ERA-Net Neuron

NEWSLETTER 19

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News From NEURON II

The Joint Transnational Call (JTC) for proposals for European Research Projects on Mental Disorders was published on January 10th, 2013. The deadline for submitting pre-proposals was March 11th, 2013. The Joint Call Secretariat received 91 pre-proposals in response to the call, involving 369 research groups from 13 countries. The deadline for submitting full proposals was June 25th, 2013, and the final results of evaluations are expected in October 2013.

The call for applications for (EPNA) 2013

EXCELLENT PAPER IN NEUROSCIENCE AWARD

was launched on July 2013.
Deadline for submission of applications is September 15th, 2013.
For further information, please visit our web page: www.neuron-eranet.eu
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Scientific Symposium 'Neurodevelopment and related disorders'

May 16-17, 2013, Reykjavik, Iceland

Forward by the symposium chair: Etienne Hirsh, Foreword

As part of the European-wide activities during the European Month of the Brain, the ERA-NET NEURON organized a workshop on neurodevelopment and neurodevelopmental disorders in Reykjavik on May 16, 2013. The symposium was well attended and addressed both researchers and the general public with a specific lecture dedicated to the lay audience.

The topic represents one of the most important and challenging aspects of neuroscience. Indeed, the development of our brain influences our entire life and thus, if this process is impaired, the consequences may last for years and may be associated with suffering, >>>

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>>>not only of the afflicted persons but also for their families and friends. The foremost goal of the workshop was to provide an overview of the research field and generate ideas on activities that NEURON II partners could jointly initiate to rapidly advance research in neurodevelopment. In the first part of the symposium, presentations focused on fundamental research questions of brain development: How can billions of neurons and glial cells (astrocytes, microglial cells and oligodendrocytes) orchestrate the development of the brain to set up complex behaviors and cognition, such as learning, hearing, vision, dream, or consciousness. In a second part, a special emphasis was put on the diseases characterized by abnormal development of the brain, such as autism, mental retardation, ADHD, language disorders, learning disorders, motor disorders and others. The symposium was concluded
by the thought-provoking concept that some diseases of the elderly may even start early during life. Altogether, this symposium emphasizes the role of developmental alteration during the whole life. It stresses also the need for understanding the role of genes in brain development, how genetically predisposed events may be altered by environment and what determines functioning of the healthy and diseased brain. New treatments will only emerge when we will be able to answer these questions.

Amparo Acker-Palmer

Amparo Acker-Palmer, Goethe University, Frankfurt, Germany

General Overview of the Nervous System

A central challenge for scientists studying neuronal development is to understand how axons and dendrites grow out to synapse to the right partners and generate a functional network. Abnormalities in dendritic and synaptic structures for example are observed in human neurodevelopmental disorders associated with mental retardation. These processes are controlled by signaling molecules that are involved in cell-to-cell communication and that coordinate the proper arrangement of cells to assure brain function and cognition. We have discovered a coordinated crosstalk of different signaling pathways including the EphB receptors and their ligands, the ephrinBs necessary for proper neuronal migration during the formation of layered structures in the brain or for neuronal communication and information processing in the nervous system. Interestingly, there is a fascinating parallelism in the development and function of the vascular and nervous systems. Both systems share complex branching patterns in the body and also employ similar molecular mechanisms to achieve such patterns. Our main interest is to understand this neurovascular link and investigate how the vascular system communicates and instructs the development and function of the nervous system to achieve brain function.

Klaus-Armin Nave

Klaus Armin Nave, Max-Planck-Institute Experimental Medicine, Göttingen, Germany

Myelin and glial cells in nervous system development

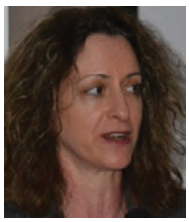
Glial cells that engage with neurons is a feature of virtually all nervous systems. Oligodendrocytes are well known for their ability to myelinate axons and to enable saltatory impulse propagation, one of the best understood concepts in neurophysiology. However, these cells also support long-term axonal integrity, as demonstrated by mouse mutants, in which oligodendrocytes make myelin but lose their ability to maintain axon function and survival. This neuroprotective function appears independent of myelin itself. In fact, axonal support may have been the primary role of axon-associated glial cells in nervous system evolution. A major research goal is to better understand the molecular mechanisms by which neurons instruct associated glial cells to wrap axons and to support axonal integrity. One emerging mechanism is the support of axonal energy metabolisms, such as the delivery of glycolysis products. This function may be specifically important in myelinated tracts, in which axonal access to extracellular glucose is compromised by myelin itself. Ongoing research is aimed at understanding the regulation of oligodendroglial energy metabolism as a function of axonal energy needs. Perturbations of this glial support is a likely cause of reduced connectivity in the brain and the loss of higher brain functions.

S. Wendy Roberts

S. Wendy Roberts, University of Toronto, Canada

Overview of Developmental Disorders and Focus on Autism

Using Autism Spectrum Disorders (ASD) as a model of neurodevelopmental disorders, links can be identified between clinical and basic science research.
As hundreds of mini neurodevelopmental syndromes are identified using current genetic methodology, overlaps are apparent in pathways leading to intellectual disability, language disorders and ASD. There is an urgent need to identify basic mechanisms such as those involved in cell signalling and synaptogenesis that may be disrupted by genes associated with ASD and other neurodevelopmental disorders.
Clinically, understanding commonly disrupted pathways should facilitate development of novel therapeutics for various neurodevelopmental disorders.
Generic approaches to enhance early brain development may enrich brain function for all children and eventually enhance economic health and wealth of nations! Dawson and Rogers' documentation that earlier intervention produces better outcomes, and reinforces the need for very early generic intervention starting as early as 12 months, developed in concert with careful study of behavioral outcomes as well as atypical neuronal mechanisms found in the individual.
Families want to be listened to, to be part of stakeholder teams with scientists and policy makers, in order to have input into research priorities and to help to plan studies that will answer their most important questions.



