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NEUR 301/401: Biological Mechanisms of Brain Disorders
Syllabus

Credits: 3

Course Director: David M. Katz, PhD, Departments of Neurosciences & Psychiatry, School of Medicine

Weekly schedule: 3 class meetings per week (MWF), 50 minutes each

Course Description: This course is designed to introduce students to a broad range of neurological and neuropsychiatric diseases and disorders in order to understand how genetic and environmental perturbations can disrupt normal brain function. The primary focus will be on understanding the biological bases of nervous system dysfunction. For each disease discussed, the subject matter will be organized to explain how normal brain function is impacted, the biological mechanisms underlying dysfunction (including still-unanswered questions) and current efforts to develop effective treatments (translational research). With this approach, students will gain an understanding of disease presentation, how animal models and human studies are being used to elucidate pathophysiological mechanisms, and opportunities and challenges in the development of new therapies. The class format will be a mix of lecture-based sessions and discussions of scientific journal articles.

Learning Objectives:

After participating in this course, students should be able to:

1. Explain the biological mechanisms underlying a broad range of brain disorders
2. Critically analyze and interpret preclinical studies of human disease reported in the scientific literature
3. Illustrate the utility and limitations of animal models for developing effective therapies for neurological disorders
4. Identify critical gaps in our current understanding of biological mechanisms and treatment strategies for brain disorders

Instructor contact information:

