14:15 - 15:45

NEUROPHYSIOLOGY OF BEHAVIOR IN DROSOPHILA MELANOGASTER

Aram Megighian - Department of Biomedical Sciences - University of Padua

Abstract: Organisms respond to stimuli from the environment by generating behavioral responses (adaptive behavior) composed of coordinated actions or inactions that aim to obtain the best advantage for the organism itself in evolutionary terms (survival of the individual and survival of the species). The processing of these adaptive behavioral responses requires the use of the most complex nervous activities (cognition) and resides in basic psychophysiological mechanisms that are shared in the various organisms (vertebrates as well as invertebrates) such as selective attention and decision making processes. In vertebrates, some macroscopic anatomical structures are involved in the processes that govern adaptive responses. These structures are present both in humans and primates as well as in animals distant from them such as other mammals or fish or agnates. These structures, however, are absolutely not identifiable in the nervous system of invertebrates, which is completely different from a macroscopic point of view from that of vertebrates. Yet, as mentioned, even invertebrates present adaptive responses with characters similar to those of vertebrates. Has evolution acted from the outside by selecting particular nervous structures to process these responses? Or, on the contrary, are these generated by nervous microcircuits present in both invertebrates and vertebrates, where the extreme flexibility in the responses of the latter is obtained by the redundancy of these microcircuits? The aim of my current research is to identify these microcircuits in invertebrates, using the analysis of visuomotor behavioral responses in a model animal such as the fruit fly and exploiting its genetic manipulability.

Biosketch: The first theme of my research is developed within the research group "Neurotoxin, Neuroparalysis and Neurodegeneration Lab" (formerly Montecucco Lab, now directed by Prof Ornella Rossetto), where my contribution is directed to the functional study by means of intra- and extracellular electrophysiological techniques of the mammalian neuromuscular synapse under normal conditions, during the pathological processes that determine its acute or chronic damage and finally during the regenerative processes of repair from damage. I came to this research topic after having dealt in the early part of my career with the physiological mechanisms that regulate the functional relationship between motor neuron and skeletal muscle within the motor unit.

In 1996-97 I was Research Scientist in the Neurobiology Laboratory of Prof. G. Harris, Dept. of Biology at San Diego State University, USA. During this period I developed a method of intracellular in vivo recording of action potentials (evoked through stimulation of cephalic motor centers) and minis of the indirect flight muscles of adult individuals of Drosophila melanogaster, the fruit fly. In this experimental animal model it is in fact possible to combine sophisticated genetic and molecular techniques with equally sophisticated techniques of anatomical, behavioral and electrophysiological analysis. Since about 60% of the genes of D. melanogaster are homologous to those of humans, the fruit fly represents a valid experimental model for the study of genetic function.

My attention has been turned to the study of the genes (and the proteins expressed by them) involved in the molecular nanomachine that regulates synaptic release, using as an experimental model the neuromuscular synapse of the adult and the third stage larva of the fruit fly. Using intracellular recording techniques with current- and voltage-clamp methods, I analyzed the role of the CASK protein which, by forming a complex with MUNC-18 and neurexin, regulates synaptic release. In another series of experiments conducted on transgenic animals with mutation of a single amino acid in the proteins SNAP25 and Syntaxin, I investigated whether the SNARE complexes combine to form a rosette supercomplex around the point of contact between the neurotransmitter vesicle and the presynaptic membrane, thermodynamically favoring the fusion between the two membranes.

The second research theme developed from these studies. My attention has progressively shifted from the study of the neuromuscular synapse as a model of chemical synapse, to the analysis of nerve circuits in the same ani-

mal model (giant fiber pathway, electroretinographic responses) and then to simple behavioral analyses (sleep, epileptogenic responses) and, currently, to complex behavioral analyses (visual-motor and olfactory-motor responses) in fixed or free tethered flight condition.

15:55 - 17:25

FUNCTIONAL IMAGING AND CONNECTOMICS IN ZEBRAFISH FROM BRAIN ACTIVITY TO FUNCTIONAL NEURONAL ARCHITECTURES: AN INTEGRATED FRAMEWORK TO INVESTIGATE CIRCUIT MECHANISMS

Marco Dal Maschio - Department of Biomedical Sciences - University of Padua

Abstract: Understanding the brain mechanisms supporting sensory processing or the execution of behavioral programs is a challenging task, also in suitable model organisms. The lecture will describe first some of the main challenges one has to address and it will then present possible methods and strategies currently available one could adopt in the research. A framework tying together functional brain recordings, neuronal activity modulation, behavior tracking and connectomics will be shown as current building blocks of an approach for the dissections of the brain mechanisms.

