ERA-NET NEURON

NEWSLETTER 40

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Announcements from NEURON Cofund2

DON'T MISS

NEURON's EPNA2022 Call:

"Excellent Paper in Neuroscience" Award - thematic focus on Sensory Disorders

If you a first author of an outstanding scientific article on sensory disorders published in 2021 - you may be eligible to apply with a chance to win 3000€ and an invitation for a special lecture

Submission deadline:
30 Sep 2022 | 19:00 CEST

Coming up!

Lay Audience Webinar

"Covid & Mental Health"

Dr. Livia de Picker

21 October 2022 | 17:30 CEST

Connect here

DON'T MISS

NEURON's Networking Groups Call on:

Chronic Pain

Submission deadline:
8 Nov 2022 | 14:00 CET

STAY TUNED!

NEURON's JTC2023

Pre-announcement coming in December 2022

www.neuron-eranet.eu/

Funded by the European Commission

More information can be found on our website
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From the desk of the coordinator | September 2022

Dear Readers,

The summer holidays have rejuvenated us all and we, at NEURON Cofund2, are back and fully engaged in the final evaluation by the panel of experts of the full proposals submitted under the JTC2022 on 'Cerebrovascular Diseases'.

In May, we were delighted to hold our traditional Foresight Symposium in hybrid format in Bonn, Germany. The topic of the symposium was 'Mechanisms of Resilience and Susceptibility in Mental Health' and it was organized by NEURON partners Etienne Hirsch (INSERM) and Bernard Poulain (CNRS). The symposium included presentations from renowned scientific experts and a discussion panel, led by NEURON's coordinator, Marlies Dorlöchter, in which scientists and representatives from patient organizations discussed the key issues that need to be addressed in research on this topic. More on the Foresight Symposium on page 4.

During the month of July, ERA-Net NEURON was enthusiastically involved in the largest neuroscience conference in Europe, the Federation of European Neuroscience Societies (FENS) Forum 2022 that took place in Paris, with several program contributions – two special lectures and one networking event. Furthermore, ERA-Net NEURON was represented in the panel discussion on research policy views on the future development of brain research, which was organized and moderated by the European Brain Council (EBC) as part of the European Brain Research Area (EBRA) project (Further details on all of NEURON activities in FENS2022 can be found here). On a related note, you might want to **save the date** for the upcoming EBRA Final Conference that will take place on **October 11th, 2022** in Brussels, Belgium. This conference is part of the Brain Innovation Days 2022 event organized by EBC to bring together key opinion leaders and stakeholders from the ever-growing brain innovation ecosystem to create synergies and showcase the importance of brain innovation.

We are also enthusiastic about the launching of **two new calls!** The first, this year's excellent paper in neuroscience award 2022 (EPNA2022) on the thematic focus of 'sensory disorders'. This annual call represents ERA-Net NEURON's dedication to support and promote early career researchers (ECRs) by recognizing remarkable and outstanding scientific publications by ECRs in the field of disease-related, translational, neuroscience. The EPNA2021 awardee, Steffen Tiedt, is featured in a personal interview in this newsletter (page 12). The second call is a new initiative by ERA-Net NEURON – a call for networking groups on the topic 'chronic pain'. This new call scheme does not fund experimental research, but is rather meant to address cross-cutting challenges in the research field of chronic pain, to build knowledge on specific aspects, identify gaps, and find solutions for urgent issues, such as interoperability of data and method harmonization.

Lastly, ERA-Net NEURON had long pledged to inform, connect and interact with the public on the topics of neuroscience and mental health through various outreach activities. In this regard, we would like to invite you all to the next webinar in ERA-Net NEURON's lecture series for lay audience on the extremely relevant topic of **'Covid and Mental Health'**. In the webinar that will take place on **October 21st, 2022 at 17:30 CEST**, Dr. Livia de Picker from University Psychiatric Hospital Duffel, Belgium, will talk about the various implications of the Covid19 pandemic on mental health. Feel free to spread the word and invite your friends and family to join this open webinar provided as a free service to the public by ERA-Net NEURON.

