Neuroscience of Pain

Fall 2023, ACN 6372-001, HCS 6372-001

Instructor: Kate Sadler, PhD, katelyn.sadler@utdallas.edu, BSB 10.538 (office), 972-883-2406 (office)
Class meeting time/location: M + W, 2:30-3:45 pm, GR 4.301
Office hours: by appointment

Course description

This is a systems-oriented neuroscience course that covers the anatomical and physiologic basis for different forms of pain. The course emphasizes the similarities and differences between the different forms of pain and describes the basic features of neural signaling/processing of pain signals in primary afferents, the dorsal horn of the spinal cord, and the brain. This includes the transmission of signals that occurs in the tracts and nuclei of the ascending neural pathways and the processing that occurs at different levels of the central nervous system. Also included is the anatomy and the function of the descending systems that can control transmission of pain signals. Peripheral and central sensitization and the basis for such phenomena as hyperalgesia and allodynia are discussed. The course will also include discussion of the physiological and molecular basis for treatment of pain.

Course objectives

At the end of this course, students will be able to:

1. List and describe the basic mechanisms involved in sensing noxious stimuli.
2. Describe how noxious stimuli can activate pain circuits in the dorsal horn of the spinal cord and in the caudal part of the trigeminal nucleus.
3. List anatomical components and basic physiology of sense organs for noxious stimuli.
4. List the anatomical components of the ascending pain pathways.
5. List the anatomical components of the descending pain pathways.
6. Describe the similarities and differences between peripheral and central sensitization and understand the basic principles underlying these two forms of sensitization
7. Describe the anatomical and functional basis for such phenomena as hyperalgesia, allodynia and "wind-up."
8. Describe how hyperalgesia is related to sensitization.
9. Define pain terminology including neuropathy, neuropathic pain, hyperalgesia, analgesia, allodynia, etc.
10. Compare and contrast the difference between somatic pain and visceral pain.
11. List the neural transmitter substances involved in pain processing.
12. Describe 2-3 examples of pain relief with a focus on pharmacology.
13. Describe 1-2 examples of non-pharmacological approaches to pain biology.

Course format

This course is organized so that one scientific topic is covered per week. Except for weeks 1, 3, and 4, class will take the following structure each week:

- **Before coming to class on Monday:** students are expected to complete the assigned readings. Students will complete a reading guide (5 pts; can complete as many times as possible) while reviewing these materials.
- **In class on Monday:** Dr. Sadler will give a 30-40 min lecture on a given topic. Students will then work in groups on an in-class review (5 pts; can complete as many times as possible). Correct answers to the review activity will be discussed as a class.
- **Before coming to class on Wednesday:** students will submit their 'muddiest point' on eLearning by 11:59 pm on Tuesday. The 'muddiest point' is a topic on which you need clarification or a remaining question that you have regarding Monday's material. Students will also read the journal club article(s) assigned for Wednesday's session.
- **In class on Wednesday:** Wednesday classes will start with a review of the 'muddiest points' submitted after Monday's class. Dr. Sadler will lead the discussion of these points. The remainder of Wednesday's class will be a journal club format. Students will work in pairs/groups to present 2-3 classic or modern primary literature papers that were pre-selected by the instructor throughout the

semester (25 pts each). All students – even those not presenting—are expected to participate in the paper discussion. Students will grade each presentation given by their classmates (5 pts each).

Students can access all readings, lectures, assessments, and exams on our eLearning site.

Exams

All exams are take home. Exams will be available on eLearning from 3:45 pm Wednesday – 2:30 pm the following Monday. I appreciate that you may consult with your classmates during the open exam period but know that plagiarism is NOT tolerated. Answers provided on your exam should be unique from your classmates. Any evidence of plagiarism and cheating will result in an automatic zero for the assignment and forwarding to the University honor code system. It is your responsibility to understand what constitutes plagiarism and cheating. If you have questions, ask. Ignorance cannot be used as an excuse. Information on UTD's academic policy can be found here: https://www.utdallas.edu/conduct/dishonesty/.

Textbook

There is **no required textbook** for this course. Rather, students will read peer-reviewed published papers on each lecture topic. All readings are available on our eLearning site. The following books are recommended for students who want additional reading material on this topic:

- "Wall & Melzack's Textbook of Pain, 6th edition", McMahon, Stephen et al. (2014). ISNO10: 0702040592, available in the UTD library. This is more or less the bible of pain. Highly recommend.
- "Understanding Pain: Exploring the Perception of Pain", Cervero, Fernando (2014). ISBN-10: 0262526069, available on Amazon for <$25

Course grading

Assignment	Due when?	Possible points	# of assignments	Total points
Reading guide	2:30 pm Monday	5	15	75
In class activity	3:45 pm Monday	5	14	70
Journal club assessment	3:45 pm Wednesday	5	14	70
Journal club presentation	varies	80	1	80
Muddiest point	11:59 pm Tuesday	3	14	42
Exam 1	2:30 pm Sept 25	150	1	150
Exam 2	2:30 pm Oct 30	150	1	150
Exam 3	2:30 pm Dec 11	150	1	150
Just because.	n/a	0	n/a	(20)
TOTAL POINTS POSSIBLE				**787**

Grades will be assigned as follows:

Grade	%
A	93.5 - 100
A-	89.5 – 93.4
B+	86.5 – 89.4
B	83.5 – 86.4
B-	79.5 – 83.4
C+	76.5 – 79.4
C	67.5 – 76.4
F	< 67.4

Course policies

- This course does not have an attendance policy but select assignments can only be completed in class (*e.g.,* in class activity, journal club assessments). There are 20 extra points built into the grading scheme. These points cover the in class activities students would miss if they were unable to attend 2 class meetings. No make-up work is offered if a student misses 1 or 2 classes. If a student plans to be absent from class for an extended period (> 2 classes), they must contact Dr. Sadler at least 1 week in advance to discuss make-up work policies. Unplanned extended absences should be communicated to Dr. Sadler as soon as possible.