Biosketch: Marco Dal Maschio is Associate Professor of Physiology at Università degli Studi di Padova (Italy). He graduated in Physics in 2002 and completed his PhD in Biotechnology in 2006, both at Università degli Studi di Padova. He was PostDoctoral Fellow from 2008 to 2012 at the Italian Institute of Technology (Italy), dept. Neuroscience and Brain Technologies, and from 2013 to 2018 at the Max Planck for Neurobiology (Germany), dept. Genes - Circuits - Behavior. His main research expertise is at the interface between Neurotechnologies and Neuroscience in particular taking advantage of and developing light-based technologies to investigate brain mechanisms of visuomotor integration in normal and pathological conditions.

17:35 - 19:05

SOMATOSENSORY DIFFERENCES AND NEUROINFLAMMATION IN GENETIC MODELS OF AUTISM SPECTRUM DISORDERS

Yuri Bozzi - Center for Brain/Mind Sciences (CiMEC) - University of Trento

Abstract: Sensory differences are a common feature in autism spectrum disorders (ASD). Similarly, sensory deficits have been described in mice lacking ASD-associated genes. In this lecture, I will summarize the current approaches to investigate behavioral and neuroanatomical differences in mouse models of ASD, focusing on the recent work carried out in my laboratory. Specifically, we recently investigated somatosensory abnormalities in Cntnap2 and Shank3b mutant mice, two well-characterized mouse models of ASD. Our work showed that both mutant mice display impaired whisker-dependent texture discrimination accompanied by altered activity and functional connectivity of the primary somatosensory cortex. In order to better characterize the neurobiological substrates of these defects in Cntnap2 and Shank3b mutant mice, we focused on the cerebellum, a region involved in somatosensory integration and social cognition. Our work showed severe neuroinflammation in the cerebellum of both Cntnap2 and Shank3b mutants. Interestingly, cerebellar inflammation and social deficits could be rescued by an antioxidant/anti-inflammatory treatment in both Cntnap2 and Shank3b mutant mice. Our data indicate that Cntnap2 and Shank3b mutant mice are reliable models to investigate the

relationship between somatosensory differences, social cognition, and neuroinflammation in ASD.

Biosketch: graduated in Biology from the University of Pisa in 1991, and received his PhD in Neurobiology from the Scuola Normale Superiore in Pisa in 1996. After four years in France, he returned to Italy as a researcher at the CNR Institute of Neuroscience in Pisa. He moved to the University of Trento in 2009, where he has held the position of Full Professor of Physiology at the Mind/Brain Center (CIMeC) since 2017. In October 2022, he was appointed Director of the CIMeC. His research concerns the neurobiological basis of autism. He is the author of more than 90 articles in international journals and more than 100 presentations at national and international conferences. He has been engaged in intensive scientific outreach activities throughout the country for about 15 years.

21:00 - 22:15

SPECIAL LECTURE

ROSARIO RIZZUTO - UNIVERSITY OF PADUA

09:15 - 10:45

MOLECULAR AND CELLULAR PHYSIOPATHOLOGY OF CONGENITAL MIGRAINE MOLECULAR, CELLULAR AND CIRCUIT MECHANISMS OF MIGRAINE: A MULTISCALE APPROACH IN GENETIC MOUSE MODELS OF THE DISEASE

Daniela Pietrobon - Department of Biomedical Sciences, University of Padua

Abstract: Migraine is much more than an episodic headache. It is a complex brain disorder, characterized by a global dysfunction in multisensory information processing. The molecular, cellular and circuit mechanisms of the primary brain dysfunctions that underlie migraine onset and altered sensory processing remain largely unknown and are major open issues in the neurobiology of migraine. Genetic mouse models of a rare monogenic form of migraine with aura (FHM) provide a unique experimental system to tackle these key unanswered questions. In FHM1 knock-in mice carrying a pathological gain-of-function mutation in the neuronal voltage-gated calcium channel CaV2.1, we studied i) the unitary excitatory and inhibitory synaptic transmission at different cortical synapses and the excitatory-inhibitory balance at core microcircuits mediating feedback intracortical inhibition and feedforward thalamocortical inhibition (using patch-clamp recordings in brain slices), and ii) the cortical network activity evoked by either visual stimuli in awake head-fixed mice or whisker stimulation in anesthetized mice (using local field potentials and multiunit firing activity recordings). In FHM2 knock-in mice carrying a pathological loss-of-function mutation in the astrocytic 2 Na, K ATPase, we studied the rate of K+ and glutamate clearance by astrocytes during neuronal activity in brain slices and the glutamate changes evoked by whisker stimulation in the somatosensory cortex in awake head-fixed mice (using patch-clamp recordings and glutamate imaging with a genetically-encoded sensor). In both knock-in mouse models we studied the mechanisms underlying their enhanced susceptibility to cortical spreading depression, the phenomenon that underlies migraine aura and may trigger the headache mechanisms. I will describe the functional alterations we have uncovered in the cerebral cortex of these mouse models of migraine and discuss the insights into the molecular, cellular and circuit mechanisms of migraine obtained from these findings.

