COURSE DATA

Data Subject	
Code	40145
Name	Experimental neurobiology
Cycle	Master's degree
ECTS Credits	15.0
Academic year	2023 - 2024

Study (s)

Degree	Center	Acad. year	Period
2074 - M.D. in Basic and Applied Neurosciences	Faculty of Biological Sciences	1	Second term

Subject-matter

Degree	Subject-matter	Character
2074 - M.D. in Basic and Applied Neurosciences	6 - Specialty in experimental neurobiology	Optional

Coordination

Name	Department
GARCIA VERDUGO, JOSE MANUEL	21 - Cellular Biology and Parasitology
MARTINEZ RICOS, JOANA	17 - Human Anatomy and Embryology
TERUEL MARTI, VICENT MANUEL	17 - Human Anatomy and Embryology

SUMMARY

The experimental and applied neurobiology subject is located in the second semester of the Master's Degree in Basic and Applied Neurosciences of the University of Valencia. It shares a teaching period with Cognitive and Affective Neuroscience. It consists of six major blocks: A) Diseases that affect the nervous system, B) Neurobiology of addiction, C) Neuronal plasticity, D) Stem cells and cell therapy, E) Information processing in neural circuits, and F) Applied neurosurgery.

This itinerary includes the main advances in recent years in neuroscience and allows the analysis of the range of future possibilities and projection of the discipline by approaching cutting-edge aspects of neuroscience, such as degenerative processes, neural plasticity, regenerative processes in the nerve, stem cells, cell therapy, pain, neurological, mental pathologies, as well as neurobiology of drug addiction. We will begin with the genetic and molecular bases of the many diseases and pathologies that affect the nervous system (neurodegenerative, neurosensory, sensory-motor neuropathies, traumatic pathologies

such as spinal cord injuries, ischemic pathologies such as cerebrovascular accidents, etc.) . Some are rare in the population, the so-called rare diseases such as Friedreich's ataxia or Huntington's disease, with a marked family inheritance. Others are much more prevalent, of multifactorial aetiology, and in some cases with a genetic basis, so their study is much more complex, such as Alzheimer's disease, Parkinson's disease and many psychiatric diseases. The identification of the genes and/or risk factors for neurological and psychiatric diseases with a genetic load is crucial for their correct diagnosis and for the knowledge of the functions that are altered in the cell, a requirement that enables the search for effective therapies. In the case of traumatic pathologies of the nervous system, such as head injuries, spinal cord injuries or peripheral nerve injuries, the cause of the pathology is an external aggression that triggers a cascade of cellular and molecular events. Neural injuries of ischemic origin also cause the activation of cytotoxic pathways. In these two cases, the prognosis and the design of new therapies depend on the knowledge and control of the molecular bases responsible for cell damage. We will continue with an introduction to the clinical aspects of psychiatric illness and translational research in mental health.
Along with the genetic basis, students will be provided with an integrated view of the molecular and cellular bases responsible for neurodegenerative diseases, focusing on the presentation of the most widely used cellular and animal models in research on the mechanisms of neurodegeneration.

Another aspect to consider in this matter is the neurobiology of drug addiction. Addiction is a chronic and relapsing disease with a very difficult therapeutic approach. This is mainly due to the lack of knowledge that still exists today about the molecular and cellular bases of the phenomenon. Detailed knowledge of the effects that different drugs of abuse have on the brain is crucial for understanding, redefining and proposing new therapeutic strategies useful for the treatment of this disease. The contents of this second part are aimed at showing the student the advances made in this field of neurobiology in relation to the knowledge of the molecular and cellular bases of both the acute and chronic action of drugs and phenomenon of relapse, the main difficulty with which the therapist who treats these patients is robbed.

In a third block, we will refer to the phenomena of neuronal plasticity in the adult nervous system. This plasticity ranges from phenomena at the molecular level to structural remodeling. Given that molecular/neurochemical plasticity phenomena related to learning and memory or the interaction of the endocrine system and the nervous system will be addressed in other modules of this master's degree, the teaching in the Experimental and Applied Neurobiology module will focus in structural plasticity. In this part of the module, the remodeling of neurites, dendritic spines and synapses will be studied. An overview ofthe regions of the adult brain that show this remodeling, the extrinsic and intrinsic factors that induce/modulate it, as well as the molecular mechanisms that support this structural plasticity. The involvement of adult structural plasticity in some mental disorders will also be discussed. In this blog we will also address the plasticity phenomena that occur in the nervous system in response to injuries. We will analyze which regions of the nervous system have the spontaneous capacity for axon regeneration, reconnection and remodeling in response to aggression, and which regions do not have this capacity.regenerative We will reveal the cellular and molecular keys to these regional differences and the possible targets for therapeutic action based on them.

