Università degli Studi dell'Insubria

Centro di Ricerca in

Neuroscienze

GIORNATA SCIENTIFICA 2020

16 settembre 2020

Centro NeuroScienze

Università degli Studi dell'Insubria

***Segreteria del Centro**: Dipartimento di Biotecnologie e Scienze della Vita, Via J.H. Dunant n. 2, 21100 Varese VA - Tel. 0332 421392, E-mail: Centro.Neuroscienze@uninsubria.it*

Indice

Giornata Scientifica 2020

PRESENTAZIONE DEL CENTRO DI RICERCA IN NEUROSCIENZE

Il Centro di Ricerca in Neuroscienze è stato fondato nel 2003 presso l'Università dell'Insubria. L'obiettivo del Centro è stato, dalla sua nascita, quello di costituire un punto di incontro tra i gruppi di ricerca dell'area biomedica e clinica presenti nell'Ateneo, favorendo lo scambio di conoscenze e la nascita di collaborazioni su tematiche attinenti alle Neuroscienze.

Il Centro opera organizzando periodiche riunioni dei laboratori di ricerca dei suoi membri, afferenti a diversi Dipartimenti dell'Ateneo, in cui i giovani collaboratori sono invitati a presentare comunicazioni sulle loro attività. Inoltre, il Centro collabora all'organizzazione di Seminari specialistici e divulgativi su tematiche neuroscientifiche, promuovendo la conoscenza dei meccanismi fisiologici e patologici alla base del funzionamento del sistema nervoso. Il Centro è affiliato al Consorzio NeuroMi - Milan Center for Neuroscience.

Gli organi direttivi del Centro si compongono del Direttore e del Consiglio Scientifico. Il Centro di Ricerca in Neuroscienze ha avuto come Direttori, in passato, la prof.ssa Daniela Parolaro, il prof. Riccardo Fesce, il prof. Mauro Fasano ed il dr. Sergio Balbi. Il Direttore attuale, per il triennio 2020-2022, è la dr.ssa Lia Forti, ed il Consiglio Scientifico è composto dai professori Marco Cosentino, Charlotte Kilstrup-Nielsen, Cristina Roseti e Silvia Sacchi.

REGOLAMENTO
DEL CENTRO DI RICERCA
IN NEUROSCIENZE

INDICE

Art. 1 - Denominazione del Centro

1. Presso l'Università degli Studi dell'Insubria è istituito il Centro di Ricerca in Neuroscienze.

Art. 2 - Sede del Centro

1. Il Centro afferisce al Dipartimento di Biotecnologie e Scienze della Vita, è ivi funzionalmente e logisticamente allocato e usufruisce degli spazi, dei finanziamenti, delle attrezzature tecnico-scientifiche e del personale messi a disposizione dal Dipartimento o da altri enti pubblici o privati.

Art. 3 - Finalità del Centro

1. Il Centro ha lo scopo di:
   a. 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;
   b. 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;
   c. trasmettere e scambiare informazioni sulle tematiche sopraindicate tra le unità di ricerca del settore operanti presso altri dipartimenti o istituzioni di ricerca o laboratori di aziende industriali;
   d. contribuire alla formazione di ricercatori, esperti e docenti delle discipline ricomprese nelle sue finalità;
   e. promuovere rapporti con altre istituzioni di ricerca in Italia e all'estero, per proporre progetti a livello locale, nazionale ed internazionale, al fine di configurarsi come nodo di network di eccellenza nell'ambito delle Neuroscienze;
   f. favorire il confronto, la diffusione e la divulgazione delle conoscenze mediante comunicazioni, convegni, corsi, iniziative editoriali e pubblicistiche e ogni altro programma formativo ed in- formativo utile al perseguimento delle sue finalità;
   g. provvedere all'acquisizione e gestione di apparecchiature, strumenti scientifici e servizi tecnici in dotazione al Centro.

Art. 4 - Attività del Centro

1. Nell'ambito dell'attività del Centro verranno organizzati seminari, attività di aggiornamento e convegni, nazionali ed internazionali, relativi ad argomenti di cui all'art. 3 e nel rispetto delle disposizioni in vigore per l'amministrazione universitaria.
2. Tali attività potranno essere svolte anche in collaborazione con Enti pubblici e privati ed associazioni con interessi convergenti.
3. Nel rispetto della normativa vigente e con finanziamenti specificamente destinati a tale scopo dai finanziatori potranno essere istituiti premi di ricerca o borse di studio.
4. Rientra tra le attività del Centro la possibilità di curare la pubblicazione di articoli, testi e rapporti sugli argomenti elencati nell'articolo 3.

Ogni anno il Centro predisporrà una relazione sull'attività svolta. L'attività del Centro è verificata ogni due anni dal Senato Accademico, sentito il Nucleo di Valutazione, nelle forme, nei tempi e nei modi previsti dallo Statuto di Ateneo e dal Regolamento generale di Ateneo.

Art. 5 - Aderenti al Centro

1. Oltre ai professori e ricercatori proponenti, possono aderire al Centro:
   a. professori e ricercatori dell'Università dell'Insubria, di altri Atenei italiani e stranieri;
   b. studiosi afferenti a centri e enti di ricerca pubblici e/o privati;
   c. professionisti esperti nei settori di attività del Centro;
2. L'adesione al Centro può essere richiesta mediante domanda di adesione corredata da curriculum scientifico e/o professionale e dalla descrizione dettagliata dei temi di interesse, che devono essere in linea con le finalità del Centro. Sulla domanda di adesione si esprime entro 30 giorni il Consiglio Scientifico del Centro. Contro il diniego decidono definitivamente gli organi accademici competenti.
3. I componenti del Centro che sono esterni all'Università dell'Insubria possono esprimere solo parere consultivo sulle materie oggetto di deliberazione da parte del Centro e non concorrono alla formazione del numero legale.
4. Possono svolgere attività nell'ambito del Centro, oltre agli aderenti, a seguito di deliberazione favorevole del Consiglio Scientifico, laureandi, specializzandi, dottorandi di ricerca, borsisti, assegnisti di ricerca ed altro personale di enti di ricerca e/o strutture pubbliche o private.
5. Per il personale esterno alle Università ammesso a frequentare le strutture del Centro, sulla base di specifici accordi, il Direttore Scientifico del Centro dovrà accertare l'esistenza di idonea copertura assicurativa, relativa a infortuni e responsabilità civile.
6. Il Centro si avvale per il proprio funzionamento di personale messo a disposizione da Dipartimenti dell'Università o da terzi mediante convenzioni con l'Università.
7. Il Centro può utilizzare, previa approvazione del Dipartimento ospitante, i locali e le apparecchiature in dotazione alle strutture ove afferiscono gli aderenti al Centro.

