Relazione

sulle attività svolte dal Centro di Ricerca in Neuroscienze nell'anno 2020

Il Centro di Ricerca in Neuroscienze (di seguito denominato "il Centro"), afferente al Dipartimento di Biotecnologie e Scienze della Vita dell'Università dell'Insubria, è stato istituito nell'anno 2003 (Regolamento emanato con Decreto Rettorale n. 4938 il 3 marzo 2003). Il Regolamento del Centro è stato riformulato nel luglio 2020 (ultime modifiche approvate dal Senato Accademico il 15 luglio 2020).

1. Componenti

Gli attuali componenti del Centro sono Professori e Ricercatori dell'Università degli Studi dell'Insubria, affiliati al Dipartimento di Biotecnologie e Scienze della Vita (DBSV), al Dipartimento di Medicina e Chirurgia (DMC), o al Dipartimento di Scienza e Alta Tecnologia (DiSAT):

Tiziana Alberio (DiSAT)
Sergio Balbi (DBSV)
Elena Bossi (DBSV)
Camilla Callegari (DMC)
Marco Cosentino (DMC)
Mauro Fasano (DiSAT)
Lia Chiara Forti (DBSV)
Cristina Giaroni (DMC)
Stefano Giovannardi (DBSV)
Charlotte Kilstrup-Nielsen (DBSV)
Franca Marino (DMC)
Marco Mauri (DBSV)
Alberto Passi (DMC)
Cristina Roseti (DBSV)
Tiziana Rubino (DBSV)
Silvia Sacchi (DBSV)
Erica Zamberletti (DBSV)

2. Direttore e Consiglio Scientifico

Il 27 gennaio 2020 sono state rinnovate le cariche direttive del Centro (Direttore e Consiglio Scientifico) per il triennio 2020-2022: l'attuale Direttore del Centro è la Dr.ssa Lia Chiara Forti, ed il Consiglio Scientifico è composto dai Professori Marco Cosentino, Charlotte Kilstrup-Nielsen, Cristina Roseti, Silvia Sacchi.

3. Obiettivi dell'istituzione e linee di ricerca

Il Centro di Ricerca in Neuroscienze ha lo scopo di promuovere la ricerca nell'ambito delle Neuroscienze, ovvero sulla biologia cellulare, genetica, biochimica e fisiologia delle cellule nervose, sulla neurofarmacologia e neuroimmunologia, sulle patologie funzionali e degenerative del sistema nervoso, e favorire lo sviluppo di un approccio interdisciplinare e multidisciplinare per approfondire le conoscenze nel campo delle Neuroscienze raccordando le competenze dei gruppi operanti presso l'Università degli Studi dell' Insubria.

Le linee di ricerca degli afferenti al Centro sono elencate qui di seguito (con breve descrizione, in lingua inglese):

Tiziana Alberio, Mauro Fasano - *Laboratorio di Biochimica e Proteomica Funzionale*

The Biochemistry and Functional Proteomics lab research is mainly focused on protein biochemistry. Our projects focus on Parkinson's Disease with two main goals: the elucidation of pathogenetic mechanisms and the discovery of peripheral biomarkers. We both use standard biochemistry methods and proteomics to find proteins and pathways involved in neurodegenerative processes. We employ in-house routines to statistically analyze omics data and the systems biology approach to interpret complex results. We have established several collaborations to describe Parkinson's Disease specific mechanisms from general pathways of neurodegeneration and we are often involved in other neuroscience projects in order to analyze and interpret complex data.

Elena Bossi, Cristina Roseti - *Laboratorio di Fisiologia Cellulare e Molecolare*

Our research topics are focused on the structure, function and regulation of ion channels and membrane transporters involved in numerous diseases, such as Parkinson and chronic pain. By using electrophysiological techniques, molecular biology, immunochemical, biochemical and fluorimetric techniques, several proteins involved in the membrane translocation of ions and solutes have been studied and characterized by the laboratory of cellular and molecular physiology. Electrogenic membrane transporters are the main subject of research: the protein belonging to neurotransmitter sodium symporter or SLC6 family, like GAT1, GlyT1, DAT and B0AT1 are studied. Moreover, other transporters involved in neurotransmission are also investigated, like SLC1 glutamate transporters and in gut-brain relationships also SLC15a family (PEPT1 oligo-peptides transporters) is also deeply studied. Recently we have also investigated some TRP channels and their role in chronic pain onset and persistence. The proteins are studied in heterologous systems: Xenopus oocytes or cell lines. In these cells cDNAs coding for wild type or recombinant proteins are transfected or membrane collected from healthy or pathological human tissue transplanted. The functional and/or pharmacological characterization is usually conducted by two-electrode voltage clamp, but also by uptake using fluorescent probes and HPLC methods. Quantification or alteration in protein expression is studied by immunochemistry or qPCR approaches.