Finally, in the cell therapy section, we aim for the student to become familiar with stem cells in general and their use in neurodegenerative diseases with cell loss, as well as in other types of cell therapies that are they can apply in pathologies of the nervous system. In the first case, we will identify the areas with adult neurogenesis and the factors that control the migration, differentiation and proliferation of stem cells. We will talk about the activation, differentiation and transplantation techniques of these cells, their relationship with aging and especially with the formation of tumors. There are numerous data linking glioblastomas to stem cells. In these sections, therefore, a broad overview will be given of the three major characteristics involving stem cells: the reparative aspects, aging and tumors. We will also focus on other types of cells that are already being used in patients, or that are close to therapeutic application, in the

different types of pathologies of the nervous system. For example, we will talk about the use of Schwann cells and olfactory enveloping glia in the repair of traumatic injuries of the peripheral nerves and the central nervous system, or about the cell therapies that have been used and that are proposed to be used in patients with Parkinson's disease, multiple sclerosis, amyotrophic lateral sclerosis, among others.

In the fifth block we will review the anatomy and function of certain circuits that have been discussed in previous modules, but we will approach their study from an electrophysiological perspective. On the one hand, the functional anatomy of some components of the limbic system (hippocampus, amygdala and prefrontal cortex) will be reviewed and the cellular and electrophysiological mechanisms underlying various processes in which these structures are involved will be described, such as learning and memory, spatial orientation or stress management. It is intended that the students are familiar with the relationship between certain neural functions and specific electrophysiological states. The next step will therefore be to establish the relationship between certain pathologies and the detection of oscillatory patterns and aberrant neural activities that characterize them, which will be developed in more detail in the sixth blog, on applied neurosurgery..Some cases that are currently well defined will be explained, such as epilepsy or schizophrenia, as well as several motor-type disorders, and the relevance of identifying these patterns for the design of approaches neurosurgery, such as deep brain stimulation, which will be developed in more detail in the sixth block, applied neurosurgery. In the practical part we will work on modelling, and analysis of oscillations.

The practical load of the subject aims for the student to know the basics of the experimental methods used in the study of the nervous system, and to acquire skills in experimental design and the use of the most common techniques in this field, to be able to interpret the results of the experiments (and therefore be able to understand the articles), to know new tools and know how to apply them to solve specific problems.

PREVIOUS KNOWLEDGE

Relationship to other subjects of the same degree

There are no specified enrollment restrictions with other subjects of the curriculum.

Other requirements

OUTCOMES

2074 - M.D. in Basic and Applied Neurosciences

- Students should apply acquired knowledge to solve problems in unfamiliar contexts within their field of study, including multidisciplinary scenarios.
- Students should be able to integrate knowledge and address the complexity of making informed judgments based on incomplete or limited information, including reflections on the social and ethical responsibilities associated with the application of their knowledge and judgments.

- Students should communicate conclusions and underlying knowledge clearly and unambiguously to both specialized and non-specialized audiences.
- Students should demonstrate self-directed learning skills for continued academic growth.
- Ser capaz de aplicar las técnicas de búsqueda, identificación, selección y recogida de información científica especializada, así como de los métodos que se han de tener en cuenta a la hora de examinar críticamente cualquier clase de fuentes y documentos científicos.

- Saber comunicar el conocimiento sobre neurociencia y sus implicaciones a públicos especializados y no especializados de un modo claro y sin ambigüedades, usando la lengua propia y el inglés.
- Saber aplicar el método científico a los estudios en neurociencias y poseer el espíritu crítico requerido para distinguir la información científica rigurosa de la pseudociencia
- Conocer los mecanismos biológicos básicos de la patología del sistema nervioso
- Ser capaz de comprender y conocer las implicaciones de las nuevas terapias en las actuaciones sobre patologías del sistema nervioso
- Comprender la validez y utilidad así como adquirir destreza en el manejo de modelos celulares y animales de enfermedad
- Saber trabajar en equipos multidisciplinares y diseñar estrategias experimentales multidisciplinares en el ámbito de las neurociencias para la resolución de problemas biológicos complejos
- Saber trabajar de manera responsable y rigurosa en el laboratorio, considerando los aspectos de seguridad, manipulación y eliminación de residuos así como del correcto uso de los animales de experimentación y los principios éticos para la investigación en humanos.
- Conocer los principios éticos y legales de la investigación científica en neurociencias
- Comprender las aproximaciones experimentales y sus limitaciones, así como interpretar resultados científicos en neurociencias y saber elaborar y redactar informes que los describan
- Adquirir destrezas en el manejo de las metodologías empleadas en las neurociencias y en el registro anotado de actividades, así como en el manejo de programas informáticos para la obtención y análisis de los datos y la exposición de los resultados
- Students should possess and understand foundational knowledge that enables original thinking and research in the field.