Department of Neurosciences

David M. Katz, PhD

Room E712, Robbins Bldg, School of Medicine

Office hours TBD

david.katz@case.edu

216-368-6116

David Friel, PhD

Room E647, Robbins Bldg, School of Medicine

Office hours TBD

ddf2@case.edu

216.368.4930

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Lin Mei, PhD

Room E750A, Robbins Bldg, School of Medicine

Office hours TBD

lin.mei@case.edu

216.368.4928

Jerry Silver, PhD

Room E661, Robbins Bldg, School of Medicine

Office hours TBD

jxs10@case.edu

216.368.2150

Wen-Cheng Xiong, PhD

Room E721, Robbins Bldg, School of Medicine

Office hours TBD

wxx119@case.edu

Richard Zigmond, PhD

Room E701, Robbins Bldg, School of Medicine

Office hours TBD

rez@case.edu

216.368.4614

Department of Neurology

Wei Xiong, MD

University Hospitals-Cleveland Medical Center

Office hours TBD

wei.xiong@uhhospitals.org

216.844.3192

Department of Psychological Sciences

Heath Demaree, PhD

Mather Memorial Building 126B

Office hours TBD

heath.demaree@case.edu

216.368.6468

Lee Thompson, PhD

Mather Memorial Building 127A, Cleveland Hearing and Speech 334

Office hours TBD

lee.thompson@case.edu

216.368.6477

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	NEUR301/401	Biological Mechanisms of Brain Disorders	
FALL	2019		
26-Aug	Introduction	Course introduction & overview of nervous system disease	Katz
28-Aug		Functional organization of the nervous system 1	Katz
30-Aug		Functional organization of the nervous system 2	Katz
2-Sep		Labor Day	
4-Sep		Electrophysiology of neurons	Friel
6-Sep		How to critically analyze preclinical studies of human disease	Katz
9-Sep	Genetic disorders	Genetic etiologies and gene therapy in neurological disease	Friel & Katz
11-Sep		Disorders of neuronal excitability 1	Friel
13-Sep		Disorders of neuronal excitability 2	Friel
16-Sep		Neurodevelopmental disorders 1	Katz
18-Sep		Neurodevelopmental disorders 2	Katz
20-Sep		Neurodevelopmental disorders 3	Katz
23-Sep		Interim exam 1	
25-Sep	Neurodegenerative Disorders	Alzheimer's disease 1	W-C Xiong
27-Sep		Alzheimer's disease 2	W-C Xiong
30-Sep		Parkinson's disease 1	W-C Xiong
2-Oct		Parkinson's disease 2	W-C Xiong
4-Oct		Amyotrophic lateral sclerosis 1	W-C Xiong
7-Oct		Amyotrophic lateral sclerosis 2	W-C Xiong
9-Oct	Metabolic & auto-immune disorders	Auto-immune disorders of the neuromuscular junction 1	Mei
11-Oct		Auto-immune disorders of the neuromuscular junction 2	Mei
14-Oct		Multiple sclerosis 1	Silver
16-Oct		Multiple sclerosis 2	Silver
18-Oct		Interim exam 2	
21-Oct		Fall Break	
23-Oct		Peripheral neuropathies	Zigmond
25-Oct		Neuro-immune mechanisms in peripheral nerve injury	Zigmond
28-Oct	Pain, stroke & trauma	Pain 1	Niemi
30-Oct		Pain 2	Niemi
1-Nov		Pain 3	Niemi
4-Nov		Stroke 1	W Xiong
6-Nov		Stroke 2	W Xiong
8-Nov		Stroke 3	W Xiong
11-Nov		Interim exam 3	
13-Nov		Spinal cord injury & regeneration 1	Silver
15-Nov		Spinal cord injury & regeneration 2	Silver
18-Nov		Spinal cord injury & regeneration 3	Silver
20-Nov		Neuropsychiatric disorders	Neuropsychiatric consequences of early life trauma 1
22-Nov	Neuropsychiatric consequences of early life trauma 2		Katz
25-Nov	Neuropsychiatric consequences of early life trauma 3		Thompson
27-Nov	Neurobiology of addiction disorders 1		Demaree/Thompson
29-Nov	Thanksgiving		
2-Dec	Neurobiology of addiction disorders 2		Demaree/Thompson
4-Dec	Neurobiology of addiction disorders 3		Demaree/Thompson
6-Dec	Final Exam		

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Class Format: Note: Most class sessions will be lecture-based. At the discretion of each instructor, some sessions will be structured as discussions of assigned readings from the scientific literature, led either by the instructor or by a graduate enrollee (see below).

Prerequisites: Undergraduate: BIOL 216 or PSCL 352; Graduate: Permission of instructor

Reading: The textbook is Sontheimer, H. Diseases of the Nervous System. Other readings will be assigned as needed throughout the course. Exam material will be derived from lectures, assigned readings in the textbook and assigned journal articles.

Grading: For final letter grades for both graduate and undergraduate students, the tentative scale is 90% and above = A, 80% and above but below 90% = B, etc., but these ranges may be adjusted ("curved"), at the discretion of the instructor. For undergraduate enrollees, grading will be based on exam performance (90%) and class participation (10%). For graduate enrollees, grading will be based on exam performance (75%) and class participation (10%); in addition, graduate enrollees will be required to present, and lead a discussion of an article from the primary scientific literature. Performance will be graded and will account for 15% of a graduate enrollee's grade. The presenting student will be required to provide a concise contextual background to the paper being discussed, to demonstrate mastery of all of the data figures and to be able to thoughtfully summarize the strengths, weaknesses and impact of the paper.

Exams: There will be a total of four short essay exams: three interim exams held during class time and one final exam held during Finals Week. Each of the four exams will contribute equally to the exam-based component of the student's grade.

Paper discussions: Articles from the scientific literature will be included in the required reading assignments at the discretion of each instructor. Material from these papers will be discussed in class and will appear on exams.

Course policies:

General

To do well in this course, you need to attend classes, take detailed notes during the lectures, and participate in discussions. Lecture slides will be posted as soon as possible after class, and you are strongly advised to augment them with your own notes. Anything that is mentioned in class is fair game for exams, regardless of whether it is written on a slide or not.

Disability Accommodations

In accordance with federal law, if you have a documented disability, you may be eligible to request accommodations from Disability Resources. In order to be considered for accommodations you must first register with the Disability Resources office. Please contact their office to register at 216.368.5230 or get more information on how to begin the process. Please keep in mind that accommodations are not retroactive.

