



## MEDICINE AND SURGERY

**Course: Neuropharmacology**

**Year: 5<sup>th</sup>**

**Period: 1<sup>st</sup> semester**

**Credits: 3**

### **Objectives**

*The neuropharmacology course will discuss the drug-induced changes in functioning of the nervous system. In particular, it will provide both knowledge and conceptual understanding of the use and action of various classes of drugs in the treatment of different human diseases affecting the brain. The course will also aim to provide understanding of the molecular mechanisms at the basis of brain diseases as possible new drug targets for more effective therapies.*

*By the end of the course student will be able to:*

- List the major drugs and drug classes currently used in medical practice and describe their pharmacology including their indications, mechanisms of action, physiological effects, pharmacokinetic properties, major adverse effects and clinically significant drug interactions.*
- Apply knowledge of the pharmacology of the major drugs and drug classes currently used in medical practice, together with both disease-specific and patient specific factors to select the most appropriate medication(s) for the effective pharmacotherapy of a given disease or condition in a specific patient*
- Demonstrate an understanding of the molecular, cellular and physiological mechanisms underlying the pathophysiological changes that occur in the etiology of the most common disease states and describe how targeting these mechanisms with the appropriate choice of drug(s) can act to effectively treat, cure, or mitigate the underlying disease causes and/or symptoms*
- Describe the effective use of non-pharmacological therapeutic interventions in the treatment of specific brain diseases, conditions and symptoms*

### **Prerequisites**

*A deep understanding of the main concepts of neuroanatomy, neuronal physiology and neuronal cell biology are strictly required.*

### **Contents**

#### **LESSON 1: Drug targets in the CNS**

##### ***Learning Outcomes Addressed***

- *Describe synaptic targets of drug action in the processes of neurotransmitter synthesis, release, reuptake, degradation, postsynaptic action.*
- *Define the concept of synaptopathy.*
- *List the major roles of astrocytes and microglia in the brain and their potential exploitation as novel drug targets*
- *Introduce the concept of neuroinflammation and define the mechanisms of cell-to-cell communication in brain*

#### **LESSON 2: The Neurovascular Unit: barrier for drugs and drug target**

##### ***Learning Outcomes Addressed***

- *Define the cellular components of the Neuro Vascular Unit and their function*
- *Introduce the concept of lymphocyte transendothelial migration and the consequences of T Cells infiltration during brain inflammation and pathological conditions*
- *Introduce brain diseases involving activation of the immune system with a specific focus on Multiple Sclerosis (MS)*



- *List symptoms of MS, risk factors, pathogenesis and disease course*
- *Define MS therapeutical landscape and list disease-modifying treatments*

### **LESSON 3: Drug Therapy of Neurodegenerative Diseases**

#### **Learning Outcomes Addressed**

- *Explain how genes, molecules, cells, and neural circuits interact in the generation of neurodegenerative disorders*
- *Describe current research efforts in neurodegenerative diseases with a focus on Alzheimer's Disease*
- *Describe mechanisms of action and adverse effects of drugs used for the treatment of Alzheimer's Disease*
- *Introduce the effective use of non-pharmacological interventions for prevention and treatment of Alzheimer's Disease*

### **LESSON 4: Parkinson's disease: current and emerging therapies**

#### **Learning Outcomes Addressed**

- *Briefly define symptoms of PD*
- *Describe alterations of neuronal circuits and pathological hallmarks of PD*
- *Describe dopamine biosynthesis and metabolism*
- *Describe mechanisms of action and adverse effects of the major classes of drugs used for the treatment of PD*
- *Introduce emerging pharmacological treatment for PD*

### **LESSON 5: Autophagy in neurodegeneration: perspectives and new pharmacological approaches**

#### **Learning Outcomes Addressed**

- *Describe what is autophagy, what are the different types of autophagy*
- *Define genetics of autophagy and signaling pathways controlling autophagy and describe substrates of autophagy*
- *Appreciate the link between loss of autophagy and neurodegeneration.*
- *Describe the main drugs used for stimulating or inhibiting autophagy*
- *Appreciate the critical limitations of the currently available drugs.*
- *Define the rationale for targeting autophagy in neurodegenerative diseases*

### **LESSON 6 AND 7: Antiepileptic drugs**

#### **Learning Outcomes Addressed**

- *Briefly describe the pathophysiology and genetic of epilepsy*
- *Introduce epilepsies as disorders of neuronal excitability and describe the network alterations leading to seizures.*
- *List the different types of seizure and introduce the concept of status epilepticus*
- *List classes of antiepileptic drugs (AEDs).*
- *Identify the mechanisms of action, routes of administration, adverse effects and drug interactions for antiepileptic drugs acting on calcium and sodium channels.*
- *Identify the mechanisms of action, routes of administration, adverse effects and drug interactions for antiepileptic drugs targeting the GABAergic system*
- *Introduce and describe AEDs with mixed mechanisms of action.*
- *Discuss the rationale and clinical use of the various classes of AEDs*

