disease progression starts slowly and is characterized by continuous worsening without distinct relapses. Relapsing progressive MS is a rare subtype, observed in about 1% of patients, in which a progressive increase in disability from the onset is superimposed by occasional relapses.

The pathological hallmark of MS is the presence of focal areas of inflammation and demyelination in the brain and spinal cord white matter. Traditionally, MS has been considered to be an autoimmune disease in which dysregulated auto-reactive T cells in the periphery enter the CNS and, together with macrophages and B cells, proceed to destroy various CNS elements, particularly myelin. This concept has been reinforced by experimental animal models such as experimental allergic encephalomyelitis (EAE) in which immunization with myelin, myelin proteins, or myelin protein peptides induced immune-mediated destruction of CNS myelin. The pathological similarities between the MS animal model experimental allergic encephalomyelitis (EAE) and MS provided a unifying hypothesis for their pathogenesis. Traditionally, MS has been considered to be an autoimmune disease in which dysregulated auto-reactive T cells in the periphery enter the CNS and, together with macrophages and B cells, proceed to destroy various CNS elements, particularly myelin. On the other hand, axonal pathology, even though mentioned as early as 1936, remained controversial and the axonal component of MS pathogenesis received less attention. It is now demonstrated that multiple MS lesions of the brain and spinal cord indeed include demyelination, inflammation, gliosis and axonal damage. Since the late 1990s, MS research has refocused on the role of axonal pathology and neurodegeneration in MS pathogenesis. Progressive axonal loss provided a logical explanation for the transition from RRMS to SPMS and for continuous and irreversible neurological decline in SPMS. The neurodegeneration reflected by brain and spinal cord atrophy correlates with disease progression.
Controversy around …

The primary autoimmune hypothesis

Based on the overwhelming evidence that the disease has an inflammatory phenotype, it has been assumed that the pathophysiology of MS begins with an immune dysregulation then leading to an attack of the CNS. Thus, the current concept still describes MS as a primary demyelinating inflammatory disease of CNS leading to secondary axonal degeneration. However, clinical experience has raised some troubling inconsistencies that cast reservation on this assumption, and some authors now question whether inflammatory demyelination is primary or secondary in the disease process, suggesting that MS might instead be a degenerative disorder. Several authors have suggested alternative models which propose that MS is a primary progressive disease in which there is a putative underlying degenerative process that would in turn trigger an autoimmune reaction, ranging from weak to strong.

In a recent article, Styts et al. propose that MS results from a convolution between progressive cytodestruction and a variably primed immune system. Thus, in this model, the true primary event in MS might be cytodegenerative, with the inflammatory events reflecting secondary - but still very important - reactions, as during the HIV form of MS. If true, primary progressive MS would reflect more accurately the initiating events involved in the disease, and EAE, the most commonly used animal model of MS would better describe autoimmune inflammatory processes than the real cause of MS. The creation of transgenic mice in which oligodendrocytes are deficient for peroxisomes offers a model in which a phenomenon of axonal degeneration may proceed demyelination and be followed by a strong inflammatory component[5].

B cells vs T cells

Recent studies support the concept that demyelination may occur by different mechanisms - including T-cell mediated demyelination, antibody-mediated demyelination and primary oligodendrocyte death - in different subpopulations of MS patients. B cells and antibodies account for the most prominent immunodiagnostic feature in patients with MS, namely oligodendroglial bands. The identification of myelin oligodendrocyte glycoprotein (MOG) as a target for autoantibody-mediated demyelination in EAE resulted in the re-evaluation of the role of B cells responses to myelin autoantigens in the immunopathogenesis of multiple sclerosis. However, the literature regarding antibodies to MOG in MS patients is confusing and contradictory. Nevertheless, recent studies, however, have described high levels of antibodies to confirm computationally correct MOG in MS. In adult MS, such antibodies are rarely found and then only at low levels[4]. In rat models of MOG-induced EAE, demyelination is antibody-dependent and reproduces the immunopathology seen in many cases of MS. In contrast, in mice inflammation in the CNS can result in demyelination in the absence of a MOG-specific B cell response, although if present this will enhance disease severity and demyelination[5].