Art. 6 - Organi del Centro

1. Sono organi del Centro:
   a. il Direttore Scientifico;
   b. il Consiglio Scientifico.

Art. 7 - Direttore Scientifico

1. Il Direttore Scientifico del Centro è eletto dal Consiglio Scientifico del Centro fra i professori di prima e di seconda fascia e i ricercatori dell'Università degli Studi dell'Insubria aderenti al Centro ed esterni al Consiglio stesso. Il Direttore è nominato con decreto del Direttore del Dipartimento a cui afferisce il Centro.

2. Il Direttore dura in carica tre anni e può essere confermato. Almeno tre mesi prima dalla scadenza del triennio il Consiglio Scientifico procede alla designazione del Direttore Scientifico.
3. La durata del mandato del Direttore Scientifico coincide con quella del Consiglio Scientifico.
4. Il Direttore scientifico:
   a. rappresenta il Centro, ne sovrintende e coordina l'attività, mantiene i rapporti con le autorità accademiche;
   b. convoca e presiede il Consiglio Scientifico, ne coordina l'attività e provvede all'esecuzione delle deliberazioni assunte;
   c. presenta al Consiglio Scientifico, all'inizio di ogni anno di attività, il programma dettagliato delle ricerche unitamente al preventivo dell'utilizzazione dei fondi disponibili nell'anno;
   d. predispone e sottopone al Consiglio Scientifico e al Consiglio del Dipartimento a cui afferisce il Centro, la relazione sull'attività svolta nell'anno, sui fondi ottenuti e sulla loro utilizzazione;
   e. designa un Vice Direttore tra gli aderenti al Centro che lo supplisce in caso di impedimento o di assenza.

Art. 8 - Consiglio Scientifico

1. Il Consiglio Scientifico del Centro è composto dal Direttore Scientifico, e da 4 membri eletti dall'assemblea degli aderenti, tra i membri del Centro.
2. Il Consiglio Scientifico è nominato con decreto del Direttore del Dipartimento a cui afferisce il Centro e dura in carica tre anni.
3. Il Consiglio Scientifico:
   a. individua e programma le linee dell'attività scientifica del Centro;
   b. approva il programma delle ricerche e il piano finanziario annuale proposto dal Direttore Scientifico;
   c. approva il rendiconto finale predisposto dal Direttore Scientifico;
   d. delibera sulle questioni riguardanti l'amministrazione dei fondi del Centro;
   e. delibera sulle forme di collaborazione e convenzione con altri Organismi pubblici e privati;
   f. delibera in merito alle richieste di nuove adesioni al Centro.
4. Il Direttore Scientifico convoca il Consiglio Scientifico almeno due volte all'anno o quando non meno di un terzo dei membri ne facciano richiesta. La convocazione è inviata, anche solo mediante posta elettronica, almeno 5 giorni prima della data fissata per la riunione.
5. Le riunioni del Consiglio Scientifico sono valide se è presente un terzo dei componenti. Le deliberazioni sono valide se approvate da più della metà dei presenti; in caso di parità prevale il voto del Direttore Scientifico.
6. Di ogni riunione viene redatto verbale, che viene approvato dal Consiglio Scientifico.

Art. 9 - Finanziamenti

1. Il Centro opera con i finanziamenti derivanti da:

a. Ministero dell'Università e della Ricerca Scientifica ed altri ministeri interessati nell'area di ricerca;
b. Consiglio Nazionale delle Ricerche;
c. eventuali contributi del Dipartimento di Biotecnologie e Scienze della Vita;
d. Regioni, enti locali ed altri Enti pubblici o privati, imprese o Fondazioni;
e. Unione Europea o altri organismi internazionali;
f. eventuali contributi di altri organismi italiani o stranieri;
g. donazioni e lasciti;
h. entrate diverse.

Art. 10 - Amministrazione

1. Il Centro è qualificato come centro di costo del Dipartimento e ad esso si applicano le norme previste dallo Statuto di Ateneo e dal Regolamento per l'amministrazione, la finanza e la contabilità.
2. La gestione amministrativa e contabile fa capo al Dipartimento di Biotecnologie e Scienze della Vita.

Art. 11 - Modifiche al regolamento

1. Le modifiche al presente regolamento sono proposte dal Consiglio Scientifico con la maggioranza qualificata dei 2/3 degli aventi diritto al voto e approvate dagli organi accademici competenti.

Art. 12 - Cessazione del Centro

1. Il centro cessa su proposta degli aderenti, con delibera approvata a maggioranza qualificata dei 2/3 e comunicata agli organi accademici competenti e nei casi stabiliti dall'art 62 dello Statuto dell'Università degli studi dell'Insubria.

Art. 13 - Norma di rinvio

1. Per quanto non previsto nel presente regolamento si applicano lo Statuto, il Regolamento per l'Amministrazione, la Finanza e la Contabilità ed il Regolamento Generale di Ateneo dell'Università degli Studi dell'Insubria.