Academic Integrity

Any violation of the University's Code of Ethics will not be tolerated. All forms of academic dishonesty including cheating, plagiarism, misrepresentation, and obstruction are violations of academic integrity

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standards and will result in a minimum penalty of receiving a zero for the assignment, the potential for failing the entire course. Cheating includes copying from another's work, falsifying problem solutions or laboratory reports, or using unauthorized sources, notes or computer programs. Plagiarism includes the presentation, without proper attribution, of another's words or ideas from printed or electronic sources. It is also plagiarism to submit, without the instructor's consent, an assignment in one class previously submitted in another. Misrepresentation includes forgery of official academic documents, the presentation of altered or falsified documents or testimony to a university office or official, taking an exam for another student, or lying about personal circumstances to postpone tests or assignments. Obstruction occurs when a student engages in unreasonable conduct that interferes with another's ability to conduct scholarly activity. Destroying a student's computer file, stealing a student's notebook, and stealing a book on reserve in the library are examples of obstruction.

In addition, the incident will be reported to the Dean of Undergraduate Studies and Academic Review Board for undergraduates or Senior Associate Dean of Graduate Studies, for Graduate Students. The CWRU Statement of Ethics for graduate students can be found here:
<http://case.edu/gradstudies/about-the-school/policies-procedures/>

Mental health and other issues

It is very difficult to do your best work while struggling with a mental health issue. All students have access to University Counseling Services (<https://students.case.edu/counseling/>); this is a service that is included in your tuition. Together with Disability Resources, UCS can help you manage your mental health and academic responsibilities. Please take advantage of these resources. Counseling services at University Health & Counseling Services are located at 220 Sears Building. Walk-ins for on-site counseling are available Monday-Wednesday and Friday from 8:30 AM to 4:45 PM and Thursday from 9:30 AM to 4:45 PM. A counselor can be reached by phone 24 hours per day, 7 days per week by calling (216)-368-5872. This is available for students as well as faculty seeking consultation regarding students.

For crises, additional information can be found here:
<https://students.case.edu/wellness/info/emergencies.html>

More information about University Health & Counseling Services can be found here:
<https://students.case.edu/departments/wellness/>

The following links from SAMHSA, NIMH, and NAMI contain additional helpful information about mental health.

<https://www.samhsa.gov/topics>

<https://www.nimh.nih.gov/index.shtml>

<https://www.nami.org/Learn-More>

Detailed topic list

Unit 1: Introduction – 5 hours

David Katz, PhD (Neurosciences & Psychiatry), Richard Zigmond, PhD (Neurosciences)

A. Functional organization of the nervous system

1. Basic neuronal & glial cell biology (Zigmond) – 1 hr
2. CNS & PNS – basic structure & function (Katz) – 2 hrs

B. Origins and classification of neurological disease processes – (Katz) 1 hr

1. Congenital vs acquired
2. Neuronal vs glial vs vascular etiologies
3. Metabolic vs infectious vs auto-immune
4. Localization & time course (focal vs diffuse, acute, slow progressing, fast progressing)

C. How to critically analyze preclinical studies of human disease – (Katz) 1 hr

1. Promises and pitfalls of animal models of human disease
2. How to read a scientific journal article

Unit 2. Genetic disorders of the nervous system – 6 hours

David Katz, PhD; David Friel, PhD (Neurosciences)

A. General principles of genetic etiologies and gene therapy in neurological disease (Friel & Katz) – 1 hr

1. Types of mutations
2. Developmental timing
3. Global vs targeted expression
4. Cellular and circuit-level effects
5. Gene therapy strategies

B. Disorders of Neuronal Excitability – Friel

1. Normal physiology – 1 hr
 - a. Membrane excitability & synaptic transmission
 - b. Brief review/overview of cerebellar pathways and motor control
2. Ataxia – an example of a ‘movement disorder’ – 1hr
 - a. Episodic ataxia Type 2 (EA2) (Loss of channel function)
 - b. Familial Hemiplegic Migraine Type 1 (FHM1) (Gain of channel function)
 - c. Spinocerebellar Ataxia Type 6 (Defective expression/targeting)

