CASE STUDY
Drugs & the Brain: Case-based Instruction for an Undergraduate Neuropharmacology Course

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In order to transform a traditional large non-majors general education (GE) neurobiology lecture (Drugs & the Brain) into an active learning course, we developed a series of directed mini-cases targeting major drug classes. Humorous and captivating case-based situations were used to better engage and motivate students to solve problems related to neuropharmacology and physiology. Here we provide directed cases, questions and learning outcomes for our opiates mini-cases. In addition, we describe how case studies were incorporated into our course and assessed using peer review and online quizzing. An in-depth analysis of the overall course transformation on student exam performance, opinions and instructor evaluations can be found in the *JUNE* article *Don't Believe the Gripe! Increasing Course Structure in a Large Non-majors Neuroscience Course.*

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BACKGROUND AND CONTEXT

In this paper, we describe our new set of mini-cases about opiate drugs designed for an introductory neurobiology, pharmacology and physiology course. This course fulfills non-majors general education requirements for the biological sciences at the University of California, Irvine and thus we wanted to incorporate best teaching practices grounded in discipline-based education research (American Association for the Advancement of Science, 2011; Stevens, 2011; Ledbetter, 2012). Because of its large size (150-350 students) our Drugs & the Brain course has always been taught in a traditional way that provided students with power point lectures and multiple choice exams.

We decided to introduce an active learning component to Drugs & the Brain as well as online quizzing and peer review in order to increase course structure. Previous studies have shown that increasing course structure and providing daily problem solving can help students that are less prepared (Freeman et al., 2011). Case studies provided an ideal way to incorporate a form of case-based learning that would promote student thinking and target the specific content of our pharmacology course (Yadav et al., 2007; Stevens, 2011; Herreid and Schiller, 2013; Wiertelak et al., 2016).

A total of seven sets of mini-cases were produced that covered major drug classes including, psychomotor stimulants, opiates, antidepressants, anti-psychotics, sedative-hypnotics and hallucinogens. Each set included three individual mini-cases with directed questions designed to cover basic core concepts of neurobiology and pharmacology. These included: action potential, neurotransmitter synthesis and release, agonists, antagonists, receptor subtypes, behavioral paradigms, binding graphs, dose-response graphs, drug delivery, drug metabolism, neural circuitry, addiction, withdrawal, receptor regulation, tolerance & sensitization.

While writing the case studies, we sought to also incorporate humor, history, and popular culture and to provide emotionally stimulating content that students would enjoy. Our set of mini-cases on opiates provides a good example of what is contained in all of the seven sets of case studies.

Student materials and implementation notes are available from the corresponding author or from cases.at.june@gmail.com.

CLASSROOM MANAGEMENT OVERVIEW

Student groups of 3-5 students were pre-assigned by the instructor before the beginning of the course. Classes were held during the fall quarter on Tuesdays and Thursdays for 80 minuntes in a large auditorium. Students worked with their group-mates during the Tuesday class on an assigned case, using their textbook (Grilly and Salamone, 2011), computers, tablets or phones for reference. During the Tuesday session, the instructor circumnavigated the lecture hall, interacting with groups, fielding questions and guiding problem solving. Students were required to turn in their completed case work prior to attending class on Thursday by uploading them into the software platform Canvas (https://www.instructure.com/). During the Thursday lecture, the instructor walked students through the correct answers for the completed case questions during, providing additional background information about the relevant topic. The Thursday lecture also prepared students for peer review, suggesting details to consider when grading the worksheets.

LEARNING OBJECTIVES

Content Objectives for the opiate mini-cases:

At the end of case #1, students will be able to:

- Identify symptoms related to opiate overdose. Represent the visual pathway.

- Describe a treatment that is currently available to reverse overdose and be able to describe its action.
- Discuss how relapse following opiate withdrawal can lead to overdose.
- Diagram one of the mechanisms by which opiate receptors control vesicle release.
- Explain how opiates regulate GABA release and subsequently Dopamine release.
- Describe the neural pathways that underlie addiction.

At the end of case #2, students will be able to:

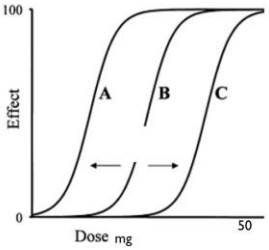
- Describe concepts of tolerance, cross-tolerance, dependence, sensitization and desensitization.
- Analyze how cross-tolerance develops in the synapse.
- Relate the action of cross-tolerance in the synapse to a dose-response curve.
- Extrapolate how a change in chemical structure influences a drug's ability to pass the blood brain barrier.
- Predict withdrawal symptoms from a drug's response.
- Compare the types of drugs that might have been prescribed to alleviate opiate withdrawal symptoms in the early 1900s with drugs used today.
- Explain why Methadone's intensity of response and withdrawal make it an ideal replacement drug for heroin.
- Identify a receptor that is not an opioid receptor that could desensitize in response to opiate use.

At the end of case #3, students will be able to:

- Describe how opiate addiction is diagnosed.
- Compare and contrast the psychological and physiological symptoms of addiction and provide examples of both.
- Explain why opiates have strong potential for dependence and abuse.
- Describe how a drug's potential for abuse is measured in the laboratory and identify a behavioral paradigm used to measure this.
- Theorize why withdrawal from Cocaine is different from Heroin and graph how the intensity of their abstinence syndrome might compare.
- Give an example for why withdrawal symptoms alone cannot fully account for opiate addiction.