With this, we wish you good health and welcome you to keep up with our activities on our website, by following us on twitter and by joining our LinkedIn community, in order not to miss further information on our calls and events.

Sincerely yours

Foresight Symposium on Mechanisms of Resilience and Susceptibility in Mental Health

May 11th, 2022

The Foresight Symposium on 'Mechanisms of Resilience and Susceptibility in Mental Health', which was organized by NEURON partners Etienne Hirsch (INSERM) and Bernard Poulain (CNRS) as a hybrid meeting last May in Bonn, was an enlightening full day of lectures by seven experts in the field, whose lecture summaries can be found following this introduction, and two patient representatives: Peter Kinderman from Mental Health Europe and Raluca Nica from Gamian Europe. The symposium included enriching discussions with the speakers, five scientific advisory board (SAB) members that attended the meeting, patient representatives and NEURON partners.

Every year, one out of six people in the EU are affected by mental health problems, leading to costs of over 600 billion euros. In accordance, the topic of resilience and susceptibility in mental health was previously highlighted in the 2020 update of NEURON's Strategic Research Agenda (SRA) as a priority for research efforts. Therefore, this symposium was organized to discuss the susceptibility, protection, and resilience factors for mental health, including brain-related (genetics, stress, nutrition, perinatal infections or environmental hazards exposure), mind-related (emotions, behavior, interactions with others) or societal factors (cultural, economic, political, environmental). The aim of this symposium can be divided into five main objectives:

(i) Reviewing the mechanistic understandings of mental disorders
(ii) Reviewing the role of vulnerability and protection factors in mental disorders
(iii) Reviewing the importance of resilience in mental health
(iv) Developing prevention, intervention and care strategies for mental disorders
(v) Discussing the opportunity of a call for research on vulnerability, protection and resilience in mental disorders

Following this symposium NEURON funding organizations, agreed on the importance of working towards better understanding of vulnerability, protection and resilience in mental health. This symposium served as an important consultation step for the NEURON funding organizations to receive a scientific update on the topic and to develop the upcoming call text. We are grateful to the experts, whose insights greatly assist us in developing valuable activities for brain research and mental health.

Ruth Feldman

Early interaction and bonding

Prof. Ruth Feldman

Center for Developmental Social Neuroscience, Reichman University, Israel
Yale Study Child Center, Yale Medicine, USA

Biobehavioral synchrony corresponds to the autonomic, brain-to-brain and hormonal synchrony during a social interaction. It begins its development within the first year of life through parent-child interactions, making it a crucial period for mental health as this feature's healthy development conditions the ability to bond with other people throughout life.

Progress of research has led to the description of the parenting brain in human, which is divided into three networks: the empathy, mentalizing and emotion networks. Parenting brain only fully activates during synchronous social moments, and a dysfunction of this wiring leads to a disturbed mothering behavior. When functional, it allows the tuning of child's brain to social life through right-to-right brain theta synchrony between the adult's central region and the child's occipito-temporal region. An important feature of biobehavioral synchronization is oxytocinergic synchronization.

Research on this subject led to the development of synchrony-based psycho-educational interventions, for example to enhance the bonding between mothers suffering from post-partum depression and their babies. However, new studies are needed to explore the behavioral synchrony, oxytocinergic system and affiliative brain in young subjects. Getting new insights on these three elements will allow the establishment of new strategies to promote mental health at an early age.

Pierre Gagnepain

Post-traumatic stress disorder and resilience

Pierre Gagnepain

INSERM
Neuropsychology and Human Memory Imaging Department, University of Caen, France

Post-traumatic stress disorder (PTSD) is an anxiety disorder affecting trauma victims' daily life of which the most characterizing symptoms are the persistency of intrusive traumatic memories and hyper-arousal. Although research still needs to improve the current understanding of pathological processes behind PTSD, it must also focus on resilience factors allowing individuals to remain healthy after a trauma.