Membri del Centro

Tiziana Alberio
Dipartimento di Scienza e Alta Tecnologia
Università dell'Insubria

Sergio Balbi
Dipartimento di Biotecnologie e Scienze della Vita
Università dell'Insubria

Elena Bossi
Dipartimento di Biotecnologie e Scienze della Vita
Università dell'Insubria

Camilla Callegari
Dipartimento di Medicina e Chirurgia
Università dell'Insubria

Marco Cosentino
Dipartimento di Medicina e Chirurgia
Università dell'Insubria

Mauro Fasano
Dipartimento di Scienza e Alta Tecnologia
Università dell'Insubria

Lia Forti
Dipartimento di Biotecnologie e Scienze della Vita
Università dell'Insubria

Cristina Giaroni
Dipartimento di Medicina e Chirurgia
Università dell'Insubria

Stefano Giovannardi
Dipartimento di Biotecnologie e Scienze della Vita
Università dell'Insubria

Charlotte Kilstrup-Nielsen
Dipartimento di Biotecnologie e Scienze della Vita
Università dell'Insubria

Franca Marino
Dipartimento di Medicina e Chirurgia

Università dell'Insubria

Marco Mauri
Dipartimento di Biotecnologie e Scienze della Vita
Università dell'Insubria

Alberto Passi
Dipartimento di Medicina e Chirurgia
Università dell'Insubria

Cristina Roseti
Dipartimento di Biotecnologie e Scienze della Vita
Università dell'Insubria

Tiziana Rubino
Dipartimento di Biotecnologie e Scienze della Vita
Università degli Studi dell'Insubria

Silvia Sacchi
Dipartimento di Biotecnologie e Scienze della Vita
Università degli Studi dell'Insubria

Erica Zamberletti
Dipartimento di Biotecnologie e Scienze della Vita
Università degli Studi dell'Insubria

Linee di ricerca dei membri del Centro

Tiziana Alberio, Mauro Fasano
Biochemistry and Functional Proteomics Laboratory

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
Laboratory of Cellular and Molecular Physiology

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
Center of Research in Medical Pharmacology

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 Forti
Laboratory of Cellular Neurophysiology

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
Laboratory of enteric nervous system physiopharmacology

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
Laboratory of Molecular Biology

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
Neuropsychopharmacology Group

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 pathogenesis 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
Laboratory "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.

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Centro NeuroScienze
Università degli Studi dell'Insubria
UNIVERSITÀ DEGLI STUDI DELL'INSUBRIA
DBSV Dipartimento di Biotecnologie e Scienze della Vita
Scientific Day
Center for Research in NeuroScience
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

Programma

10:00 **Opening Address**

Lia Forti
Director of the Center for Research in Neuroscience

10:10 **First session**

Chair: Lia Forti

Ivano Caselli
Dissociative disorders and brain dysfunctions: findings from scientific literature

Isabella Barbiero
Molecular mechanisms of microtubule derangement in CDKL5 deficiency disorder, and target-based therapies

Erica Zamberletti
Cannabidivarin treatment rescues autism-like behaviors and reduces hippocampal microglia activation induced by prenatal valproic acid exposure in rats

Emanuele Schiavon
Acute stress effects on synaptic properties and excitability in pyramidal neurons of the rat prelimbic prefrontal cortex

11:30 **Coffee break - Sponsor presentation**

11:45 **Second session**

Chair: Silvia Sacchi

Silvia Sacchi
Investigating the metabolism of D-amino acids, atypical signaling molecules in neurotransmission

Tiziana Romanazzi
Obeticholic acid effects on dopamine transporters expressed in Xenopus laevis oocytes

Angela Di Iacovo
Glutamate transporter EAAT2 in LRRK2-associated Parkinson's disease

12:45 **Lunch**

14:30 **Third session**

Chair: Marco Cosentino

Luca Magistrelli
Potential role of CD4+ T Lymphocytes transcription factors in the development of long-term motor complications in Parkinson's Disease

Alessia Furgiuele
Dopaminergic modulation of the immune response and role in Parkinson disease

Adeena Shafique
Linking phenotype to genotype: proteome signatures of neurodegenerative disorders sharing the same gene mutation

Stefania Fozzato
Characterization of two nociceptors: TRPM8 and TRPV4 transplanted in Xenopus laevis oocytes from patients affected by chronic pain

16:00 -17:00 **Plenary lecture**

Howard E. Gendelman
Brain Immunity, COVID-19 and Neurodegenerative Disease

Plenary lecture

Howard E. Gendelman

Dr. Gendelman is Margaret R. Larson Professor of Internal Medicine and Infectious Diseases and Chair of the Department of Pharmacology and Experimental Neuroscience at the Nebraska Medical Center, Omaha, NE.

The major focus for his research is on the role played by glial inflammatory activities in brain disease. The work bridges immunology, neuroscience and pharmacology and crosses disease barriers for studies of HIV-1-associated neurocognitive disorders, Parkinson's disease (PD) and amyotrophic lateral sclerosis (ALS). The major goal is to use immune-based approaches to reverse nerve cell damage.

He has published so far nearly 500 original papers, reviews, books and book chapters, which received more than 42.000 citations. Founder and Editor-in-Chief of the Journal of Neuroimmune Pharmacology (Springer-Nature).

More info at:
https://www.unmc.edu/pharmacology/faculty/primary-faculty/gendelman/index.html

Brain Immunity, COVID-19 and Neurodegenerative Disease

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the etiological agent of coronavirus disease 2019 (COVID-19). SARS-CoV-2, is a positive-sense single-stranded RNA virus with epithelial cell and respiratory system proclivity. Like its predecessor, SARS-CoV, COVID-19 can lead to life-threatening disease. Due to wide geographic impact affecting an extremely high proportion of the world population it was defined by the World Health Organization as a global public health pandemic. The infection readily spreads from person-to-person through liquid droplets by cough, sneeze, hand-to-mouth-to-eye contact and to less degrees through contaminated hard surfaces. Close human proximity accelerates SARS-CoV-2 spread. COVID-19 is a systemic disease that can move beyond the lungs by blood-based dissemination to affect multiple organs. These organs include the nervous system. The primary cause of SARS-CoV-2 mortality is acute respiratory distress syndrome by macrophage activation and resultant inflammatory activities. These inflammatory activities cause a broad spectrum of neurological impairments that include dizziness, confusion, cerebrovascular disease, muscle pain, ataxia and seizures. The early cell-based portal for viral entry is through the angiotensin-converting enzyme 2 receptor. Viral origins are zoonotic with genomic linkages to the bat coronaviruses but without an

identifiable intermediate animal reservoir. There are currently few therapeutic options, and while many are being tested what is now of proven merit includes steroids, remdesivir and convalescent plasma. Better understanding of the epidemiology, molecular biology, pharmacology, and pathobiology of SARS-CoV-2 is needed to provide the insights directed to curtailing this disease outbreak