Biosketch: After graduating in Chemistry at the University of Padova (1979), during the first part of her career (1979-1986), Daniela Pietrobon worked on energy transduction in mitochondria and kinetic modelling of mitochondrial proton pumps (as a research fellow and CNR researcher at the University of Padova and as visiting scientist at the Weizmann Institute of Science in Israel). Then, as visiting scientist at Harvard Medical School, she focused her research activity on the biophysics of cardiac voltage-gated Ca2+ channels and back in Padova, as associate professor of Physiology, on the biophysics and physiology of neuronal voltage-gated Ca2+ channels and the effect of pathological mutations on human recombinant Ca2+ channels (1987-1999). Since 2000 she is full Professor of Physiology at the University of Padova and works on the functional characterization of genetic mouse models of migraine and migraine pathophysiology.

10:55 - 12:25

USE OF ADENO ASSOCIATED VIRAL VECTORS IN THE BRAIN: SOMETIMES EASIER SAID THAN DONE

Marco Mainardi - Department of Biomedical Sciences - University of Padua

Abstract: Adeno associated viral vectors (AAVs) are universally used to express a variety of recombinant proteins in brain cells. Through the capability of AAVs to infect postmitotic cells, neurons can be (seemingly) easily transduced with fluorescent reporters, optogenetic and chemogenetic actuators, proteomic probes, just

to cite a few. AAV-borne constructs can be used alone, as a mix of multiple AAVs, or combined with transgenic mouse lines to obtain conditional expression. Moreover, an steadily growing array of engineered capsid serotypes allows targeting of the brain via systemic delivery with increasing efficiency, often eliminating the need for time-consuming stereotaxic injections.
However, the versatility of AAV-mediated gene transduction in the brain must not be mistaken for a "shake-and-bake" ease of use. Employing a new construct, or even adapting a published one to different experimental conditions often requires a painstaking and lengthy optimization process, which requires a good amount of trial-and-error.
Through the discussion of AAV basics and of cases taken from my own experience, we will try to extract some principles for good AAV practice, as well as learning something new about synaptic plasticity.

Biosketch: Marco Mainardi graduated with honors in Biomolecular Science and Technology from the University of Pisa in 2006. The following year he obtained the Licentiate Diploma in Biology with honors at the completion of the Ordinary Course at the Scuola Normale Superiore, where he also obtained, in 2010, the Postgraduate Diploma in Neurobiology with honors, under the supervision of Lamberto Maffei and Matteo Caleo. After three years as a research fellow and fellow of the Accademia dei Lincei at the CNR Institute of Neuroscience in Pisa, he moved to the Institute of Physiology at the Catholic University of Rome as a fixed-term researcher. In 2017 he returned to Pisa, as a fixed-term researcher in the Biology Laboratory of the Scuola Normale Superiore. In 2019, he won a researcher position at the CNR Institute of Neuroscience. He is currently a CNR first researcher and is about to start as an associate professor of Physiology at the University of Padua.
Marco Mainardi works on strategies to manipulate the plasticity of nerve circuits and has authored more than 40 publications in international journals.

12:35 - 14:05

SYNAPTIC DYSFUNCTION AND MEMORY DEFICIT IN MODELS OF NEURODEGENERATION

Nicola Origlia - Neuroscience Institute - National Research Council, Pisa

Abstract: A common feature of neurodegenerative disorders is that they originate in specific areas of the brain and then spread to progressively larger regions over time, following an anatomically defined pattern of connections. Extensive literature identifies synaptic dysfunction as an early mechanism affected in the disease, which correlates with cognitive decline. However, how synaptic dysfunction originates and propagates in the affected brain is still largely obscure, and it is now one of the most compelling question in neuroscience research. Experimental models can help to propose new biological mechanisms mediating the progression of neurodegeneration and offer the opportunity to test pharmacological treatments.

Biosketch: Nicola Origlia, neurobiologist, holds a PhD and a specialisation in pharmacology from the University of Pisa. He has carried out research in the field of neuroscience at prestigious institutes (CNR; SISSA; Columbia University, NY) and has participated in and led international research projects (NIH, Telethon, AHAF, Alzheimer's Association). He has held positions as Associate Professor of Physiology for biotechnology (University of L'Aquila) and medical students (University of Pisa), and is a lecturer in Neurobiology for the Master of Science in Neuroscience course at the University of Pisa. Since 2011 he has been a researcher at the CNR Institute of Neurosciences, where he heads a research laboratory dedicated to the study of neurobiological mechanisms underlying neurodegenerative phenomena.

