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# Testi del Syllabus

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Resp. Did.	<b>CESCA FABRIZIA</b>	<b>Matricola: 031484</b>
Docenti	<b>CESCA FABRIZIA, 3 CFU LEGNAME GIUSEPPE, 3 CFU MORETTI RITA, 3 CFU</b>	
Anno offerta:	<b>2019/2020</b>	
Insegnamento:	<b>897SM - NEUROLOGIA</b>	
Corso di studio:	<b>SM54 - NEUROSCIENZE</b>	
Anno regolamento:	<b>2019</b>	
CFU:	<b>9</b>	
Settore:	<b>BIO/09</b>	
Tipo Attività:	<b>B - Caratterizzante</b>	
Anno corso:	<b>1</b>	
Periodo:	<b>Secondo Semestre</b>	
Sede:	<b>TRIESTE</b>	

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## Testi in italiano

### Lingua insegnamento

English

### Contenuti (Dipl.Sup.)

The Neuropathology course combines core teaching of fundamental aspects of major neuropathological diseases, with emphasis on the cellular and molecular causes of neurodegeneration and their clinical presentation, and on the role of glial cells in neurodegenerative pathologies and disorders of cognition. The course will also address how hypotheses can be tested in relevant model systems and utilised to develop novel therapeutic strategies.

The course contents will be organized as follows:

Glial Neuropathology (prof. F. Cesca): Classification and evolution of glia and astroglia; membrane channels, receptors and transporters; ion signaling; gliotransmission; functions of astroglia. Glial pathology: A1/A2 activated astrocytes, glial scar, Alexander disease, epilepsy, Huntington's disease. Improved in vivo calcium imaging techniques; pre-synaptic astrocytic processes (PAPs), astrocyte-to-neuron communication in synaptic plasticity and neural circuit activity. Humanized mice; astrocytes and cognitive disorders: Rett syndrome, MDD.

Molecular Neuropathology (prof. G. Legname): Molecular mechanisms in neurodegeneration; Prion diseases; Prion-like events in major neurodegenerative diseases; Proteinopathies; Protein changes in physiological and pathological conditions: Prion protein, alpha-synuclein and Lewy bodies, TDP-43, Beta-amyloid, Tau protein; Alzheimer's Disease; Parkinson's Disease; Creutzfeldt-Jakob Disease, Multiple Sclerosis; Bovine Spongiform Encephalopathy; Drug screening.

Clinical Neuropathology (prof. R. Moretti): Alzheimer's Disease: clinical presentation and diagnostic criteria; neuronal loss, amyloid cascade hypothesis, tau hyperphosphorylation, APOE4, altered glutamate, calcium theory; neuroinflammation; genetic hypotheses; Vascular and subcortical

dementias; Movement disorders, Parkinson's disease: clinical presentation and diagnostic criteria; dopaminergic pathways; dopamine depletion: pathological and therapeutic implications; Reward mechanisms: neural circuits and neurotransmitters involved; Addiction mechanisms: neural circuits and neurotransmitters involved; Sleep and sleep disorders, dream theory; ARAS system: mono- and polysynaptic pathways; Brain death; Brain Metabolism, ischemia and its relevance in clinical practice: Apoptosis and neuroinflammation; endothelium damage; Seizure and Epilepsy.

## Testi di riferimento

Verkhratsky A. and Butt A. 'Glial Physiology and Pathophysiology', Wiley-Blackwell, ISBN: 978-0-470-97853-5 (2013)

Kandel E.R et al., Principles of Neural Science, 5th Edition McGraw Hill Medical.

Aminoff. MJ .Neurology and General Medicine, Churchill and Livingstone, 7 Ed.

Scientific articles and reviews on specific topics will also be provided during classes.

CD-ROM with slides could be provided.

## Obiettivi formativi

The course seeks to provide the basic tools for the understanding of the physiopathological, symptomatological, diagnostic and therapeutic aspects of some of the most important neurodegenerative diseases, and their modeling in animals.

The feasibility of these models and the potential for translating the arising experimental data into sound clinical practice, will be addressed. The lab's models will be developed in clinical practice, showing the major common sharing points and the most important differences in clinical context.

1. Knowledge and understanding: main brain pathologies starting from basic neurophysiological up to cellular and animal models arriving to clinical context, focusing on both the neuronal and glial contribution to the onset and development of the various diseases;

2. Applying knowledge and understanding: the students should be able to understand and implement experimental strategies in order to investigate specific mechanisms of different pathologies;

3. Making judgments: the students should be able to develop critical capacities to read and understand or criticize scientific papers, to organize and implement strategies to obtain or critically analyze scientific data;

4. Communication skills: students should be able to employ technical language, in order to write with major supervision a scientific paper or organize a scientific oral communication;

5. Learning skills: students should be able to organize, implement and carry on a scientific knowledge, in order to begin an experiment and with major supervision begin their steps in lab experimental sessions.