### **LESSON 8: Pharmacological treatment of anxiety disorders**

#### **Learning Outcomes Addressed**

- *Define pathogenic clusters of anxiety and stress*
- *Classify and briefly describe the main clinical features of anxiety disorders.*
- *Describe the mechanism of action, pharmacological effects and pharmacokinetics of anxiolytics/hypnotics.*
- *Describe adverse effects and important drug interactions of anxiolytics/hypnotics and list the problems encountered with the continued use of these drugs.*
- *Introduce the molecular distinction between anxiolytic and sedative effects of anxiolytics/hypnotics*
- *Introduce the use of non-pharmacological approaches, such as psychotherapy and cognitive behavioral therapy in anxiety disorders.*

## **LESSON 9 AND 10: Pharmacological treatment of depression**

### **Learning Outcomes Addressed**

- *Describe the Biology of Depression: from the monoamine theory to the altered neuroplasticity.*
- *List the different classes of antidepressants.*
- *Understand the primary sites of action of antidepressant drugs*
- *List the pharmacokinetic properties, major adverse effects and clinically significant drug interactions for the different classes of antidepressants*
- *Describe the management of symptoms upon antidepressant discontinuation*
- *Describe some of the proposed mechanisms underlying the delayed therapeutic effects of antidepressant drugs.*
- *Introduce the use of non-pharmacological in depression*

## **LESSON 11: Pharmacological Treatment of Psychosis**

### **Learning Outcomes Addressed**

- *Describe the significance of the term psychosis*
- *Describe the neurodevelopmental hypothesis of schizophrenia*
- *Introduce schizophrenia as a synapse disorder and introduce genetic and environmental components contributing to the disease.*
- *List the positive and negative symptoms of schizophrenia*
- *Describe the mechanisms of action and adverse effects of typical and atypical antipsychotic drugs*
- *Design a treatment plan for the patient with schizophrenia that incorporates interventions for optimal outcomes.*
- *Describe the therapeutic objectives for managing bipolar disorder*

## **LESSON 12: Drug of Abuse and Addiction.**

### **Learning Outcomes Addressed**

- *Understand the neurobiological basis of addiction*
- *Classify drugs of abuse: stimulants, depressants and hallucinogenic agents.*
- *Describe the mechanisms of action, the effects and the pharmacokinetics of the major drugs of abuse*
- *Describe the signs and symptoms of withdrawal from the major drugs of abuse*
- *Discuss the currently available pharmacological options for the treatment of drug addiction and new approaches for this disorder.*

## **LESSON 13: The Gut Microbiota: A New Player in Brain Disorders**

### **Learning Outcomes Addressed**

- *Understand the main concepts underlying gut-brain interplay*
- *Describe the main evidence linking gut microbiota dysfunction and neurological diseases.*
- *Discuss new pharmacological perspectives targeting gut microbiota for the cure of brain disease.*

## **LESSON 14: NEW PERSPECTIVES FOR THE PHARMACOLOGICAL TREATMENT OF BRAIN DISEASES**

### **Learning Outcomes Addressed**

- *Students are encouraged to propose a relevant topic in the field of neuropharmacology which will be matter of discussion of the last lecture. The goal is to explore emerging concepts or new therapeutic perspectives which may be relevant for still incurable brain disorders.*

### **Teaching Methods**

*Frontal or on-line lessons.*



### Verification of learning

*The final exam will consist of multiple choice questions. Questions will be arranged in distinct sections covering the main topics of the course, each including 3 or 6 questions according to the topic.*

### Texts

- **Goodman and Gilman's the Pharmacological Basis of Therapeutics, 13th Edition** by Randa Hilal-Dandan; Bjorn Knollman; Laurence Brunton. ISBN: 9781259584732 - Publication Date: 2018
- **Rang and Dale's Pharmacology, ed.9 2020** by James M. Ritter; Rod J. Flower; Graeme Henderson; Yoon Kong Loke; David MacEwan; Humphrey P. Rang. ISBN: 9780702074486 - Publication Date: 2020
- **Basic and Clinical Pharmacology, ed.14** by Bertram G. Katzung; Anthony J. Trevor. ISBN: 9781259641152 - Publication Date: 2018
- **Molecular Neuropharmacology: A Foundation for Clinical Neuroscience**, 3e Eric J. Nestler, MD, PhD, Steven E. Hyman, MD, David M. Holtzman, MD, Robert C. Malenka, MD, PhD