Abstract

Dissociative disorders and brain dysfunctions: findings from scientific literature

Ivano Caselli

PhD Student in Clinical and Experimental Medicine and Medical Humanities, University of Insubria, Varese (VA), Italy
Department of Medicine and Surgery, Section of Psychiatry, University of Insubria, Varese (VA), Italy

Dissociation is a mental process which involves disruptions of usually integrated functions of consciousness, perception, memory, identity, and affect. It consists in a complex heterogeneous phenomenon that implicate a wide range of psychological (as depersonalization, derealization, numbing, and amnesia) and somatoform symptoms (e.g. analgesia). Dissociation mechanism may be a protective strategy to cope with overwhelming emotions in traumatic/stressful events, suggesting an interaction between genetic, neurobiological and cognitive predispositions and stressful life events. A link between dissociative states/traits and altered activity in brain regions involved in emotion processing and memory, interception and attention regulation (insula), self-referential processes, cognitive control, and arousal modulation have been shown for several disorders. Neuroimaging research in psychiatry has been increasingly used in recent years to identify some of the neurobiological mechanisms of psychiatric disorders. Harricharan et al. have identified a central role played by the periaqueductal gray (PAG) in defensive responses. In dissociative disorders, high levels of elaborative memory encoding and reduced size of parietal lobe have been highlighted. In borderline personality disorder (BPD), dissociation is primarily stress-related and appears to have substantial impact on affective-cognitive functioning. Irle et al. have been suggested that borderline personality disorder (BPD), in which dissociative symptoms are quite frequent, is related to the reduced size of parietal lobe. Neuroimaging genetic studies that associate genetic and epigenetic variation with neural activity or structure provide an opportunity to link genes to psychiatric disorders in order to identify potential dysfunction. Clinical work would benefit from developing biomarkers that could facilitate the early identification of heterogeneous subtypes of psychopathology. van der Kruijs and collegues identified that HRV, EEG and (functional) MRI are sensitive methods to detect psysiological changes related to dissociative disorders such as FNSS, and can possibly provide more information about their aetiology to provide biomarker for earlier identification of patients at risk and appropriate treatment of dissociative conditions. In the context of the studies in neuroimaging research, it is considered useful to provide an overview of the most relevant findings in associations between dissociative disorders and brain dysfunction.

Keywords: Dissociation; Dissociative Disorders; Neuroimaging; Biomarkers; Neural correlates; Brain dysfunction; Neurosciences.

Molecular mechanisms and target-based strategy to correct microtubule derangement in vitro and in vivo models of CDKL5 deficiency disorder

Barbiero I.[1], De Rosa R.[1], Zamberletti E.[1], Gabaglio M.[1], Tramarin M.[1], Peroni D.[1], Bianchi M.[2], Rubino T.[1], Kilstrup-Nielsen C.[1]

[1]*Department of Biotechnology and Life Sciences, University of Insubria, Busto Arsizio, Italy*
[2]*Institute of Neuroscience (TCIN). Trinity College Dublin, Ireland*

Mutations in CDKL5 cause a rare neurodevelopmental pathology called CDKL5 deficiency disorder (CDD) characterised by severe infantile seizures, intellectual disability, hypotonia, and impairment of motor, language and hand function skills.
Loss of CDKL5 both in vitro and in vivo leads to altered neuronal morphology that involves specific cellular structures such as the growth cone, axon, dendritic tree and spines. These alterations can in part explain the delayed neuronal maturation that is at the base of the cognitive impairment associated with CDD in patients and in animal models. A key to understand such defects may be provided by current findings that describe for the first time a role of CDKL5 in regulating microtubule (MT) dynamics. In particular, we recently identified IQGAP1 as a novel interactor of CDKL5. IQGAP1 is a scaffold protein that regulates cytoskeleton organization by linking the actin and MTs through its association with the MT plus end binding protein (+TIP) CLIP170. We found that in CDKL5 silenced cells CLIP170 is arranged in a closed/hypo-functional conformation that reduces its affinity for IQGAP1 and MTs, interfering with proper MT dynamics. In line with these results, through live-imaging and biochemical studies we have gathered evidence indicating that synaptic defects in Cdkl5-KO neurons and brains can be linked to impaired invasion of MTs into dendritic spines. Importantly, the open conformation of CLIP170 can be induced by the neuroactive steroid pregnenolone (PREG). Indeed, CLIP170 acts as an intracellular receptor for PREG that promotes MT dynamics by blocking CLIP170 in its active conformation. Accordingly, we found that treatment of CDKL5 deficient cells with pregnenolone-methyl ether (PME), a non-metabolized derivative of PREG, favours the opened/active conformation and improves CLIP170 MT-binding, MT dynamics and supports neuronal maturation in Cdkl5-KO neurons. Further we found that sub-chronic administration of PME to fully symptomatic Cdkl5-KO mice improved hippocampal-dependent learning and memory behaviour and favours spine maturation. Interestingly, the positive effect on cognitive deficits is maintained also one week after treatment discontinuation.
Altogether, these results shed light on the molecular mechanism through which CDKL5 exerts its role on neuronal maturation and suggest CLIP170 as a novel candidate for the development of target-based therapies.