Marco Cosentino, Franca Marino - *Centro di Ricerca in Farmacologia Medica*

Our main research interests concern neuro- and immunopharmacology with particular regard to the neuroendocrine modulation of immune response. Recent research: pharmacological modulation of endogenous catecholamines in human lymphocytes and its functional relevance in health and disease such as multiple sclerosis and Parkinson's disease. Other interests: clinical pharmacology and pharmacogenetics, pharmacoepidemiology and pharmacovigilance, pharmacology of herbal medicines.

Lia Chiara Forti – *Laboratorio di Neurofisiologia Cellulare*

The recent research topic in the lab is the study of functional effects of acute stress (AS) on synaptic transmission and membrane excitability of neurons in the rodent prefrontal cortex (PFC). Our expertise includes electrophysiological patch-clamp recordings, field potential recordings, planar multielectrode arrays recordings and Ca^{2+} imaging, in brain slices and cultured cells. We are exploring AS effects on miniature and spontaneous synaptic currents and membrane firing regulation in different regions and layers of the PFC. My past interests have been mainly focused on cerebellar physiology, including patch-clamp and Ca^{2+} imaging studies of synaptic inputs to cerebellar granular layer interneurons, regulation of their pacemaker firing, and axonal action potential propagation in molecular layer interneurons.

Cristina Giaroni – *Laboratorio di fisiofarmacologia del sistema nervoso enterico*

Our main research topics are centered on the cellular and molecular mechanisms involved in the adaptive changes occurring in the enteric nervous system which underlay the pathophysiology of main gut diseases, such as intestinal ischemia/reperfusion injury, intestinal inflammation and irritable bowel syndrome. In this regard, we are currently focusing our research on the relevance of the enteric microenvironment and the microbiota in the development of enteric neuropathies underlying intestinal ischemia and inflammation

Charlotte Kilstrup-Nielsen – *Laboratorio di Neurobiologia Molecolare*

The research focus of the laboratory of Molecular Neurobiology is to characterize the functions of X-linked kinase CDKL5 in the nervous system and the consequences of its deficiency, leading in humans to a severe neurologic disorder. The goal of our studies is to provide data that can pave the way for therapeutic approaches. For these studies we make large use of *Cdkl5*-KO neurons and mice. We have through our studies contributed significantly to the current knowledge of CDKL5 functions and the consequences of some pathologic mutations. We also showed that in neurons, CDKL5 levels are tightly controlled by phosphorylation-dependent degradation. Our present focus is to characterize synaptic defects in CDKL5 deficient neurons and the role of CDKL5 in regulating microtubule dynamics. We have demonstrated that surface expression of the AMPA-receptor subunit GluA2 is reduced in *Cdkl5*-KO neurons but can be restored upon treatment with the antidepressant drug Tianeptine. Regarding microtubules, we have identified the +TIP CLIP170 as an import downstream effector of CDKL5 possibly representing a novel druggable target for CDKL5 deficiency disorder.

Tiziana Rubino, Erica Zamberletti - *Gruppo di Neuropsicofarmacologia*

Ongoing research lines in the lab are aimed at evaluating: 1) The therapeutic potential of some phytocannabinoids in models of autism; 2) The role of the endocannabinoid system in the pathogeneqsis of psychiatric disorders; 3) The ability of cannabidiol to modulate the long-term negative consequences of adolescent delta-9-tetrahydrocannabinol exposure on the brain; 4) the role of the endocannabinoid system in adolescent brain maturation/remodeling

Silvia Sacchi – Laboratorio *"The Protein Factory 2.0"*

We work in molecular mechanisms involved in the regulation of the catabolism of the atypical neuromodulators D-serine (D-Ser) and D-aspartate (D-Asp) in the brain. D-Ser is an essential activator of the NMDA receptors since it acts as the principal co-agonist, while D-Asp is an alternative agonist. Alterations in their metabolism have been shown to affect the receptor functionality, thus being implicated in several neurological disorders, among which schizophrenia, AD and ALS. In particular, we are interested in deciphering how the functional properties of the two human FAD-dependent flavooxidases responsible for the degradation of D-Ser and D-Asp - D-amino acid oxidase (hDAAO) and D-aspartate oxidase (hDDO), respectively - are modulated (cofactor/ligand binding, interaction with regulatory proteins, subcellular localization, degradation pathway). Indeed, despite their relevant physiological role, little is known about the processes entailed in establishing hDAAO and hDDO