## Prerequisiti

Basic knowledge in subjects such as chemistry, biochemistry, anatomy and physiology is required.

## Metodi didattici

Lectures and frontal lessons.

Neuroimaging, as well as electroencephalography will be displayed.

## Altre informazioni

The material used during the lessons will be made available in moodle.

## Modalità di verifica dell'apprendimento

Profs Cesca and Legname: students will undergo a final oral examination (mandatory), where the various issues covered in the course will be addressed and discussed. The exam may also entail the critical presentation of a scientific paper (in the form of a Journal Club) chosen by the candidate. Marks for the single modules will be attributed for a maximum of 30/30. To pass the exam (18/30) the student should show sufficient knowledge of the subjects addressed during the lessons. To get the maximum score (30/30 lode) the student should demonstrate to have acquired an excellent knowledge of the topics addressed during the lessons, and a remarkable ability to expose and critically discuss the various subjects.

Prof. Moretti: the evaluation will consist in 2 partial written examinations in itinere, or in a single final written examination. The examination will include 15 multiple-choice questions. Marks will be attributed for a maximum of 30/30 lode. To pass the exam (18/30), the student should answer correctly to at least 7 questions, to get the maximum score (30/30 lode) the student should answer correctly to all the questions.

The final mark will be the average of the marks of the three modules.

## Programma esteso

Glial Neuropathology (dr. F. Cesca): Astroglia: introduction, morphology, types of astroglia, syncytial networks. Astroglia physiology: ion channels, neurotransmitter receptors (glutamate, purinergic, GABA), membrane transporters. Calcium signaling in astroglia, store-operated calcium entry (SOCE), calcium waves. Signaling mediated by sodium, chloride, potassium ions and protons. Gliotransmission: release of neurotransmitters and neuromodulators. Functions of astroglia: neurogenesis and gliogenesis, neuronal guidance, synaptogenesis, neurovascular units, the blood-brain barrier (BBB), brain microcirculation, neuronal metabolism (lactate shuttle), neuroimaging, extracellular ion homeostasis, ROS, water and neurotransmitter homeostasis (glutamate-glutamine and GABA-glutamine shuttle), synaptic transmission, systemic homeostasis. Neuroglia in pathology: Functional and morphological definition of reactive astrogliosis, Wallerian degeneration, excitotoxicity, microglia activation. How to culture rodent astrocytes. A1/A2 activated astrocytes: identification, activation by microglia, proposed role in pathology. Glial scar: positive and negative functions, and still debated issues. Alexander disease: cellular and molecular features. Epilepsy: main functions of astrocytes that are altered under epileptic conditions, gliosis in epilepsy, adenosine therapy. Huntington's disease: contribution of astrocytes to the pathology. Improved in vivo calcium imaging techniques: compartmentalization of calcium signals at somas and processes, correlation with synaptic activity. Pre-synaptic astrocytic processes (PAPs): molecular composition and function. Astrocyte-to-neuron communication in synaptic plasticity and neural circuit activity: main molecular players and multi-scale coordination of brain states and higher brain functions. Humanized mice: biomedical applications of glial chimeric animals. Possible implications of astrocytes in cognitive disorders. Contribution of astrocytes to Rett syndrome: in vitro and in vivo evidence. Evidence of the role of astrocytes in depression disorders.

Molecular Neuropathology (prof. G. Legname): Molecular mechanisms in neurodegeneration; Prion diseases; Prion-like events in major neurodegenerative diseases; Proteinopathies; Protein changes in physiological and pathological conditions: Prion protein, alpha-synuclein and Lewy bodies, TDP-43, Beta-amyloid, Tau protein; Alzheimer's Disease; Parkinson's Disease; Creutzfeldt-Jakob Disease, Multiple Sclerosis; Bovine Spongiform Encephalopathy; Drug screening. The course covers all major aspects at the molecular level of neurodegenerative diseases. Students should have a strong background in biochemistry and molecular biology.

Clinical Neuropathology (prof. R. Moretti): Clinical and neuroimaging aspects of different forms of dementia, with clinical presentation and diagnostic criteria of Alzheimer's Disease; neuropathology of neuronal loss, amyloid cascade hypothesis, tau hyperphosphorylation, APOE4, altered glutamate, calcium theory; neuroinflammation; genetic

hypotheses. Vascular and subcortical dementias; principal differences and hemodynamic basis of small vessel disease. Principal common factors between AD and sVAD. Movement disorders, Parkinson's disease: clinical presentation and diagnostic criteria; dopaminergic pathways; dopamine depletion: pathological and therapeutic implications. Apoptosis and neuro-inflammation and endothelium damage. Reward mechanisms: neural circuits and neurotransmitters involved; Addiction mechanisms: neural circuits and neurotransmitters involved. Sleep and sleep disorders, dream theory; ARAS system: mono- and polysynaptic pathways; coma and Brain death. Seizure and Epilepsy.



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