Cannabidivarin treatment rescues autism-like behaviors and reduces hippocampal microglia activation induced by prenatal valproic acid exposure in rats

Erica Zamberletti[1], Marina Gabaglio[1], Cristina Manenti[1], Daniela Parolaro[2], Tiziana Rubino[1]

[1]Department of Biotechnology and Life Sciences, University of Insubria, Busto Arsizio (VA), Italy; [2]Zardi-Gori Foundation, Milan (Italy)

Autism Spectrum Disorder (ASD) is a group of neurodevelopmental conditions characterized by widespread abnormalities of social interactions and communication, severely restricted interests and highly repetitive behavior. Although there are therapies that may help reduce associated symptoms, no approved medication is available for treating the core symptoms of ASD. Neuroinflammation and altered inflammatory responses, together with synaptic alterations, have been reported in animal models of autism spectrum disorder (ASD)-like behaviors. If brain inflammation plays a role in the development of ASD, then administration of compounds able to reduce neuroinflammatory responses could possibly help relieving symptoms of the disease. Phytocannabinoids seem to exert anti-inflammatory and neuroprotective properties, either directly or indirectly, in animal models of neurodegeneration, motor-related disorders and nervous system injuries. In addition, some phytocannabinoids have been shown to modulate symptoms and traits commonly altered in autism spectrum disorder (ASD), including motor and cognitive functions, sociability and anxiety. However, no studies have specifically investigated the effect of any of these compounds in animal models of ASD.
Here, we explored the effect of sub-chronic cannabidivarin (CBDV) administration on autism-like behaviors induced by prenatal valproic acid (VPA) in rats. Male offspring of VPA-treated dams (500 mg/kg i.p.; GD 12.5) received CBDV using two different protocols. Symptomatic treatment with CBDV (0.2, 2, 20, 100 mg/kg i.p.; PND 34-58) was performed to assess the effect of CBDV on autism-like behaviors. Preventative CBDV treatment (2, 20 mg/kg i.p.; PND 19-29) was conducted to test CBDV's ability to affect the appearance of autism-like traits. At the end of both protocols, behavioral testing was carried out to assess sociability and preference for social novelty, short-term memory, locomotor activity and compulsive self-grooming. CBDV 20 mg/kg in symptomatic rats ameliorated social impairments, social novelty preference, short-term memory deficits, repetitive behaviors and hyperlocomotion. Preventative CBDV treatment at the same dose prevented sociability and social novelty deficits, short-term memory impairments and hyperlocomotion, without affecting stereotypies.
Neurochemical analysis carried out 24 hours after discontinuing symptomatic CBDV treatment in the prefrontal cortex and hippocampus revealed that prenatal VPA exposure significantly increased the expression of GFAP, CD11b and TNFα and triggered microglia activation restricted to the hippocampus. Remarkably, CBDV treatment (20 mg/kg) completely

normalized the levels of all neuroinflammatory markers and restored microglia morphology in this brain region.
Overall, these data support the ability of CBDV treatment to ameliorate some aspects of the autism-like phenotype induced by prenatal VPA exposure in male rats. Although this study does not provide a direct correlation, we found that CBDV's behavioral effects are associated with the rescue of neuroinflammatory markers and microglia morphology in the hippocampus.

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Acute stress effects on excitability and synaptic properties of pyramidal neurons in the rat prefrontal cortex, and their modulation by ketamine

E. Schiavon[1], F. Salerno-Scarzella[1], L.Musazzi[2], M.Popoli[3], L. Forti[1]

[1]Center for Neuroscience Research and Dept. of Biotechnology and Life Sciences, University of Insubria, Varese (VA) Italy
[2]School of Medicine and Surgery, University of Milano-Bicocca, Italy
[3]Department of Pharmacological and Biomolecular Sciences,University of Milano, Italy

Stress is a major risk factor for a variety of psychiatric disorders, including depression, anxiety and post-traumatic stress disorder (PTSD). The cellular and functional changes underlying the adaptive or maladaptive behavioral effects of a single acute stressor are not well understood. In the medial prefrontal cortex (mPFC) of rodent models, both chronic and acute stress protocols affect glutamate neurotransmission. Moreover an overall decrease of neuronal firing and functional connectivity are reported in models of chronic stress, while no information is available for acute stress. The inescapable footshock (FS) protocol is an acute stress procedure considered a model of PTSD-like behavior. In the male rat, FS rapidly (1-2 hrs) increases the number of synaptic spines and enhances the amplitude of spontaneous excitatory postsynaptic currents (sEPSCs) in L2/3 pyramidal neurons (Pyr) of the prelimbic mPFC. FS also increases $[K^+]$-evoked Glu release from frontocortical synaptosomes. Within 24 hrs (and up to 2 weeks), FS induces atrophy and retraction of prelimbic Pyr apical dendrites. Glu release from frontocortical synaptosomes remains elevated at least 24 hrs after FS, but it is unclear whether this corresponds to enhanced glutamatergic transmission in the prelimbic area in more physiological preparations. Ketamine is a non-competitive antagonist of NMDARs, with fast-acting antidepressant activity when used at low, subanesthetic doses. Ketamine was proposed as a prophylactic treatment before or after traumatic stress to reduce the risk of PTSD development, however studies of its action after acute stress are scarce.

The first aim of our work was to explore the sustained (~24hr) effect of FS stress on Glu transmission in pyramidal neurons of the prelimbic mPFC, and its regulation by ketamine at antidepressant dosage. We recorded synaptic currents 24 hrs after FS in visually identified layer 2/3 Pyr of prelimbic mPFC in slices from adult male rats. We compared animals subjected to a 40-min session of FS protocol, injected with ketamine (10mg/kg) 6 hrs after FS, and controls (CTR). sEPSCs frequency had a minor decrease in FS-stressed animals, with no change in amplitude or kinetics, however ketamine after FS increased sEPSC frequency and peak amplitude and accelerated their rise and decay. We also analysed miniature excitatory postsynaptic currents (mEPSCs), reflecting quantal release in the absence of action potentials. mEPSCs in the FS group showed non significant changes in frequency and ampitude *vs* CTR. Ketamine after FS

slightly increased mEPSC frequency and peak amplitude and accelerated their kinetics.

Our second aim was to explore possible rapid and sustained changes in membrane excitability in prelimbic L2/3 Pyrs of FS-stressed animals. We analysed the number of spikes evoked by somatic current injection (f-I relation) 1 hr (FS-1h) or 24 hrs after FS; in the latter case a group of animals was injected with ketamine 6 hrs after FS (FS-Ket) and compared to saline-injected FS-stressed animals (FS-24h), and saline or ketamine-injected non-stressed animals. Interestingly, the slope of the f-I relation significantly increased in FS-1h vs. control. This effect was lost in FS-24h, however an increase in excitability was still visible at 24hrs in FS-Ket, but not in ketamine-treated non-stressed animals, vs saline-injected controls.