cellular levels and activity. Investigating them will provide crucial information concerning the regulation of D-Ser and D-Asp levels in the brain, with remarkable implications for the understanding of the modulation of NMDAR-mediated neurotransmission in physiological and pathological conditions. Furthermore, since the precursor L-Ser, synthesized via the so called "phosphorylated pathway", is the key rate-limiting factor for maintaining steady-state levels of D-Ser in the adult brain (it is converted to the D-enantiomer by serine racemase), we recently started to study the enzymes catalyzing the different biosynthetc steps: phosphoglycerate dehydrogenase (PHGDH), phosphoserine aminotransferase (PSAT) and phosphoserine phosphatase (PSP). Again, the factors affecting the amount and the activity of these enzymes are still largely elusive. Thus we are investingating the L-Ser pathway using various biochemical approaches, cell model systems and brain samples, with the ambitious aim to identify potential molecular targets and propose alternative strategies to modulate D-Ser levels.

4. Finanziamenti

Il Centro non ha attualmente fonti di finanziamento proprie: le attività del Centro (vedi sotto, par. 5 e 6) sono svolte all'interno delle strutture e dei servizi resi disponibili dall'Ateneo. Le linee di ricerca caratterizzanti il centro sono portate avanti dai singoli Laboratori afferenti grazie a finanziamenti propri.

5. Organizzazione di workshop, convegni, eventi

i) Il Centro ha organizzato nel settembre 2020 una **Giornata Scientifica** (vedi locandina, All.1) in cui i giovani collaboratori degli aderenti al Centro hanno presentato i risultati delle loro ricerche recenti. L'evento si è tenuto online sulla piattaforma Microsoft Teams, in rispetto delle regole sanitarie dovute all'emergenza Covid-19. L'evento ha avuto la partecipazione di 56 persone, tra aderenti al Centro, studenti dei Corsi di Laurea e Corsi di Dottorato di Ricerca dell'Insubria, uditori esterni. La Giornata si è articolata in 11 comunicazioni ed una Plenary Lecture tenuta da un esterno, il prof. H.E. Gendelman (University of Nebraska Medical Center). Il Centro ha prodotto un Libro degli Abstract della Giornata Scientifica (All.1a)

ii) Il Centro ha partecipato all'organizzazione di un "**Workshop di Neuroscienze**", previsto il 20 marzo 2020 nell'ambito della "Brain Awareness Week" (BAW), con i seminari di cinque neuroscienziati del CNR Milano, Università di Padova e Università di Roma – La Sapienza, ed una Lecture Plenaria del prof. A.Oliverio (Università di Roma – La Sapienza) (Vedi All.2, All.3). A causa dell'emergenza COVID le conferenze sono state rimandate a data da definire.

iii) Il Centro ha patrocinato l'organizzazione del ciclo "**Seminars in Cellular Neurophysiology Techniques**" per il Dottorato di Ricerca in Medicina Sperimentale e Traslazionale. Si è trattato di un ciclo di 10 Seminari Didattici organizzati da Lia Forti e tenuti sia da aderenti al Centro (Forti, Bossi, Roseti, Giovannardi) che da ospiti esterni. Il ciclo è iniziato nel gennaio 2020. A causa dell'emergenza COVID, gli ultimi 3 Seminari sono stati rimandati a data da destinarsi. Il Seminario dei prof. Giovannardi e Schiavon, previsto per il 28 febbraio, si è tenuto online su piattaforma Teams il 15/05/2020.

iv) Il Centro ha patrocinato l'organizzazione di alcuni Seminari da parte di suoi aderenti:

20/4/20 Cristoforo Comi (UniUPO)
"20 anni di ricerca in neuroimmunologia clinica e sperimentale all'Università del Piemonte Orientale" organizzato dal Centro di Ricerca in Farmacologia Medica;

12/6/20 Frederico Pereira (UniCoimbra, P)
"Behavioral, glial and receptor for advanced glycation-end products signature of dopaminergic toxicants" organizzato dal Centro di Ricerca in Farmacologia Medica;

luglio 2020 (evento rimandato a data da destinarsi a causa dell'emergenza COVID): III edizione della School on Neuroimmune Pharmacology nell'ambito delle Lake Como School (qui informazioni sulla I edizione: https://bit.ly/2TU3AAD, e la II: https://bit.ly/2U48ESd). Evento organizzato dal Centro di Ricerca in Farmacologia Medica.

6. Pubblicazioni degli aderenti al Centro

Nel seguito, l'elenco delle pubblicazioni con affiliazione al Centro di Ricerca in Neuroscienze, per il quinquennio 2016-2020.