Genes and environment

Several genome-wide association study (GWAS) in MS have been performed in which the classic HLA-DRB1 risk locus stood out with remarkably strong statistical significance. In addition, P. De Jager reported recently[6] that there are now 110 established multiple sclerosis risk variants at 103 discrete loci outside of the major histocompatibility complex. However, environmental factors have also been demonstrated to play a role in the incidence of MS - such as the latitude of the country and timing of birth - suggesting that there is a subtle interplay between genes and environment in the induction of MS. Furthermore, several infectious agents have been suggested to play a role in triggering the disease. Many questions remain unanswered regarding the pathophysiology of MS. MS symptoms are quite close to those of NMO (Neuromyelitis Optica) which was for decades considered as a variant of MS. NMO (Neuromyelitis Optica Spectrum Disorder), an inflammatory disorder of the central nervous system characterized by severe attacks of optic neuritis and myelitis, is now considered to constitute a distinct entity. Some identified pathophysiological features of NMO (such as the production of aquaporin 4 antibodies in a majority of patients) have consequences on the therapeutic point of view for the treatment of NMO(SD).

A two-days event will take place on the 5th & 6th of December in Basel (Kunstmuseum): On the 5th of December, a meeting entitled “Multiple Sclerosis: recent insights and new questions” will address different hypotheses about the putative role of inflammation vs degeneration, genes vs environment and B cells vs T cells in the aetiology of the disease. We would like to express our gratitude to the organizers of the event, Dr. Raja Lindberg, Prof. Ludwig Kappos and Prof. Tobias Derfuss, as well as to all the scientists who kindly accepted to participate in the event. 

References

Dr. Fabrice Berna (born in 1978) started his medical studies in Nancy (France) in 1996. He came to Strasbourg in 2006, and worked as an assistant psychiatrist at the Department of Psychiatry of the University Hospital of Strasbourg. He did his PhD at INSERM U666 with Prof. Jean-Marie Danion on the topic of “Autobiographical memory and the self in schizophrenia”. After he graduated in 2010, he did one year post-doctoral period at the Geriatric Psychiatric Department of the University Hospital of Heidelberg (Germany), where he worked on autobiographical memory in people with mild cognitive impairment. Since he came back to Strasbourg in 2011, he continues both his clinical and research activities on schizophrenia at the University Hospital of Strasbourg and at INSERM U1114 (ex U666). His research projects have been supported in 2013 by two awards for young researchers. In January 13th-14th 2014, he and Prof. Jean-Marie Danion will organize a workshop in Strasbourg, supported by Neurex, on the topic of “Autobiographical memory and the self”.

Dr. Fabrice Berna
Psychiatrist, Inserm Unit U1114
Co-organizer of the meeting “The self from autobiographical memories to the life story. Theory and psychopathology”

Dr. Fabrice Berna, Inserm Unit UMR_S 1114

Schizophrenia is a severe mental illness, which affects about 1% of the general population. Delusions, hallucinations, disorganization of thoughts and behavior represent typical clinical manifestations of this illness, but patients also suffer from social withdrawal, apathy and severe cognitive deficits, which strongly impact their social functioning and vocational abilities. Cognitive deficits are considered as a core feature of schizophrenia: they are observed before the onset of the illness, persist and worsen into the course of the illness, and account for the diversity of patients’ functional outcomes more strongly than symptoms and other illness features.

The INSERM Unit 1114 (ex U666) entitled “Cognitive Neuropsychology and Pathophysiology of Schizophrenia” pioneered the study of cognition in schizophrenia and has acquired an expertise over the last 20 years in perception, memory and metamemory disorders in schizophrenia. This work has led to the development of cognitive remediation therapies to help patients compensate their cognitive deficits in daily life.