Overall, this work indicates that FS stress induces a rapid increase in membrane excitability of prelimbic layer 2/3 Pyrs of male rats, which parallels the increase in Glu release. Both effects are transient, as they are not apparent 24 hrs later. Ketamine treatment after FS produces a sustained increase in excitatory postsynaptic current amplitudes and neuronal membrane excitability.

Investigating the metabolism of D-amino acids, atypical signaling molecules in neurotransmission

Silvia Sacchi, Giulia Murtas, Valentina Rabattoni, Gianluca Molla, Loredano Pollegioni

"The Protein Factory 2.0", Dipartimento di Biotecnologie e Scienze della Vita, Università degli studi dell'Insubria, via J. H. Dunant 3, 21100 Varese

Despite the initial view of D-amino acids (D-AAs) as "unnatural" compounds, limited to microorganisms and invertebrates, they have actually turned out to be molecules active in the central and peripheral nervous systems of mammals, capable of modulating synaptic communication within neuronal networks. In particular, D-serine (D-Ser) and D-aspartate (D-Asp) are involved in excitatory neurotransmission through the activation of the N-methyl-D-aspartate type of glutamate receptor (NMDAR): they act as a endogenous co-agonist and agonist, respectively. Confirming their key role in controlling the receptor's activation state, altered levels of these molecules have been associated with NMDAR dysfunction and the related cognitive deficit that occurs in normal aging and neurological disorders including Alzheimer's disease, ALS and schizophrenia. We believe that an improved understanding of the processes entailed in D-AAs metabolism will offer new insights for the development of relevant strategies to treat these diseases.
For this reason, we are deeply involved in studying D-Ser and D-Asp degrading enzymes, D-amino acid oxidase (DAAO) and D-aspartate oxidase (DASPO), their biochemical properties and the mechanisms regulating their functionality. Albeit these two FAD-dependent flavoenzymes appear structurally highly conserved, they profoundly differ in quaternary structure, FAD affinity and kinetic properties and mechanism. These striking differences result in two different modes of modulation of the brain levels of D-Ser and D-Asp by the two orthologue enzymes. In addition, they appear to be regulated through different mechanisms.

OBETICHOLIC ACID EFFECTS ON DOPAMINE TRANSPORTER EXPRESSED IN *XENOPUS LAEVIS* OOCYTES

[1]Romanazzi T., [1]Briccola M., [1]Di Iacovo A., [1]Roseti C., [1]Cinquetti R., [2]Zanella D., [1]Bossi E., [2]Galli A.

[1]Department of Biotechnology and Life Sciences, University of Insubria, Varese (VA), Italy
[2]Department of Surgery, University of Alabama at Birmingham, Birmingham, AL, USA

Dopamine (DA) is a well-known neurotransmitter involved in reward-motivated behavior and addictive drugs like cocaine and amphetamines acting on its pathway. Moreover, the gut-brain axis displays significant control over motivated behavior. Recently, it was revealed that a gut-based bariatric surgery reduces reward-related behavior and psychomotor sensitization to cocaine and that the main mediator of these post-operative effects is the Takeda G protein coupled bile acid receptor (TGR5).
The main effect after bariatric surgery is an increase of circulating bile acids level into the blood and central nervous system. Obethicolic acid (OCA) is a hydrophobic bile acids analogue which is a selective agonist of nuclear farnesol-X-receptor (FXR) and plasma membrane receptor TGR5. This receptor is expressed in intestine, ileum, colon and central neural system. Dopamine transporter (DAT) is a 12 transmembrane domain protein and it is responsible for dopamine (DA) homeostasis. DAT acts mediating re-uptake of dopamine from synaptic cleft thereby terminating the postsynaptic dopamine action. DAT is electrogenic transporter and can be studied by electrophysiological techniques.
The aim of this study is to verify the possible pharmacological interaction between DAT and OCA, in presence of DA.
mDAT was expressed in *Xenopus laevis* oocytes and by two electrode voltage clamp technique transport current was recorded. The data showed that OCA alone does not elicit any measurable current. In dose - response experiments where the OCA concentration was increased from 1nM to 10μM in the presence of fixed dose of DA at 30μM, the transport associated current was not altered. When the OCA was used at 10μM concentration and the DA perfusion was increased from 300nM to 30μM, the increase of DA transport current was not changed by the presence of OCA, but the kinetic analysis to determine I_{max} and $K_{0,5}$ revealed that the latter value was slightly decreased in the presence of OCA consequently with an increase of the affinity for DA.
These preliminary results shed a light on the possible direct mechanism of OCA on DAT activity. Next step will be performed co-expressing DAT and TGR5 to study a possible TGR5 mediated impact on the DA transport in the presence of OCA. Moreover, because of cocaine well-known effect on DAT, it will be necessary to investigate also the role of OCA on DAT in the presence of addictive drugs.

Glutamate transporter EAAT2 in LRRK2-associated Parkinson's disease

[1]Angela Di Iacovo, [1]Martina Briccola, [1]Tiziana Romanazzi, [1]Raffaella Cinquetti, [2]Ludovica Iovino, [2,3]Laura Civiero, [1]Elena Bossi, [1]Cristina Roseti.

[1]Department of Biotechnology and Life Sciences, University of Insubria, Varese (VA), Italy
[2]Department of Biology, University of Padova
[3]IRCCS San Camillo Hospital, Venice