Magistrelli L, Storelli E, Rasini E, Contaldi E, Comi C, Cosentino M, Marino F. Relationship between circulating CD4+ T lymphocytes and cognitive impairment in patients with Parkinson's disease [published online ahead of print, 2020 Jul 17]. *Brain Behav Immun*. 2020;S0889-1591(20)30584-5. doi:10.1016/j.bbi.2020.07.005

De Francesco E, Terzaghi M, Storelli E, Magistrelli L, Comi C, Legnaro M, Mauri M, Marino F, Versino M, Cosentino M. CD4+ T-Cell Transcription Factors in Idiopathic REM Sleep Behavior Disorder and Parkinson's Disease [published online ahead of print, 2020 Jul 10]. *Mov Disord*. 2020;10.1002/mds.28137. doi:10.1002/mds.28137

Zilocchi M, Colugnat I, Lualdi M, Meduri M, Marini F, Corasolla Carregari V, Moutaoufik MT, Phanse S, Pieroni L, Babu M, Garavaglia B, Fasano M, Alberio T. Exploring the Impact of PARK2 Mutations on the Total and Mitochondrial Proteome of Human Skin Fibroblasts. Front Cell Dev Biol. 2020 Jun 11;8:423. doi:10.3389/fcell.2020.00423. PMID: 32596240; PMCID: PMC7300190.

Zilocchi M, Finzi G, Lualdi M, Sessa F, Fasano M, Alberio T. Mitochondrial alterations in Parkinson's disease human samples and cellular models. Neurochem Int. 2018 Sep;118:61-72.
doi: 10.1016/j.neuint.2018.04.013. Epub 2018 Apr 26. PubMed PMID: 29704589.

Alberio T, Forlani G, Lualdi M, Tosi G, Accolla RS, Fasano M. Neonatal Fc receptor is involved in the protection of fibrinogen after its intake in peripheral blood mononuclear cells. J Transl Med. 2018 Mar 14;16(1):64. doi: 10.1186/s12967-018-1446-2. PubMed PMID: 29540212; PubMed Central PMCID:PMC5853075.

Malty RH, Aoki H, Kumar A, Phanse S, Amin S, Zhang Q, Minic Z, Goebels F, Musso G, Wu Z, Abou-Tok H, Meyer M, Deineko V, Kassir S, Sidhu V, Jessulat M, Scott NE, Xiong X, Vlasblom J, Prasad B, Foster LJ, Alberio T, Garavaglia B, Yu H, Bader GD, Nakamura K, Parkinson J, Babu M. A Map of Human Mitochondrial Protein Interactions Linked to Neurodegeneration Reveals New Mechanisms of Redox Homeostasis and NF-κB Signaling. Cell Syst. 2017 Dec 27;5(6):564-577.e12. doi:10.1016/j.cels.2017.10.010. Epub 2017 Nov 8. PubMed PMID: 29128334; PubMed Central PMCID: PMC5746455.

Monti C, Colugnat I, Lopiano L, Chiò A, Alberio T. Network Analysis Identifies Disease-Specific Pathways for Parkinson's Disease. Mol Neurobiol. 2018 Jan;55(1):370-381. doi: 10.1007/s12035-016-0326-0. Epub 2016 Dec 21. PubMed PMID: 28004338.

Fasano M, Monti C, Alberio T. A systems biology-led insight into the role of the proteome in neurodegenerative diseases. Expert Rev Proteomics. 2016Sep;13(9):845-55.
doi: 10.1080/14789450.2016.1219254. Epub 2016 Aug 22. Review. PubMed PMID: 27477319.

Di Pierro A, Bondi H, Monti C, Pieroni L, Cilio E, Urbani A, Alberio T, Fasano M, Ronci M. Experimental setup for the identification of mitochondrial protease substrates by shotgun and top-down proteomics. EuPA

Open Proteom. 2016 Feb 22;11:1-3. doi: 10.1016/j.euprot.2016.02.002. eCollection 2016 Jun. PubMed PMID: 29900104; PubMed Central PMCID: PMC5988556.

Fasano M, Alberio T, Babu M, Lundberg E, Urbani A. Towards a functional definition of the mitochondrial human proteome. EuPA Open Proteom. 2016 Jan 7;10:24-27. doi: 10.1016/j.euprot.2016.01.004. eCollection 2016 Mar. PubMed PMID: 29900096; PubMed Central PMCID: PMC5988588.