Among cognitive deficits in schizophrenia is autobiographical memory impairment. These deficits are important to consider due to their deleterious impact on patients’ social functioning and quality of life. Autobiographical memory entails traces of experiences (emotions, images, feelings) relating to past personal events. It also comprises knowledge about ourselves, about our past and also our beliefs, dreams or imaginations. Therefore, autobiographical memory is more than a simple cognitive function since it represents an essential component of the self. Locking autobiographical memory as the “memory of the self” has led researchers like Martin Conway (see Conway, 2005) to put forward cognitive models showing the reciprocal relationships between autobiographical memory and the self. Our scientific approach was grounded on Conway’s model of the Self-Memory System and the investigation of autobiographical memory in schizophrenia was thought as a way to understand the nature of the characteristics of the self in patients. In fact, alterations of the self in patients have been reported by psychiatrists since the first description of the illness. They were initially expressed in terms of “loss of inner unity of consciousness”, or “impoverished sense of self” and were considered as being the core feature of the illness. However, at that time, the descriptions referred essentially to philosophical theories.

The originality of our approach consisted in using a cognitive psychopathology approach to patients with schizophrenia in order to investigate the cognitive mechanisms underlying major symptoms of the illness such as alterations of the self or persecutory delusion. We showed that patients have difficulty to recall past personal events (Bludot et al., 2003). Patients’ autobiographical memories are vaguer, less vivid, and lack phenomenological details, which are critical to experience a sense of self during remembering (Danion et al., 2005; de Oliveira et al., 2009; Potheegadoo et al., 2012-2013). These alterations are particularly observed to understand past events that played an important role in the development of the self (Bennouna-Greene et al., 2012) or events that have occurred at critical ages for identity construction (Cuervo-Lom bard et al., 2007).

We also demonstrated that patients had difficulty to take distance from past significant events and to understand past events that played an impact on their self (Berna et al., 2011a-b). We finally provided preliminary evidence showing how persecutory delusion and autobiographical memory interact with each other in that, memories of situations associated with a feeling of malevolence from other people may contribute to the emergence of persecutory beliefs, the latter affecting in turn the way memories of similar situations are later retrieved (Berna et al., in press).

Taken together, our research has renewed the understanding of clinical symptoms of schizophrenia that were, until recently, described using a clinical or philosophical perspective. We have developed innovative methods to investigate particular aspects of autobiographical memory and brought new understanding on Conway’s model of the Self-Memory System by showing how schizophrenia alters specific components of this model.

Current research projects are oriented towards innovative methods such as the use of a wearable camera to investigate further aspects of autobiographical memory in schizophrenia and develop cognitive remediation programs adapted to patients. Fabrice Berna recently obtained two awards for young clinician researchers to support these two research projects. We are also investigating life narratives of patients with schizophrenia and patients with other clinical conditions in order to examine the structure of these narratives and later integrate our findings in the development of therapeutic interventions for patients. This issue of the self as located between autobiographical memories and life story will be the topic of a coming Neurex workshop that will take place in Strasbourg in January 13th-14th 2014 and gather the most respected and recognized researchers in this domain.

The Thalamus is the largest diencephalic structure. It is made of about 60 nuclei and is now well known for, among numerous functions, playing a key role in various aspects of cognition. Thalamic lesions, as seen after stroke, traumatic brain injury, Korsakoff syndrome or in other pathologies affecting thalamus integrity, are associated with a panel of cognitive dysfunctions including amnesia, aphasia, alterations in executive functions, attention, perseveration, etc. Beyond the traditional view considering the thalamus as an ensemble of nuclei relaying information from various subcortical areas to the cerebral cortex, and vice versa, particularly with respect to sensory and motor information, additional thalamic functions have been proposed more recently.

A Neurex meeting entitled “The Cognitive Thalamus” will take place on the December, 12th-13th, 2013 in Strasbourg, Maison de la Région, 1, Place Adrien Zeller

This meeting proposes to focus on more recent views pointing to a specific role of some of the thalamic nuclei in dynamic interactions between limbic structures (i.e., hippocampus) and cortical areas implicated in cognitive functions. There will be a particular emphasis on processes underlying memory functions.

We would like to express our gratefulness to the organizers Anne Pereira de Vasconcelos & Jean-Christophe Cassel as well as to all the scientists who kindly accepted to participate in this event.

Full program available on www.neurex.org
The 2014 session of the Bench to Bedside will take place at the ZFL, Basel, on the 7th of February 2014. Program, information and registration (from Dec. 2013) on http://www.neuronetwork.unibas.ch/

NeuroTime Erasmus Mundus Joint Doctoral program:
The Second Edition is now running…
The Third Edition is already on the starting blocks!