Among genetic abnormalities identified in Parkinson's Disease (PD), mutations of the Leucin Rich Repeat Kinase 2 (LRRK2) gene are the most common. Specifically, the G2019S LRRK2 mutation exerts its effects to enhance kinase activity.
Recent study has shown an impaired cortico-striatal glutamatergic transmission in mice carrying LRRK2 G2019S mutation. The Excitatory Amino Acid Transporter 2 (EAAT2) expressed in astrocytes is the major transporter in the brain involved in the glutamate clearance (90%). Alteration in its expression lead to a dramatic excitotoxicity, inflammation and gliosis that are common hallmarks of neurodegenerative diseases, including PD.
Our goal is to link altered glutamatergic transmission with dopaminergic degeneration in G2019S LRRK2-associated Parkinson's disease. The influence of LRRK2 (*wild-type* and mutated) on EAAT2 activity and cellular localization are investigated using Two Electrodes Voltage Clamp (TEVC) technique and immunochemistry methods on the heterologous expression system, *Xenopus laevis* oocytes.
Here, we show as transport current associated with glutamate re-uptake is increased when EAAT2 is co-expressed with LRRK2 *wild-type*, while it is significantly reduced in the presence of mutated LRRK2. The data about transporter kinetic characterization demonstrate that, compared to the *wild type* form, the mutated LRRK2 state reduces EAAT2 functionality increasing the affinity of uptake system.
Moreover, immunocytochemistry assay shows EAAT2 internalization in subcellular compartments in LRRK2 G2019S condition, resulting loss-of function of transporter and pathological effects.
Mutated phenotype is reverted upon inhibitor of LRRK2 kinase activity and this result could be an important pharmacological breakthrough.
In summary, our data suggest a functional interaction between EAAT2 and LRRK2, demonstrating an influence of the kinase on glutamate transporter activity and membrane localization and candidate G2019S mutation as potential responsible of chronic glutamate accumulation and neurodegeneration in PD.

Potential role of CD4+ T Lymphocytes transcription factors in the development of long-term motor complications in Parkinson's Disease

Luca Magistrelli[a,b], Elena Contaldi[a,c], Cristoforo Comi[a,d], Marco Cosentino[d,e], Franca Marino[d,e]

[a]*Movement Disorders Centre, Neurology Unit, Department of Translational Medicine, University of Piemonte Orientale, Novara, Italy*
[b]*PhD Program in Clinical and Experimental Medicine and Medical Humanities, University of Insubria, Varese, Italy*
[c]*PhD Program in Medical Sciences and Biotechnology, University of Piemonte Orientale, Novara, Italy*
[d]*Center of Research in Medical Pharmacology, University of Insubria, Varese, Italy*
[e]*Center for Research in Neuroscience, University of Insubria, Varese, Italy*

Introduction: motor complications represent a major challenge in long-term treatment of Parkinson's Disease (PD) patients. In this context, the role of peripheral adaptive immunity may provide new insights, since neuroinflammatory mechanisms have been proved crucial in the disease. The aim of this study was to analyze transcription factors genes involved in CD4+ T cells development in order to uncover specific molecular signatures in patients with and without motor complications.
Methods: mRNA levels of the transcription factor genes TBX21, STAT1, STAT3, STAT4, STAT6, RORC, GATA3, FOXP3, and NR4A2 were measured in CD4+ T cells from 40 PD patients, divided into two groups according to motor complications. Also 40 age and sex matched healthy controls were enrolled.
Results: We found significantly higher levels of STAT1 and NR4A2 ($p=0.004$; $p=0.003$) in patients without motor complications, whereas STAT6 was higher in patients with motor complications ($p=0.04$). ROC curve analysis confirmed STAT1 and NR4A2 as feasible biomarkers in discriminating patients without motor complications (AUC=0.76, $p=0.005$, 95% CI 0.59-0.92; AUC=0.75, $p=0.007$, 95% CI 0.58-0.90) and they both showed good positive likelihood ratios and specificity values.
Conclusions: these results highlight the relevance of peripheral immune system in long-term motor complications, thus unraveling the role of CD4+ T lymphocytes as potential therapeutic targets in PD management.

EFFECT OF DOPAMINERGIC AGENTS ON HUMAN PERIPHERAL BLOOD MONONUCLEAR CELLS: RELEVANCE FOR PARKINSON'S DISEASE

Alessia Furgiuele

Center for Research in Medical Pharmacology, University of Insubria, Varese (VA), Italy

Background: Parkinson's disease (PD) is among the most common neurodegenerative disorders. PD is characterized by a progressive loss of dopaminergic neurons in the substantia nigra pars compacta. Different lines of evidence support the peripheral immune system as a key player in PD pathogenesis, and in particular CD4+T lymphocytes may promote neurodegeneration by means of the proinflammatory cytokines TNF-α, IFN-γ and IL-17A. Dopaminergic substitution treatment is the mainstay of PD therapy, however, although dopaminergic modulation of the immune response is nowadays well established, the possible effects of dopaminergic agents in PD have never been assessed so far. Therefore, the aim of this study was to assess the effect of selected dopaminergic antiparkinson drugs on TNF-α, IFN-γ and IL-17A production by human peripheral blood mononuclear cells (PBMCs).
Methods: PBMCs were isolated from buffy coats of healthy donors by Ficoll-Paque Plus density-gradient centrifugation. Isolated PBMCs were then stimulated with anti-CD3/anti-CD28 Abs (2 μg/ml) and cultured alone or in the presence of one of the following dopaminergic agonists: pramipexole (PPX), ropinirole (ROP) and rotigotine (ROT), all at the concentration of 0.1 μM at 37°C under a 95% O_2/5% CO_2 atmosphere. Cell pellets and supernatants were collected after 48 h and TNF-α, IFN-γ and IL-17A mRNA levels and extracellular secretion were assessed respectively by RT-PCR and by ELISA.
Results: Stimulation of PBMCs with anti-CD3/anti-CD28 Abs increased TNF-α, IFN-γ and IL-17A mRNA levels (by 4-, 8- and 4-folds, respectively), TNF-α and IFN-γ secretion (from 42 to 1866 pg/mL and from 7 to 1718 pg/mL). In preliminary experiments incubation of stimulated PBMC with either PPX, ROP or ROT reduced mRNA levels of TNF-α (by 21%, 30% and 16%, respectively), IFN-γ (by 43%, 47% and 41%) and IL-17A (by 13%, 24% and 19%). Extracellular secretion of TNF-α and IFN-γ were however slightly increased by PPX (by 13% and 18% respectively), unaffected by ROP (-4% each) and reduced by ROT (by 53% and 24% respectively). Supernatants for IL-17A assay are currently stored at -80°C and will be soon processed.
Conclusions: All the dopaminergic agonists tested reduced TNF-α, IFN-γ and IL-17A mRNA levels. However, ROT, but not PPX and ROP, also resulted in reduction of proinflammatory cytokine production. In future experiments we will assess whether this pattern of effects occurs also in cells from PD patients, and to what extent it may be relevant for PD development and progression.