09:15 - 10:45

NEUROPLASTICITY IN A PRECLINICAL MODEL OF INFANTILE STROKE EXPERIENCE-DEPENDENT PLASTICITY, LEARNING AND MEMORY IN PHYSIOLOGY AND PATHOLOGY

Manuela Allegra - Neuroscience Institute - National Research Council, Padua

Abstract: The ability of the brain to reorganize its structure and function in response to intrinsic or extrinsic stimuli is defined as neuroplasticity. Plasticity of the nervous system is crucial throughout the lifespan, refining sensory systems during development, mediating learning and memory in adulthood and being the key mechanism for neuro-rehabilitation in case of injury and for the prevention of neurodegenerative disorders later in life. Using in vivo recording techniques (extracellular LFP recordings and calcium imaging), we will explore neuroplasticity in physiological and pathological conditions and we will describe how neuronal circuits of the hippocampus and neocortex can rewire their activity during learning and memory, and in response to brain injury.

Biosketch: She graduated in Neurobiology at the University of Pisa in 2009 under the supervision of Prof Yuri Bozzi. She obtained a PhD in Neurobiology at the Scuola Normale Superiore of Pisa in 2014, working in Prof Matteo Caleo's lab, where the main focus of her research activity was the study of neuroplasticity mechanisms in physiological and pathological conditions, using the visual system of rodent models. In 2017, Dr Allegra moved to Paris and joined the laboratory of Prof Christoph Schmidt-Hieber at Institut Pasteur. Here she was awarded a Marie Curie individual fellowship and her research activity was mainly focused on the hippocampal function in memory encoding and recall. In 2020, she was appointed a permanent research position by the CNR and she joined the Neuroscience Institute in Padua, where she has started her own research group with a starting grant from Fondazione CaRiPaRo.

11:00 - 12:30

IMMUNE SYSTEM AND SYNAPTOPATHIES INVESTIGATING THE INTERPLAY OF INNATE IMMUNITY AND BRAIN IN NEURODEVELOPMENT

Elisabetta Menna - Neuroscience Institute - National Research Council, Milan

Abstract: Maternal infections and prenatal inflammation are recognized risk factors for neurodevelopmental diseases. Astrocytes are glial cells essential for synapse formation and refinement, but they also may react to inflammatory environment affecting neuronal network homeostasis. However, how an inflammatory episode occurring during foetal development influences astrocyte generation and phenotype remains largely unknown.

In the brain, the innate immune molecule Pentraxin3 (PTX3) is produced by astrocytes and promotes the maturation of excitatory synapses. Its expression is induced by inflammatory stimuli both in mouse and in human iPSC-derived astrocytes. By using a mouse model of maternal immune activation (MIA) to mimic a viral or bacterial infection, with Poly(I:C) or LPS respectively, we demonstrated that astrocytes from MIA offspring retain a long-lasting molecular signature related to the type of immunogen used when analyzed three weeks after the maternal insult. When in co-cultures with wild-type neurons, MIA-derived astrocytes affect synapse formation and functional maturation.

We demonstrated that MIA affects PTX3 levels in the cerebral cortex, but not in the hippocampus, of the offspring, during the first and second postnatal weeks, a critical period for synapse development. Interestingly,

also the number of astrocytes is altered exclusively in the cerebral cortex at this stage. These results underscore, for the first time, the contribution of astrocytes to the long-term alterations observed during brain development following prenatal inflammation.

Biosketch: My research is focused on the study of the mechanisms involved in the formation and function of the synapses and in defining how these processes get wrong in neuro-developmental diseases, such as ASD and intellectual disability. Inflammation has been recognized as an important factor contributing to CNS injury, my research aims at defining whether prenatal inflammation or deregulation of immune molecules affect synaptic protein networks and function, thus increasing the risk of neurodevelopmental disorders. These lines of research resulted in the identification of key immune molecules and signalling pathway which directly affect synaptic protein networks and synapse physiology (PTX3, IL1beta and IL6). The main objective of my research is to identify new targets suitable for therapeutic intervention or preventive strategies in humans. I'm also investigating the impact of SARS-CoV-2 infection on the central nervous system and, in particular, whether the inflammatory response triggered by SARS-CoV-2 infection during pregnancy may affect infant neurodevelopment.

13:45 - 15:15

SPECIAL LECTURE

PIETRO PIETRINI - SCUOLA IMT ALTI STUDI LUCCA

SEDI DI SVOLGIMENTO DELLE LEZIONI

28 agosto: Complesso Interdipartimentale "A. Vallisneri", viale G. Colombo 3/ Via U. Bassi 58b
29 agosto: Campus di Biologia e Biomedicina "Fiore di Botta", Via del Pescarotto 8
30 agosto: Complesso Interdipartimentale "A. Vallisneri", viale G. Colombo 3/ Via U. Bassi 58b