C. Neurodevelopmental disorders – Katz - 3 hours

1. Rett syndrome
 - a. Clinical presentation
 - b. Genetic & molecular etiology
 - c. Mechanisms of brain circuit dysfunction
 - d. Evidence for reversibility
 - e. Translational research and therapy development
2. Spinal muscular atrophy
 - a. Clinical presentation

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- b. Genetic & molecular etiology
- c. Mechanisms of brain circuit dysfunction
- d. Translational research and therapy development

Unit 3: Disorders of the aging brain – 6 hours

Wen-Cheng Xiong, PhD (Neurosciences)

A. Alzheimer's disease (AD) – 3 hrs

1. Clinical presentation
2. History of AD research
3. Current understanding of AD:
 - a. genetic & molecular risk factors
 - b. pathological mechanisms
4. Translational research & therapy development

B. Parkinson's disease (PD) – 3 hrs

1. Role of the basal ganglia in motor control
2. Clinical presentation
3. History of PD research
4. Current understanding of PD:
 - a. genetic & molecular risk factors
 - b. pathological mechanisms
5. Translational research & therapy development

C. Amyotrophic lateral sclerosis (ALS) -2 hrs

1. Upper & lower motoneurons
2. Clinical presentation
3. Current understanding of ALS:
 - a. genetic & molecular risk factors
 - b. pathological mechanisms
4. translational research & therapy development

Unit 4: Metabolic & auto-immune disorders of the nervous system – 9 hours

Richard Zigmond, PhD, Jerry Silver, PhD, Lin Mei, PhD (Neurosciences)

A. Multiple Sclerosis (Silver) – 2 hours

1. Normal mechanisms of myelin development
2. Symptoms and etiology of MS
3. Demyelination, remyelination and axotomy in MS
4. Causes of remyelination failure in MS
5. Potential strategies to promote myelin regeneration in MS

B. Diabetic neuropathy (Zigmond) – 2 hours

1. Glucose homeostasis & diabetes (Type 1 and Type 2)
2. Vascular versus neuronal defects
3. Stocking and glove neuropathy

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4. Symptoms of numbness or pain
5. Defects in metabolism

C. Auto-immune disorders of the neuromuscular junction (Mei) – 3 hours

1. Normal signaling at the neuromuscular junction
2. Basic mechanisms of auto-immune disorders
3. Myasthenia gravis
 - a. Clinical presentation
 - b. Molecular pathophysiology and treatment

Unit 5: Stroke and trauma – 6 hours

Wei Xiong, MD (Neurology), Jerry Silver, PhD (Neurosciences)

A. Stroke (Xiong) – 3 hours

1. Overview of brain vascular anatomy & function
2. Clinical presentation of stroke, etiology & risk factors
3. Mechanisms of neuronal injury and death after stroke
4. The cutting edge of stroke therapy

B. Spinal cord injury & regeneration (Silver) - 3 hours

1. Functional anatomy of the spinal cord
2. Biology of acute versus chronic SCI
3. Pathophysiology of primary versus secondary injury
4. Barriers to CNS regeneration
5. Therapeutic strategies
 - a. Strategies to promote neuroprotection after SCI
 - b. Epidural stimulation to promote functional recovery
 - c. Promoting CNS sprouting/regeneration

Unit 6. Neuropsychiatric Disorders – 6 hours

David Katz, PhD (Neurosciences & Psychiatry), Lee Thompson, PhD (Psychological Sciences), Heath Demaree, PhD (Pending; Psychological Sciences)

A. Toxic stress and psychosocial trauma (Katz & Thompson) – 3 hours

1. Normal mechanisms of brain development: Focus on critical periods
2. Impact on early life stress on epigenetic programming, neuronal gene expression & brain function
3. Genetic risk factors & molecular mechanisms of resilience
4. Translational research and therapy development

B. Addiction disorders (Demaree & Thompson) – 3 hours

1. Normal physiology of reward circuitry in the brain
2. Clinical presentation & epidemiology
3. Neurobiology of addiction; hijacking brain reward circuitry
4. Genetic influences on addiction, including mechanisms of genetic predisposition
5. Neurobiology of recovery