Through glutamatergic neurotransmission, toxic stress alters synaptic function, neuroarchitecture and neurogenesis in the hippocampus. Stress-induced hyperexcitability leads to the over-consolidation of sensory and emotional elements and a shift from hippocampus-based memory trace to an amygdala striatum representation. This mechanism underlies the formation of intrusive and traumatic memories in PTSD. The frontoparietal system, which inhibits hippocampal hyperactivity, thereby allowing memory suppression, might reflect a fundamental resilience mechanism insulating hippocampus against stress-related alterations. Further studies are needed to confirm that the preservation of memory control processes after a trauma might indeed limit the formation of the traumatic engram.

In conclusion, mechanisms supporting the gating of hyperexcitability and flexible deactivation of fear and memory processes must be investigated as general mechanisms of resilience. Challenges for resilience research in the context of PTSD are now to investigate the temporal dynamics of resilience mechanisms following a trauma, and to design studies to track neural implementation of traumatic memories in humans.

Marion Leboyer

Role of the immune system in resilience and susceptibility in mental disorders

Prof. Marion Leboyer

University of Paris-Est-Créteil

Psychiatry and Addictology Department, Hôpitaux Universitaires Henri Mondor

INSERM U955, Institut Mondor de Recherches Médicales, France

Clear evidences point out the interactions between the immune and nervous systems and their involvement in psychiatric disorders, thereby highlighting the potential role of the immune system as a factor of resilience and susceptibility to mental disorders.

Several factors mediated by inflammation constitute risk factors for psychiatric disorders, such as childhood trauma, an unhealthy diet or fine particle pollution. This knowledge led to the establishment of a "two-hit model" where an infection or autoimmune disorder (first hit) causes non-resolved chronic inflammation, and then an infection or stress (second hit) leads to the emergence of psychiatric disorders.

Immunity seems to act as a resilience factor through the human leukocyte antigen complex, as genome wide association studies show its implication in psychiatric disorders. However, it constitutes a very dense and complex genome region and is thus complicated to study. Still, it is possible to use distribution analyses of haplotypes to identify functionally relevant haplotypes, and allele expression or quantitative trait locus to analyze functional properties.

Moreover, infection environmental triggers activate human endogenous retrovirus elements in the genome of permissive cells, leading to a self-sustained activation feedback loop for activation of HERV elements. This phenomenon might constitute a susceptibility factor in psychiatric disorders.

In the future, research needs to focus on the identification of risk and resilience factors to allow the refinement of public health interventions. Immune dysfunction needs to be studied from early psychosis to treatment resistance, to allow the development of interventions aiming at lowering inflammation and improving mental health.

Andreas Meyer-Lindenberg

Environmental risk and resilience processes in the human brain

Prof. Dr. Andreas Meyer-Lindenberg

Central Institute of Mental Health in Mannheim, Department of Psychiatry and Psychotherapy, University of Heidelberg, Germany

Urbanicity increases the risk of mental illness. Considering the continuous increase of the urban population, it is fundamental to understand how urbanicity constitutes a risk factor for mental health.

Several lines of evidence show that environmental risk factors for mental health affect neural circuits involved in the regulation of negative emotion and stress. Indeed, fMRI studies show that factors such as the size of the city one lives in, being an immigrant, or having suffered a childhood trauma, have an effect on social stress-associated brain regions. Moreover, these regions' dysfunctional activity has been linked to psychiatric disorders such as depression and schizophrenia. Overall, research indicates that risk and resilience are linked to the perigenual anterior cingulate cortex and regions regulated by it, such as ventral striatum and amygdala.

Multimodal cohort studies are essential to characterize environmental exposures and how they affect people. Identifying the mechanisms of resilience factors such as nature experience, social interaction or non-exercise activity will help developing primary prevention and interventions designed around them.