Linking phenotype to genotype: proteome signatures of neurodegenerative disorders sharing the same gene mutation.

Adeena Shafique[a], Marta Lualdi[a], Luisa Pieroni[b], Lucia Corrado[c], Sandra D'Alfonso[c], Tiziana Alberio[a], Mauro Fasano[a]

[a]*Università degli Studi dell'Insubria, Italy*
[b]*Fondazione Santa Lucia, Italy*
[c]*Università degli Studi del Piemonte Orientale, Italy*

The *C9orf72* gene mutation involving a pathologic expansion of GGGGCC hexanucleotide repeats is found in many neurodegenerative disorders, such as Amyotrophic Lateral Sclerosis (ALS) and Frontotemporal Dementia (FTD), with different clinical phenotypes.
The present study applied a shotgun proteomic approach to the primary skin fibroblasts of patients with ALS and FTD. ALS patients were characterized by having the *C9orf72* mutation, the sporadic form of the disease or some other causal genetic factor. All FTD patients in the study had the *C9orf72* mutation. The first specific aim of the study was to identify how the proteome changes in two different frames: between ALS patients with or without the *C9orf72* mutation (same clinical phenotype but different genotype); and between *C9orf72* positive ALS patients and FTD patients (different clinical phenotype but same genotype). Our second aim was to perform a systems biology analysis and identify significantly altered pathways between the different conditions. Finally, our last aim was to identify a specific panel of proteins which represents a proteomic signature that contributes to the specific disease phenotypes. Resultantly, proteins differentially expressed were identified. Multivariate analysis was performed, specifically the unsupervised principal component analysis (PCA) followed by the supervised partial least squares discriminant analysis (PLS-DA). These techniques succinctly summarised the complex data set and allowed to form a classifier that correctly classified the test subjects.

Characterization of two nociceptors: TRPM8 and TRPV4 transplanted in Xenopus laevis oocytes from patients affected by chronic pain

[2,3]Fozzato S., [1]Romanazzi T., [1]Briccola M., [1]Di Iacovo A., [1]Cinquetti R., [1]Baranzini N., [1]Grimaldi A, [1,4]Roseti C., [1,3]Surace M.F., [1,3,4]Bossi E.

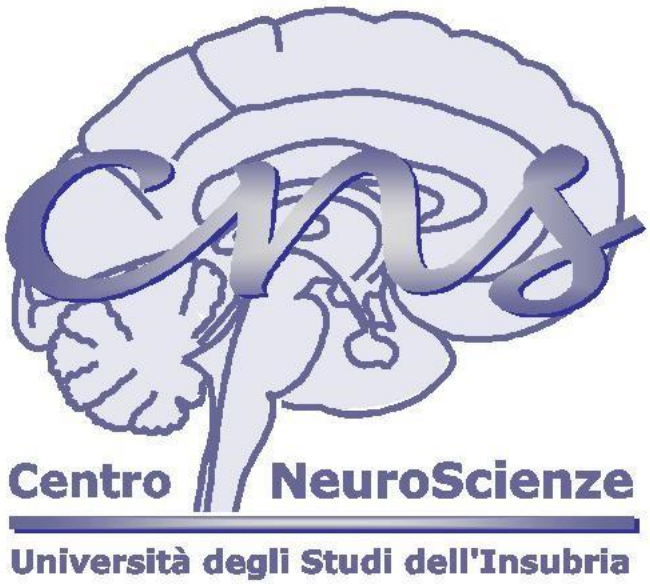
[1]Department of Biotechnology and Life Sciences, University of Insubria, Varese, Italy.
[2]Department of Medicine and Surgery, University of Insubria, Varese, Italy
[3]Interdisciplinary Research Centre for Pathology and Surgery of the Musculoskeletal System.
[4]Centre for Neuroscience Research University of Insubria

To understand the elements involved in chronic pain, in order to define a specific therapy, the expression of two selected membrane receptors was investigated in specimens harvested from patients affected by hip osteoarthritis. Transient receptor potential vanilloid 4 (TRPV4) and transient receptor potential melastatin 8 (TRPM8) were selected due to their expression in peripheral sensory neurons as molecular nociceptors together with their role in transducing thermal, chemical and mechanical stimuli. TRPV4 is a Ca2+-permeable cation channel that serves as a sensor of mechanical or osmotic signals in several musculoskeletal tissues, including cartilage, bone, and synovium. TRPM8 is a non-selective cation channel, found on both Aδ and C fiber that is activate by cold temperatures and by a number of chemical agonists such as menthol, icilin, and eucalyptol that are known to generate cool sensations. The role of TRPM8 in pain sensation has been debated: in literature the role of TRPM8 in reducing or limiting pain sensation under injury conditions has been sponsored, however, some other publications suggest that TRPM8 actually amplifies pain after injury.
The aim of this work is to verify the channels response, comparing electrophysiological behavior of Xenopus laevis oocytes transplanted with membranes extracted from coxofemoral capsule to oocytes expressing the TRPV4 and TRPM8 alone or simultaneously, after cRNA injection.
First, the presence of TRPV4 and TRPM8 was verify by immunohistochemistry in samples harvested during the necessary surgery for hip replacement in patients affected by hip osteoarthritis. Then, for the first time, membrane extracted from coxofemoral capsule were successful transplanted in Xenopus laevis oocytes and currents from TRP channels recorded.
The current elicited by temperature higher than 30 °C or lower than 18°C, by TRPV4 agonist (GSK101) and blocker (HC 067047), by TRPM8 agonist (menthol) or by Ruthenium Red (RR), a general blocker of many TRPs, were recorded and analyzed. The first data suggest that in the presence of TRPM8 activators (agonist and cold temperatures) the currents are higher than any other condition but are partially blocked by the TRPV4 activator.
Several experiments are still necessary for a better comparison of the transplanted channels from membranes of patients affected by osteoarthritis with cRNA heterologous expression. However, the

comparative approaches will allow to define the array of receptors expressed in the human samples and to personalize a potential pharmacological therapy correlated to presence of specific channels that can be identify and analyzed with this method.

Appunti

Appunti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