Bondi H, Zilocchi M, Mare MG, D'Agostino G, Giovannardi S, Ambrosio S, Fasano M, Alberio T. Dopamine induces mitochondrial depolarization without activating PINK1-mediated mitophagy. J Neurochem. 2016 Mar;136(6):1219-1231. doi:10.1111/jnc.13506. Epub 2016 Jan 13. PubMed PMID: 26710242.

Nawaz MS, Giarda E, Bedogni F, La Montanara P, Ricciardi S, Ciceri D, Alberio T, Landsberger N, Rusconi L, Kilstrup-Nielsen C. CDKL5 and Shootin1 Interact and Concur in Regulating Neuronal Polarization. PLoS One. 2016 Feb 5;11(2):e0148634. doi: 10.1371/journal.pone.0148634. eCollection 2016. PubMed PMID: 26849555; PubMed Central PMCID: PMC4746202.

Barbiero I, Peroni D, Tramarin M, Chandola C, Rusconi L, Landsberger N, Kilstrup-Nielsen C. (2017) The neurosteroid pregnenolone reverts microtubule derangement induced by the loss of a functional CDKL5-IQGAP1 complex. *Hum Mol Genet* 26, 3520-3530.

Tramarin M, Rusconi L, Pizzamiglio L, Barbiero I, Peroni D, Scaramuzza L, Guilliams T, Cavalla D, Antonucci F, Kilstrup-Nielsen C. (2018) The antidepressant tianeptine reverts synaptic AMPA receptor defects caused by deficiency of CDKL5. *Hum Mol Genet*. 27, 2052-2063.

Vigli D, Rusconi L, Valenti D, La Montanara P, Cosentino L, Lacivita E, Leopoldo M, Amendola E, Gross C, Landsberger N, Laviola G, Kilstrup-Nielsen C, Vacca RA, De Filippis B. (2019) Rescue of prepulse inhibition deficit and brain mitochondrial dysfunction by pharmacological stimulation of the central serotonin receptor 7 in a mouse model of CDKL5 disorder. *Neuropharmacology.* 144, 104-114.

Barbiero I, Peroni D, Siniscalchi P, Rusconi L, Tramarin T, De Rosa R, Motta P, Bianchi M, Kilstrup-Nielsen C. (2020) Pregnenolone and pregnenolone-methyl-ether rescue neuronal defects caused by dysfunctional CLIP170 in a neuronal model of CDKL5 Deficiency Disorder. *Neuropharmacology*, 164, 107897.

Trovò L, Fuchs C, De Rosa R, Barbiero I, Tramarin M, Ciani E, Rusconi L, Kilstrup-Nielsen C (2020) The green tea polyphenol epigallocatechin-3-gallate (EGCG) restores CDKL5-dependent synaptic defects in vitro and in vivo. *Neurobiol Dis,* 138:104791.

Frasca A, Spiombi E, Palmieri M, Valente M, Bergo A, Leva A, Kilstrup-Nielsen C, Bianchi F, Di Cunto F, Landsberger N. MECP2 mutations affect ciliogenesis: a novel perspective for Rett syndrome and related disorders. *EMBO Molecular Medicine*. [accepted for pubblication].

Prini P, Zamberletti E, Manenti C, Gabaglio M, Parolaro D, Rubino T. Neurobiological mechanisms underlying cannabis-induced memory impairment. Eur Neuropsychopharmacol. 2020 Mar 2. pii: S0924-977X(20)30061-4.

Cuccurazzu B, Zamberletti E, Nazzaro C, Prini P, Trusel M, Grilli M, Parolaro D, Tonini R, Rubino T. (2018). Adult Cellular Neuroadaptations Induced by Adolescent THC Exposure in Female Rats Are Rescued by Enhancing Anandamide Signaling. Int J Neuropsychopharmacol. 21(11):1014-1024.
Prini P, Rusconi F, Zamberletti E, Gabaglio M, Penna F, Fasano M, Battaglioli E, Parolaro D, Rubino T. (2018). Adolescent THC exposure in female rats leads to cognitive deficits through a mechanism involving chromatin modifications in the prefrontal cortex. J Psychiatry Neurosci 43(2):87-101.

Prini P, Penna F, Sciuccati E, Alberio T, Rubino T. Chronic Δ^8-THC Exposure Differently Affects Histone Modifications in the Adolescent and Adult Rat Brain. Int J Mol Sci. 2017 Oct 4;18(10). pii: E2094. doi: 10.3390/ijms18102094. PubMed PMID: 28976920; PubMed Central PMCID: PMC5666776.1

Scheggia D, Zamberletti E, Realini N, Mereu M, Contarini G, Ferretti V, Managò F, Margiani G, Brunoro R, Rubino T, De Luca MA, Piomelli D, Parolaro D, Papaleo F. (2018). Remote memories are enhanced by COMT activity through dysregulation of the endocannabinoid system in the prefrontal cortex. Mol Psychiatry. 23(4):1040-1050.