Karen Avraham

Karen Avraham, Tel Aviv University, Israel

Developmental Disorders of sensory systems: the example of deafness

A severe to profoundly deaf child is born every 1,000 births, with hearing loss in 4% of people below age 45, reaching 50% by age 80. Approximately 700 million will suffer from hearing loss by 2015, including 90 million Europeans. While this sensory defect is common, it is genetically heterogeneous, with many genetic forms of deafness, each rare. The impact of the study of the brain in this area has been emphasized by the awarding of the Brain Prize to Professors Petit and Steel for an outstanding contribution to European neuroscience in the understanding of the genetic regulation of the development and function of the ear. Next-generation sequencing (NGS) is speeding up our ability to detect disease mutations. Using NGS, we have doubled the number of mutations found for deafness in the Middle East. A mutation was found in SYNE4, a member of the LINC (LInker of Nucleoskeleton and Cytoskeleton) complex, in an Israeli family. Mice null for this protein are deaf and their outer hair cells lose the basal position of their nuclei. This discovery has led to a new mechanism for deafness. Studies in new frontiers need to be examined, including epigenetics and complex forms of hearing loss.

Yehezkel Ben-Ari

Yehezkel Ben-Ari, INSERM, Marseille, France

Neurodegenerative disorders of aging are neurodevelopmental disorders

Ionic currents like network driven patterns follow developmental sequences, differing considerably in immature and adult neurons and serving different roles. Thus, GABA depolarizes and often excites immature neurons while primarily inhibiting adult ones because of a progressive reduction of intracellular chloride mediated by a progressive expression of chloride co-transporters. In additon, seizures and a variety of insults leads to a re-expression of immature features notalby of elevated chloride and excitatory GABA (Ben-ari et al 2007). We have suggested elsewhere that neuron activity serves as a checkpoint controlling the validity of the developmental program (Ben-Ari & Spitzer, TINS 2010). Also, neurons who do not fulfill their program for instance by being misplaced or misconnected keep immature features (Ben-Ari TINS, 2008). Thus, a diuretic that reduces (Cl-) i also reduces the severity of autism in children (Lemonnier et al).
I suggest that the use of drugs that block immature but not adult ionic currents open highly promising therapeutic avenues. This approach ought to be privileged in futur programs instead of identification of more mutation to the thousand of mutation expected in autism for instance.

Ragnhildur Thora Karadottir

Ragnhildur Thora Karadottir, University of Cambridge, UK

The bright side of the brain: the role of white matter in brain function and dysfunction

The cells in our brain communicate between each other utilizing electrical signals that are converted into chemical signals at cell junctions called synapse. In the last decades neuroscience research has focused on understanding these signals between neurons, situated in the grey matter of the brain, as they are a the computational element of the brain. However, the human brain is equally segregated into grey and white matter. The brain's white matter provides a data superhighway that links ~100 billion neurons situated in the grey matter - the brain's computational area. The white matter – generated by cells named oligodendrocytes- is essential to provide fast communication between neurons crucial for us to be able to think, move, sense our environment and see. In disease, where either the neurons die, or oligodendrocytes or the white matter is damaged leading to mental and/or physical disability. Different to the grey matter the white matter has the capability of repair. This lecture introduced neuron focused on the function of the brains´ superhighways and how they may be repaired when damaged in disease.

"The bright side of the brain": A lecture to the general public

70 people signed up to attend the symposium and in addition an estimated 20-30 people showed up specifically for the lay lecture which is quite an amazing turnout in a country of only 330.000 inhabitants.

The symposium in Reykjavik on 'NEURODEVELOPMENT AND RELATED DISORDERS' was part of NEURON II activity in the EUROPEAN MONTH OF THE BRAIN. The symposium included a special lay audience presentation.

The symposium and the lay lecture were a great success. Both had been advertised widely within the academic and clinical communities. SMEs (Small and Medium Enterprises) and patient organizations were furthermore contacted and a special effort was made to invite students to the symposium. The lay audience presentation was advertised in the two main daily newspapers and on Facebook.

RANNIS, The Icelandic Centre for Research ,has had a lot of feedback from the attendees – all very favourable and many people have requested further information on the ERA-NET NEURON, so NEURON II is now firmly on the map of the Icelandic neuroscience community.

German Aerospace Centre, Project Management Agency

Federal Ministry of Education & Research (BMBF), Germany

Austrian Scuence Fund (FWF), Austria

National Authority for Scientific - Ministry of Education, Researc and Youth (ANCS - MECT), Romania

National Centre For Programmes Management, Romania

The National Centre for Research and Development (NCBIR), Poland

Medical Research Council (MRC), UK

Ministry of Health (MOH), Italy

Academy of Finland (AKA), Finland

Ministry of Science and Innovation (MICINN), Spain

National Research Agency (ANR), France

National Center for Scientific Research (CNRS), France

Institute of Health Carlos III (ISCII), Spain

National Institute for Medical Research (INSERM), France

Chief Scientist Office, Ministry of Health(CSO-MOH), Israel

National Research Fund (FNR), Luxemburg

Swedish Research Council (SRC), Sweden

Québec Health Research Funding Agency (FRSQ), Canada

Fonds Wetenschappelijk Onderzoek – Vlaanderen (FWO) Belgium

Fundação para a Ciência e a Tecnologia (FCT) Portugal

The Icelandic Centre for Research (RANNIS) Iceland

Canadian institutes of Health Research, Canada