- The information contained in the following link constitutes the **UT Dallas Syllabus Policies and Procedures** segment of the course syllabus. Please see https://go.utdallas.edu/syllabus-policies for these policies.

Course schedule

Topic	Date	Topic
1	Aug 21	**Introduction to the course, neuroscience terminology review**
	Aug 23	**Pain terminology and theories**
2	Aug 28	**Measuring pain in mice**
	Aug 30	**Measuring pain in men**
	Sept 4	No class, Labor Day
	Sept 6	M Bohic et al. (2023) Mapping the neuroethological signatures of pain, analgesia, and recovery in mice. *Neuron*; in press *Presenter:* Dr. Kate Sadler
3	Sept 11	**Primary sensory neuron anatomy and physiology**
	Sept 13	H Abdo et al. (2019) Specialized cutaneous Schwann cells initiate pain sensation. *Science* **365**(6454): 695-699
5	Sept 18	**Molecular transducers of sensory stimuli**
	Sept 20	MJ Caterina et al. (1997) The capsaicin receptor: a heat-activated ion channel in the pain pathway. *Nature* **389**: 816-824 *EXAM 1 available after class*
6	Sept 25	**Spinal cord composition** *EXAM 1 DUE before class*
	Sept 27	PW Mantyh et al. (1997) Inhibition of hyperalgesia by ablation of lamina I spinal neurons expressing the substance P receptor. *Science* **278**(5336): 275-279.
7	October 1	**Dorsal horn plasticity**
	October 4	CJ Woolf (1983) Evidence for a central component of post-injury pain hypersensitivity. *Nature* **306**(5944): 686-688
8	October 9	**Ascending pain pathways**
	October 11	S Choi et al. (2020) Parallel ascending spinal pathways for affective touch and pain. *Nature* **587**: 258-263.
9	October 16	**Cortical and subcortical pain modulation**
	October 18	Corder and Ahanonu et al. (2019) An amygdalar neural ensemble that encodes the un-pleasantness of pain. *Science* **363**(6426): 276-281.
10	October 23	**Descending pain modulation**
	October 25	HL Fields et al. (1983) The activity of neurons in the rostral medulla of the rat during withdrawal from noxious heat. *J Neurosci* **3**(12): 2545-2552 *-- and --* HL Fields et al. (1983) Evidence that disinhibition of brain stem neurons contributes to morphine analgesia. *Nature* **306**: 684-686. *EXAM 2 available after class*
11	October 30	**Neuroimmunology mechanisms of pain** *EXAM 2 DUE before class*
	November 1	A Goebel and E Krock et al. (2021) Passive transfer of fibromyalgia symptoms from patients to mice. *Journal of Clinical Investigation* **131**(13): e144201
12	November 6	**Pharmacology of common pain therapies**
	November 8	JR Vane (1971) Inhibition of prostaglandin synthesis as a mechanism of action for aspirin-like drugs. *Nature New Biology* **213**: 232-235. *-- and --* DW Dodick et al. (2019) Ubrogepant for the treatment of migraine. *New England Journal of Medicine* **381**: 2230-2241.
13	November 13	**Endogenous opioids + placebo**
	November 15	JD Levine et al. (1978) The mechanisms of placebo analgesia. *The Lancet* **312**(8091): 654-657
	November 21	No class, fall break

	November 23	No class, fall break
14	November 27	**Etiology of common chronic pain conditions + models, pt. 1**
	November 29	V Gangadharan et al. (2022) Neuropathic pain caused by miswiring and abnormal end organ targeting. *Nature* **606**: 137-145.
15	December 4	**Etiology of common chronic pain conditions + models, pt. 2**
	December 6	Sadler et al. (preprint) Gut microbiota and metabolites drive chronic sickle cell disease pain. bioRxiv doi:10.1101/2023.04.25.538342 *EXAM 3 available after class*
FINAL		*EXAM 3 DUE by 2:30 pm on Monday, December 11*

Journal club presentation schedule

Week	Date	Article	Presenter 1	Presenter 2	Presenter 3
~~4~~	~~9/11~~	~~Bessou and Perl (1969)~~			
4	9/13	Abdo et al. (2019)	Pranjal Khela	Zarreen Akhter	Maheen Mizra
5	9/20	Caterina et al. (1997)	Quincy Nauert	Eric Fisher	Anna Wilhelmy
6	9/27	Mantyh et al. (1997)	Samiul Alam	Kayla Brown	Nick West
7	10/4	Woolf et al. (1983)	Khadijah Mazhar	Hibah Shamsi	
8	10/11	Choi et al. (2020)	Navi Lanka	Avalon DeCurtis	
9	10/18	Corder and Ahanou et al. (2019)	Alexis Trail	Phuong Pham	
10	10/25	Fields et al. (1983), two articles	Marisol Mancilla Moreno	Lucy He	Gemma Torijos
11	11/1	Goebel and Krock et al. (2021)	Chelsea Garcia	Alonso Medina	
12	11/8	Vane (1971) + Dodick et al. (2019)	Shiva Nematgorgoni	Danieh Mohammad	
13	11/15	Levine et al. (1978)	Charmi Modi	Abby Harmon	Alexa Dinklang
14	11/29	Gangadharan et al. (2022)	Mariam Aladsani	Anjana Anandan	
~~15~~	~~12/6~~	~~Sadler et al. (preprint)~~			

End note: Dr. Sadler reserves the right to make changes to this syllabus as necessary. All changes will be communicated to students via eLearning.