The NeurTime program is an Erasmus Mundus Joint Doctorate program initiated by Neurex in 2011 and funded by the European Commission. It is coordinated by the University of Strasbourg.

The Second Edition of the Erasmus Mundus Joint Doctorate program was launched this October. For this new edition, eight students are enrolled in the program and will perform their PhD studies between the six universities of the consortium: the University of Strasbourg, the University of Amsterdam, the Albert-Ludwig’s University of Freiburg, the University of Basel, the Hebrew University of Jerusalem and the University of Bangalore.

In Strasbourg, the kick-off meeting took place on October 1st at the Institute of Cellular and Integrative Neuroscience (IN2, CNRS UPR 3212) and was followed by a get together with Pretzels and Alsatian soda… local specialties often new for the students coming from all over the world (Bangladesh, India, Mexico, Montenegro, Netherlands, Panama and Turkey)!

Applications for the 3rd Edition of the program (starting in October 2014) are now already open and candidates holding a Master in Natural Science (or associated fields) can apply to one (or more) of the nine proposed collaborative projects. Information can be found on our website at http://www.neurtime-erasmus.org/. ■ D.B.

Neurex supports the start-up "Polyneuron Pharmaceuticals"

In the framework of its Program “Support to start-ups”, the scientific committee of Neurex has attributed at the beginning of October a financial support to the startup Polyneuron Pharmaceuticals. The goal of the startup is to synthesize and test therapeutic molecules for the treatment of the autoimmune mediated disease “anti-MAG neuropathy”. Polyneuron Pharmaceuticals will develop a new class of drugs to treat autoimmune mediated diseases that affect the nervous system. This new class of drugs attacks selectively one disease-causing autoantibody, without affecting the rest of the immune system. Congratulations to the team and we wish all the success for their project. ■ S.K.

The Neurex "Support program for Welcome/Coming back of researchers"

The objective of this program is to encourage and support the research work performed by young teams in our academic laboratories. The deadline for applying is March, 31st, 2014. All details on www.neurex.org. ■ S.K.

Neurex supports collaborative Postdoctoral projects

A call was launched recently by Neurex for cross border collaborative fellowships. During its last meeting (October 7th), the scientific committee of Neurex evaluated the projects and attributed 4 postdoctoral grants.

The selected collaborative projects are the following:

→ LINEAGE SPECIFICATION IN THE NERVOUS SYSTEM, THE OTHER SIDE OF PLASTICITY.
   This collaborative project will run between Dr. Angela GANGRANDE (IGBMC, Illkirch / Strasbourg) and Prof. Heinrich REICHERT (BIOZENTRUM, University of Basel).

→ THE NEUROBIOLOGICAL BASIS OF INTER-GROUP BEHAVIOR IN HUMANS – INSIGHTS FROM NEUROIMAGING, NEUROPHARMACOLOGICAL MODULATION, AND ELECTRO-ENCEPHALOGRAPHY.
   This collaborative project will run between Prof. Markus HENNINGS (Department of Psychology, Laboratory for Biological and Personality Psychology, ALUFreiburg) and Prof. Daria KNOCH (Department of Psychology, Social and Affective Neuroscience, University of Basel).

→ HOW TEMPORAL EXPECTANCY TRANSLATES MOTIVATION INTO EFFORT.
   This collaborative project will run between Prof. Arne GEBERSCH (INSERM U1114, Cognitive Neuropsychology and Pathophysiology of Schizophrenia, Psychiatry Department, University of Strasbourg) and Prof. Marc WITTMANN ( Institute for Frontier Areas of Psychology and Mental Health, Freiburg).

→ THE EFFECTS OF HIGH-FREQUENCY STIMULATION IN THE STRIATUM ON COGNITIVE BEHAVIOR AND MEMORY IN RATS.
   This collaborative project will run between Dr. Robert D. KIRCH (Neuroelectronic Systems Lab, Dept. of General Neurosurgery, University Hospital Freiburg, Freiburg) and Prof. Jean-Christophe CASSEL (LNC A, University of Strasbourg - CNRS, Strasbourg).

We wish them a fruitful collaborative research. ■ S.K.
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.