Struik D, Fadda P, Zara T, Zamberletti E, Rubino T, Parolaro D, Fratta W, Fattore L. (2017). The anabolic steroid nandrolone alters cannabinoid self-administration and brain CB1 receptor density and function. Pharmacol Res. 115:209-217.

Simonnet A, Zamberletti E, Cador M, Rubino T, Caillé S. (2017). Chronic FAAH inhibition during nicotine abstinence alters habenular CB1 receptor activity and precipitates depressive-like behaviors. Neuropharmacology. 113(Pt A):252-259.

7. Collaborazioni e convenzioni

Dal 2015, Il Centro è affiliato al Consorzio NEUROMI (Milan Center for Neuroscience; https://neuromi.it/). Si tratta di un Consorzio la cui missione è la promozione della ricerca e dell'istruzione di alto livello multi-disciplinare nel campo delle Neuroscienze, rivolte alla comprensione dei meccanismi di funzionamento e malfunzionamento del sistema nervoso alle diverse età. Sono in corso di rinnovo le affiliazioni individuali degli aderenti al Centro a NEUROMI.

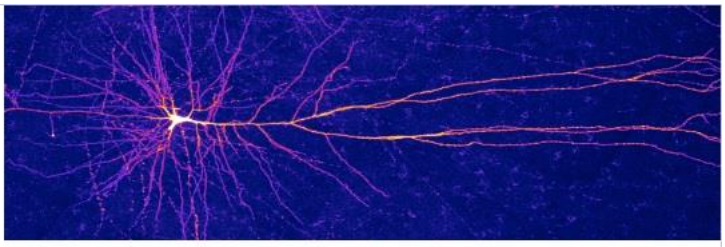
Redatto da Lia Chiara Forti

9/10/2020

Allegato 1


Centro NeuroScienze
Università degli Studi dell'Insubria
Scientific Day
Center for Research in NeuroScience
UNIVERSITÀ DEGLI STUDI DELL'INSUBRIA
DBSV Dipartimento di Biotecnologie e Scienze della Vita
16 settembre 2020
Online Event - Microsoft Teams
In order to receive the link please write to:
Centro.Neuroscienze@uninsubria.it
10:00 Welcome - Session opening
Lia Forti
10:10 Dissociative disorders and brain dysfunctions: findings from scientific literature
Ivano Caselli
10:30 Molecular mechanisms of microtubule derangement in CDKL5 deficiency disorder, and target-based theraphy
Isabella Barbiero
10:50 Cannabidivarin treatment rescues autism-like behaviors and reduces hippocampal microglia activation induced by prenatal valproic acid exposure in rats
Erica Zamberletti
11:10 Acute stress effects on synaptic properties and excitability in pyramidal neurons of the rat prefrontal cortex, and their modulation by ketamine
Emanuele Schiavon
11:30 Coffee break - Sponsors presentations
11:45 Investigating the metabolism of D-amino acids, atypical signaling molecules in neurotransmission
Silvia Sacchi
12:05 Obeticholic acid effects on dopamine transporter expressed in Xenopus leavis oocytes
Tiziana Romanazzi
12:25 Glutamate transporter EAAT2 in LRRK2-associated Parkinson's disease
Angela Di Iacovo
12:45 Lunch
14:30 Potential role of CD4+ T Lymphocytes transcription factors in the development of long-term motor complications in Parkinson's disease
Luca Magistrelli
14:50 Dopaminergic modulation of the immune response and role in Parkinson's disease
Alessia Furgiuele
15:10 Linking phenotype to genotype: proteome signatures of neurodegenerative disorders sharing the same gene mutation
Adeena Shafique
15:30 Characterization of two nociceptors: TRPM8 and TRPV4 transplanted in Xenopus Leavis oocytes from patients affected by chronic pain
Stefania Fozzato
16:00 Plenary lecture - Prof. H.E. Gendelman
"Brain Immunity, COVID-19 and Neurodegenerative Disease"
"Margaret R. Larson" Professor of Internal Medicine and Infectious Diseases, Chairman of the Department of Pharmacology and Experimental Neuroscience, and Director of the Center for Neurodegenerative Disorders at the University of Nebraska Medical Center
Dr. Gendelman's lab has a broad research experience in the diagnostics, pathogenic mechanisms and therapies for neurodegenerative disorders.
The major focus for his research is on the role played by glial inflammatory activities in brain diseases, bridging immunology, neuroscience and pharmacology for the study of HIV-1-associated neurocognitive disorders, Parkinson's disease and ALS.
17:00