Chantal Martin-Soelch

Common factors in vulnerability and resilience in mental health: General psychiatry & focus on addiction and eating disorders

Prof. Chantal Martin-Soelch

Psychology Department, University of Fribourg, Switzerland

Resilience is a key feature allowing a dynamic system or an individual to adapt successfully to disturbances threatening its viability, function and development. Several factors favor and support it, such as a properly functioning reward system.

Impaired responses to reward are evidenced in several mental disorders, suggesting that a properly working reward system could constitute a resilience factor. Of important note, several evidences point out that a dysfunctional reward system could be treated: for instance, specific psychotherapy can restore neural response to reward in depression and smoking cessation restores functional dopamine responses to reward.

An imbalance between stress reactivity and reward responses is a predictor of vulnerability to stress and thus the development of psychopathological symptoms. Interventions are to be conceived to target reward responses for the purpose of preventing from or treating these symptoms. Going forward, challenges in this field will concern new study designs and samples, with the development of prospective longitudinal studies, multi-center or cohort studies taking in account cultural differences, as well as multi-modal approaches with behavioral and clinical measures. Focusing on particular populations, such as offspring of parents with depression or trauma survivors, will help in identifying vulnerability and resilience factors. Overall, these research efforts will help the development of new treatments, stress prevention programs, and large-scale and culturally sensitive interventions to prevent the development of mental health problems after the exposure to adverse events.

Giuseppe Riva

Increase resilience through new technologies, new therapies and new patient care

Prof. Giuseppe Riva

Applied Technology for NeuroPsychology Laboratory, Institute Auxologico Italiano, Catholic University of Milan, Italy

Virtual reality (VR) consists in using computer technology to create a simulated environment using a helmet with a screen inside. It differs from 3D through the sensation of presence: the patient is a part of the scene he visualizes. VR allows the patient to relive all significant elements associated with an experience, making them available for reorganization. It compares favorably to existing treatments in several psychiatric disorders: it is used to reduce post-traumatic syndrome disorder, to lower body distortions in eating disorders, as anesthesia because if modifies neural area of pain, or to lower anxiety disorder. Treatments using VR have long-term effects that generalize with the real world.

The notion of predictive coding describes the fact that in someone's experience of the world, not only does the information flow from senses to higher faculties, but these higher faculties also predict the next input from our environment, thereby influencing one's perception before the actual sensation. Telepresence is the ability of a technology to simulate the predictive mechanisms of the brain. If the prediction is perfect, there is the feeling of presence. Scientists can use VR to monitor, manipulate and increase the patients' interaction with their environment to promote functional recovery. Furthermore, as a likeable activity, VR allows increasing patients' motivation and active participation.

The next step for VR is to be combined with sounds and vibrations to simulate one's internal reality, through proprioception, interoception and vestibular inputs. This should make people feel "for real" things that they are not feeling, by hacking directly predictive coding mechanisms of their inner body (stomach, heart and ear).

Francesca Marina Bosco

Role of metacognition in protection, resilience and vulnerability to mental disorders

Prof. Francesca Marina Bosco

Psychology Department, University of Turin, Italy

Metacognition is an innate human ability necessary for interacting with other people in a social context. It is notably composed of theory of mind (ToM), which enables self-knowledge and the understanding of other people's beliefs, emotions and desires. ToM constitutes a protective function against psychopathologies and, therefore, it is important to ensure its good development during adolescence, a critical period for psychopathological development.

ToM impairments have been described in many psychiatric disorders such as schizophrenia, alcohol abuse disorder, eating disorders, etc. Hence, ToM constitutes an interesting object of study in the scope of psychiatric disorders development. However, only a few tools have been developed to assess metacognition in patients and, moreover, the existing tools are rarely translated into other languages, making it complicated to study cross-cultural aspects in this field of research. There is also a crucial need for a greater number of reviews and meta-analyses about the more basic components of metacognition. These research advances will allow the development of programs aiming at improving metacognitive skills or preventing a metacognitive decline, and tests to evaluate the recovery processes of metacognitive deficits.