LEARNING OUTCOMES

1. Demonstrate a sufficient mastery of terminology, concepts, processes and interrelationships to address a high level of specialization in basic and applied neuroscience
2. Demonstrate understanding of the cellular and molecular mechanisms underlying the pathology of the nervous system and that enable therapeutic approaches.
3. Demonstrate the practical mastery of the experimental methodologies used in experimental and applied neurobiology.
4. Organize information and public presentations effectively with rational and scientific arguments.5. Demonstrate the ability to solve theoretical and practical questions related to the subject under study.

DESCRIPTION OF CONTENTS

1. Cellular and molecular bases of SN pathology: neurodegenerative diseases, neurological and psychiatric diseases, neurogenetics, animal and cellular models i nervous system pathology

Unit 1: Genetic and molecular bases of pathology of the nervous system. From monogenic diseases to multifactorial diseases. Mendelian genes versus genetic susceptibility factors. Nothing and atmosphere.
Unit 2: Genetic analysis in neurological diseases. Cloning of Mendelian genes. Identification of genetic vulnerability factors.
Unit 3: Molecular pathology. Mutations of loss and gain of gene function. Pathogenic potential of micro and minisatellite sequences. PolyQ neurodegenerative diseases. RNA-mediated neurodegeneration.
Unit 4: Alzheimer's disease: clinical manifestations, and cellular and molecular bases
Unit 5: Parkinson's disease: clinical manifestations and cellular and molecular bases
Unit 6: Autoimmune encephalitis: clinical manifestations and cellular and molecular bases
Unit 7: Genetic bases of psychiatric diseases. Quantitative Genetics Data. Family aggregation studies. Studies in twins.
Unit 8: Molecular genetics of psychiatric diseases: Schizophrenia, Bipolar Disorder. Findings in bonding studies. Findings in association studies. Epigenetic findings. Findings in broad genome study.
Unit 9: Methodological problems in research in psychiatric genetics. The definition of the phenotype. The gene-environment interaction. The genetics of mental illness from the Theory of Evolution.
Unit 10: Introduction to psychiatric illnesses. Case studies.
Unit 11: Translational research in Mental Health. Case studies.

2. Neural plasticity. Axon regeneration. New therapies.

Unit 12: The concept of neural plasticity in the adult nervous system. Molecular plasticity vs. structural plasticity.
Unit 13: Remodeling of axons, dendrites, dendritic spines and synapses. Molecular bases of neuronal remodeling. Techniques for studying neural plasticity.
Unit 14: Intrinsic and intrinsic factors that regulate neuronal plasticity in the adult SN.
Unit 15: Response of the adult SN to traumatic injuries.

3. Neurobiology of addiction

Unit 16: What is addiction: Definitions of drug addiction. Visions of the problem. Vulnerability to addiction. Neurobiological view of addiction: hypotheses and theories.
Unit 17: Animal models for the study of addiction: Animal models of self-administration. Preference conditioning or place aversion. Models of discrimination. Extinction resistance. Abstinence models and conditioned abstinence syndrome. Relapse models: ADE and resumption.
Unit 18: Psychostimulants, Opiates, Alcohol and Nicotine: Definitions. History of use abuse and addiction. Pharmacokinetics. Abuse and addiction potential. Mechanisms of action at the molecular, cellular and systemic levels.
Unit 19: Fundamental aspects related to the Neurobiology of Relapse.
Unit 20: Addiction treatment. Therapeutic perspectives.

4. Cell therapy. Neural stem cells. Replacement therapies in the nervous system and axon regeneration. Cancer stem cells: gliomas and neuroblastomas

Unit 21: Cell therapy in traumatic injuries of the peripheral and central nervous system.
Unit 22: Cell therapy in degenerative diseases, Parkinson's, Huntington's, ALS and ataxia.
Unit 23: Basic concepts: Adult and embryonic stem cells. Ips. Neural stem cells.
Unit 24: Comparative adult neurogenesis.
Unit 25: Cancer stem cells: gliomas and neuroblastomas. Self-renewal and expansion of tumor stem cells. Migration and invasiveness. Therapies aimed at tumor stem cells.