Allegato 2



WORKSHOP DI NEUROSCIENZE

Per la Scuola di Dottorato
Settimana del Cervello 2020
20 Marzo 2020

LA PARTECIPAZIONE E' GRATUITA

Si prega di confermare la partecipazione inviando una mail all'indirizzo mail:
brainweek2020@gmail.com

Collegio Cattaneo 9.30-15.00
Via Dunant 3, Varese

9.30 – 10.15	**Extracellular vesicles at the neuron surface: implication in Alzheimer's disease** - *Claudia Verderio*, CNR Milano
10.15 – 11.00	**Contribution of Glutamatergic transmission to synaptopathies** - *Maria Passafaro*, CNR Milano
11.00 – 11.30	Coffee break
11.30 – 12.15	**Towards a role of glial cells in Parkinson's disease** - *Laura Civiero*, Università di Padova
12.15 – 13.00	**Big Data in Neuroscience** – *Alessandro Mauro*, Università di Torino
13.00 – 14.15	Lunch break
14.15 – 15.00	**Epilepsy and neurodevelopmental diseases** - *Eleonora Palma*, Università di Roma La Sapienza

Evento aperto al pubblico

Per ulteriori informazioni:
brainweek2020@gmail.com

Aula Magna Granero Porati,
Via Dunant 3, Varese

15.15 – 17.00	**Determinismo e plasticità** – *Alberto Oliverio*, Prof. emerito, Università di Roma La Sapienza

Il Prof. Oliverio è uno studioso dei rapporti che intercorrono tra sviluppo, funzionamento cerebrale e fattori genetici, con particolare attenzione ai processi di apprendimento e memoria, e della psicobiologia dello stress.

Dipartimento di Biotecnologie e Scienze della Vita

BRAIN AWARENESS WEEK Dana Foundation

Centro di Ricerca in Neuroscienze
Università degli Studi dell'Insubria

Allegato 3

Determinismo e plasticità

Alberto Oliverio

Università La Sapienza, Roma.

Settimana del Cervello 2020

20 Marzo 2020

Aula Magna Granero Porati, Via Dunant, 3 Varese
ore 15.15

Evento aperto al pubblico

Alberto Oliverio è professore emerito di Psicobiologia all'Università La Sapienza di Roma ed ha lavorato in numerosi Istituti di ricerca internazionali. Durante la sua lunga carriera si è occupato dei rapporti che intercorrono tra sviluppo, funzionamento cerebrale e fattori genetici, con particolare attenzione ai processi di apprendimento e memoria. E' autore di oltre 400 pubblicazioni scientifiche, saggi professionali, didattici e di divulgazione tra cui i più recenti riguardano i rapporti tra comportamento e strutture cerebrali (*Geografia della mente*), tra cervello ed inconscio (*La vita nascosta del cervello*) e tra cervello e mente (*Cervello*). Nel suo ultimo libro "*Il cervello che impara*" illustra come le neuroscienze abbiano modificato le nostre conoscenze su attenzione, emozione, apprendimento, con importanti ricadute pratiche sulle modalità con cui facciamo esperienza nel corso della vita. Nel 2017, ha ricevuto il Premio Feltrinelli dell'Accademia Nazionale dei Lincei per Letteratura e Scienze.

Per ulteriori informazioni: brainweek2020@gmail.com

BRAIN AWARENESS WEEK Dana Foundation

Allegato 4 (1/3)

Seminars on **Cellular Neurophysiology Techniques**

PhD Course in
Experimental and Translational Medicine
University of Insubria

Lecturer: Dr. Lia Forti (DBSV, Busto Arsizio, University of Insubria)

Invited lecturers: prof.Elena Bossi, dr.Cristina Roseti, dr.Stefano Giovannardi, dr.Emanuele Schiavon (DBSV, University of Insubria), and others (to be announced)

Neurons are excitable cells communicating to each other mostly by electrical signals. These signals (membrane potential changes and current flowing through ionic channels) occur on very fast timescales of the order of milliseconds. Their nature and speed impose serious temporal constraints on the experimental methods used for studying neuronal physiology.

The experimental techniques that better meet neurophysiological time constraints are *electrophysiology*, the *fluorescence imaging* techniques, and the recently developed *optogenetic techniques*. The **goal** of this cycle of Seminars is to provide to PhD students in Biomedical Sciences
- the bases for understanding the principles of these techniques and the information they provide;
- the ability to read and understand studies that use these techniques;
- the ability to explore their potential, future applications and new developments.