2021 EPNA AWARDEE
Personal Interview with Dr. Steffen Tiedt

The Excellent Paper in Neuroscience Award (EPNA) initiative was first introduced by NEURON in 2009, in order to support and encourage young neuroscientists at the early stage of their career. The winners of the award receive a cash prize, as well as an invitation to present their work as special Young Investigators speakers in an international conference. This year the presentation and award took place in July at the FENS Forum 2022 conference in Paris.

The 2021 EPNA awardee is **Steffen Tiedt** (@SteffenTiedt). The award was given to Dr. Tiedt for his publication from his work in the Institute for Stroke and Dementia Research, University hospital, LMU Munich, Germany, 'Circulating Metabolites Differentiate Acute Ischemic Stroke from Stroke Mimics' published in ANN NEUROL 2020; 88: 736–746. Continue reading to learn more about Steffen and his scientific journey.

Please tell us briefly about your research interests

Our work is motivated by the heterogeneity of ischemic stroke, which poses a challenge for assigning patients to optimal treatment strategies and is a major reason for the large number of failed clinical trials. Current diagnostic algorithms are insufficient to capture both the mechanisms leading to and following stroke. We thus aim at identifying meaningful circulating signatures that inform on pathophysiological mechanisms after stroke and can be utilized as diagnostic instruments. Implementing these in clinical routine we envision stroke care to be more comprehensive and precise.

Please tell us about your scientific journey to-date

Intrigued by courses on neurophysiology during my medical studies, I conducted my MD thesis with Magdalena Götz exploring the role of STAT-signaling on the neurogenic potential of reactive astrocytes and learning the basics of experimental work. When finishing my medical studies, I aimed at working with a more translational focus and joined the group of Martin Dichgans at the ISD as a clinician-scientist conducting a joint program: a PhD in Neuroscience at the Graduate School of Systemic Neuroscience and residency in Clinical Neurology. During my PhD we initiated the CIRCULAting biomarkers after Stroke (CIRCULAS) study, which by now is one of the largest study world-wide with early and serial blood sampling in acute stroke patients. Utilizing this resource, we were the first to employ RNA sequencing for the identification of circulating miRNAs associated with stroke and to apply single-molecule array (SimoaTM) technology during the course of stroke.

What made you choose a career in your field?

I wouldn't call it a career ;-) but: First, stroke changes the lives of people instantenously. Advancing the care for these patients seems for me the obvious thing to do. Second, most scientists focus on treatments, which is great, but we can only treat if we understand human stroke pathophysiology, which we at a clinical routine level do not. We gasp for better biomarkers to advance diagnostics and thus the selection of patients for treatments. I chose to work on blood-based biomarkers, because I feel there is the greatest mismatch between what biology tells us and what we currently know and quantify. Third and last, I just like to work on clinically relevant questions with data mostly acquired from patients using complex technology such as mass spectrometry and to analyze these large datasets.

Where do you see your field of research in a few years? What are going to be the major breakthroughs?

We envision stroke care to be more precise, for example by utilizing circulating signatures. Such signatures need to be identified and point-of-care devices developed, but that will probably take longer than a few years.

What were the main challenges you had overcome in your career path and how did you overcome them?

I feel very lucky to be in the position to decide what I am working on and to have the time and the funding to do so. From a broader perspective, I am very privileged: I was born, raised and I studied in the country where I now work, so no challenges there. I was born to academics, also no challenges there. I am a man, no challenges there. The one challenge I have is to make sure that the colleagues whose work I supervise are not hit by biases and challenges arising from origin, gender etc.

What are your goals for the future and where would you like to see yourself 5 years from now?

My one scientific goal for the future is to identify blood-based biomarkers that are implemented into clinical routine.

What advice would you give your younger self or young scientists beginning their research career?

Focus on one thing. Focus on something, where your interests, passions and skills align. This is where you will succeed.