5. Information processing in neural circuits

Unit 26. Hippocampus and memory in learning and memory, and in spatial orientation: explain both the function in general and the cellular and electrophysiological mechanisms involved in these functions.
Unit 27. Modeling of memory
Unit 28. Oscillations in neural communication and markers of pathologies and neuropsychiatric treatments.
Unit 29. Oscillations in neural communication and alteration in neuropsychiatric pathologies. Analysis of oscillations in electroencephalogram.

6. Applied neurosurgery

Unit 30: Deep brain stimulation. Surgery for movement disorders.
Unit 31: Functional brain surgery.
Unit 32: Pain surgery and psychiatric surgery.

WORKLOAD

ACTIVITY	Hours	% To be attended
Theory classes	57,00	100
Laboratory practices	33,00	100
Development of individual work	40,00	0
Study and independent work	172,00	0
Readings supplementary material	60,00	0
Preparing lectures	8,00	0
Preparation of practical classes and problem	5,00	0
TOTAL	**375,00**	

TEACHING METHODOLOGY

Master class with active participation through the discussion of the most complex aspects and the resolution of doubts and questions

Laboratory practices with sample handling, problem solving, practical assumptions, preparation of practice reports, etc.

Discussion, reflection and preparation of reports on practical tasks

EVALUATION

EVALUATION SYSTEM

An exam, minimum weighting 20%, maximum weighting 80%.
Evaluation of proposed activities, preparation of papers and seminars, face-to-face or virtual. Minimum weighting 20%, maximum weighting 80%.
The final weight of each activity/exam will be weighted in the proportion of hours of the content evaluated with respect to the total of the subject.
It will be necessary to obtain a minimum of 4 points out of 10 in each of the activities and the exam to be able to take the average.

REFERENCES

Basic

- La utilització dalgun dels llibres llistats a continuació és necessària per al treball en lassignatura, per la qual cosa es recomana a lestudiant la lectura dalgun dells.
  The use of some of the books listed below is necessary for the work in the signature, for which it is recommended for students to read some of them.

  Gerd Kempermann (2005) Adult Neurogenesis: Stem Cells and Neuronal Development in the Adult Brain. Oxford University Press, USA;

  Fred H. Gage, Gerd Kempermann, Hongjun Song (editors), (2007) Adult neurogénesis, Cold Spring Harbor Laboratory Press, USA.

  Sara Gil-Perotín, Arturo Alvarez-Buylla and Jose Manuel Garcia-Verdugo. (2009). Identification and characterization of neural progenitor cells in the adult mammalian brain. Editorial: Springer. Pag. 1-104

  Damian Garcia Olmo, Jose Manuel Garcia Verdugo, Jorge Alemany, Jose A. Gutiérrez-Fuentes, (2007) Cell Therapy, McGraw-Hill , Pg. 1-405

  Strachan and Read. Human Molecular Genetics. BIOS Scient. Publ. 2004 (3ª ed) Garland Science/Taylor & Francis Group.

  Rutter M. (2006) Genes and Behavior. Blackwell. Oxford.

  Kendler K & Eaves L (2005) Psychiatric Genetics. American Psychiatric Publishing. Washington.

  Neurobiology of Addiction. GF Koob y M LeMoal (2006). Amsterdam, Academic Press.

Molecular Biology of Drug Addiction. R Maldonado (2003). New Jersey. Humana Press

Additional

- Siegel, George J.; Agranoff, Bernard W.; Albers, R. Wayne; Fisher, Stephen K.; Uhler, Michael D., editors (1999) Basic Neurochemistry: Molecular, Cellular, and Medical Aspects. Philadelphia: Lippincott,Williams & Wilkins.

Stewart A.; Weiner, William J., (2002) Parkinson's Disease: Diagnosis and Clinical Management Factor, New York: Demos Medical Publishing, Inc.

StemBook (2008) Cambridge (MA): Harvard Stem Cell Institute

Sanjuan J. (2009) Teoría de la Evolución y Medicina. Panamericana. Madrid

STRACHAN T, GOODSHIP J, and CHINNERY P. 2015. Genetics and Genomics in Medicine. Garland Science, Taylor & Francis Group, LLC. ISBN 978-0-8153-4480-3

STRACHAN and READ. Human Molecular Genetics. 2019 (5ª ed, ISNB 0815345895)