The seminar topics are listed below, organized in units 1 – 7. Each unit is structured with a Refresher lecture, a Technical lecture and a Journal Club, and requires two 2hrs-Seminars (with the exception of units 4 and 5 requiring only 1 Seminar). Units 1, 2 will be in all cases covered in the Seminar Cycle, together with a choice of other units to be discussed according to the students' interests.

A total of 10 seminars will be held weekly between January 17th and March 27th 2020, in Villa Manara, via Manara 7, Busto Arsizio.

A **presentation** of the Seminar Cycle will take place on **December 12th, 2019 at 4:00 pm** at Villa Manara.

The interested students are invited to **contact** Lia Forti at <lia.forti@uninsubria.it>

Allegato 4 (2/3)

Seminar Topics:

1. Jan 17th, 2020 - 3:30-5:30 pm
Refresher 1: Ionic Channels and Excitable Membranes
Membrane resting potential. Biophysical characterization of ion channels: voltage-dependent ion channels, ionotropic receptors.

Electrophysiological Techniques 1:
Intracellular Recordings: voltage-clamp and current-clamp.
Patch-clamp. Single-channel and whole-cell recordings.

1a. Jan 24th, 2020

3:30-4:30 pm *Journal Club 1*: on original papers studying **ionic channels and receptors** in coltured preparations with patch-clamp: biophysical properties, modulation, pharmacology

4:30-5:30 pm Heterologous expression systems. Dual electrode voltage clamp in Xenopus oocytes (Prof. Elena Bossi)

2. Jan 31st, 2020 - 3:30-5:30 pm
Refresher 2: Synaptic Transmission
Biophysical mechanisms of **neurotransmitter release**. Short and long-term **synaptic plasticity**. Diversity of synaptic mechanisms across **excitatory** and **inhibitory** synapses.

Electrophysiological Techniques 2:
Extracellular recordings (field potentials and *multi-unit* recordings). Multielectrode recordings.

2a. Feb 7th, 2020 - 3:30-5:30 pm
Journal Club 2: on original papers studying the basal properties of **synaptic transmission** in coltures and in *ex-vivo* preparations (slices), and the **plasticity** properties of specific **synaptic connections**, using patch clamp, intracellular and extracellular recordings.

3. Feb 14th, 2020 - 3:30-5:30 pm
Refresher 3: Input Integration and firing patterns In Neurons.
Propagation of synaptic potentials in dendrites. Generation and propagation of action potentials in axons and dendrites: diversity of firing patterns across neuronal subtypes and underlying mechanisms.

3a. Feb 21st, 2020 - 3:30-5:30 pm
Journal Club 3: on original papers studying **neurological disorders:** alterations of neuronal membrane excitability and firing patterns, of synaptic transmission, and of network excitability in specific pathologies.

Invited Seminar : GABAR and nAChR dysfunctions in human diseases (dr. C. Roseti)

4. Feb 28th, 2020 - 3:30-5:30 pm
Optical Techniques
(dr. S. Giovannardi) - Fluorescence Microscopy
- Exogenous fluorescent markers: Fluorometric measurement of Ca^{2+} ion dynamics (*Ca^{2+} imaging*) and pH dynamics (*pHluorins*)
- Confocal microscopy and multiphoton microscopy
- Fluorometric measurement of membrane potential (with *voltage-sensitive dyes*)

Allegato 4 (3/3)

- Local control of the dynamics of [Ca^{2+}] and other molecular species activated through UV photolysis of photosensitive *caged compounds*

(dr.Emanuele Schiavon)

- Genetically engineered fluorescent markers
- [Ca^{2+}] imaging *in-vivo* with two-photon microscopy

4a. Mar 6th, 2020 - 3:30-5:30 pm

Journal Club 6: on original papers using optical techniques (to be chosen)

5. Mar 13th, 2020 - 3:30-5:30 pm *[to be confirmed]*

Optogenetics [Invited Lecturer, *to be announced*]: Technique for stimulating/inhibiting the firing of specific neuronal subtypes genetically engineered to express opsins. Opsins are proteins that can form photosensitive ionic channels, opened or closed by light. This technique can be used for measuring neuronal input/output properties, and for studying animal behaviour (from worms to mammals) in conditions of specific and local neuronal activation or inactivation.

5a. Mar 27th, 2020 - 3:30-5:30 pm

Journal club 7: on original papers using optogenetics techniques

Students will be also invited to attend the Neuroscience Seminars that will be organized by DBSV and the Center for Neuroscience at the University of Insubria during the Brain Awareness Week (March 20, 2020)

For information:

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