Below are example excerpts from the opiate case studies:

From case 2. You are a multi-dimensional time-traveler from a future where unemployment rates are very high, causing many time travelers to take up professions in past years… You have just moved to a quaint rural area outside of St. Louis to start your own medical practice treating families and farmers in the year 1914…. You find medical practice fairly easy, but you are surprised by the treatments used in the past. Many of your patients were casually prescribed opiate containing medications for common conditions like coughs or aches and pains. Your most recent patient was kicked by a horse and now has a broken leg and is in a lot of pain. You need to decide how to treatment based on your knowledge (while sticking to treatments available in this era).



Assume that the curve labeled B is for an average person's response to opiate treatment for effectively reducing pain when in medical distress.

Which curve, A or C, best represents the dose of opiates that your patient will need to treat the pain for their broken leg if they are already taking opiates regularly as a cough suppressant?

From case 3. You are a medical researcher who investigates the effects of endogenous and exogenous ligands on opioid receptors. You have a research partner in the same lab who investigates how opiates are metabolized in the body. Both of you are at an elementary school for red ribbon day, talking to children in the 6th grade... Unfortunately, you are both the worst at communicating to children or even the lay public... Your own children are very disappointed in you both being unable to simplify your responses… Do your best to answer the kids' questions below.

A smart kid named Brian asks you to prove that opiates have a strong potential for abuse. Explain to Brian how a given drug's potential for abuse is tested in laboratory settings. What behavior is measured and how?

Your partner chimes in to explain that addicts are often merely avoiding withdrawal… This does not soothe the children. You correct your partner in front of the children, much to their delight. You do not believe that withdrawal can possibly account for opiate addiction. Why not? It seems like a perfectly plausible idea.

CASE EVALUATION

Each group of students worked on completion of one case of the full set of opiate mini-cases. The submission of answers to the questions provided was followed by a question and answer review lecture with the instructor, covering all of the cases. After students had discussed all of the case study questions in depth and took notes on how to grade the questions, they participated in peer review. Each submission was randomly assigned to 3-5 individual students using the Canvas automated peer review process. Students had to correct at least 3 submissions from their peers that were different from the case they had turned in to canvas, ensuring that all students thought deeply about each of the cases. Students were provided a short quantitative rubric called ANTS (based on the UCI anteater mascot) to provide an overall score for the worksheets.

Accurate: The answer is accurate, meaning that the group solved the problem right according to our class review.
Net: The group completed all of the assigned questions for their section with adequate answers.
To the point**:** The answers provided get to the point of the question and do not wander around or provide large amounts of irrelevant information.
Scientific**:** The answers incorporated scientific data and information from the textbook for support as opposed to personal opinion.

Each of the above criteria was graded for 1 pt. and peer reviewers were able to assign a fraction of a point for each category. The average score for quantitative peer review for all 7 case studies ranged from 3.75-3.95, with a mean of 3.87out of 4 achievable points. This suggested that peers graded the group assignments generously. In addition to the quantitative rubric, students were required to provide written feedback on each case study explaining their grading. This type of evaluation was spot checked each week to ensure that students were providing constructive feedback to peers. Examples of typical feedback include the following:

- *"Next time I would incorporate more scientific words into the study, such as "sensitizing, stereotypy, condition autonomic", etc... Also, some questions were on the right path, just missing little details to complete it."*
- *"You failed to mention on #3 that VTA is a component of the reward system."*
- *"Question six was incorrect as the correct answer given in class was B to A because the rats in group A had a faster reaction in less time than the control group, proving a sensitivity to cocaine."*
- "*Some of the information felt "googled" in comparison to what the text book provided. This made one or two of your answered seem guessed or unconfident in terms of delivery."*
- *"This case study response was very clear, so that even though I was correcting, I learned a few more things too."*

Following the completion of peer review, students gained access to a short weekly quiz on the week's topic. Each quiz was composed of 8 questions worth 0.5 pts. each for a total of 4pts per quiz. Unlike the thought problems assigned in the case studies, quiz questions were mostly lower-level Bloom's questions of recall and application that served to reinforce basic content (Bloom et al., 1956).

Examples of quiz questions:

Some anesthetic drugs and painkillers may not work as well for alcoholics. This is likely caused by....
a. cross tolerance
b. loss of cyp450 enzymes
c. a larger rough endoplasmic reticulum
d. overactive acetaldehyde dehydrogenase

Cannabinoids activate G-proteins that shut down vesicle release of Ach, NE, 5-HT, DA, GABA & Glutamate. They do this by blocking which of the following…
a. Na+ channels
b. K+ channels
c. Ca++ channels
d. 5-HT2 receptors

The average score on quiz questions for weekly topics ranged from 2.9-3.8 with an overall mean of 3.35 out of 4 achievable points.

We further assessed the impact of case studies by comparing scores on exam questions to those of students from the traditional lecture course. These findings and a detailed review of student opinion about the case study teachings and their impact on teaching evaluations can be found in the *JUNE* article "*Don't believe the Gripe! Increasing Course Structure in a Large Non-majors Neuroscience Course*" (Nagel and Nicholas, 2017).

SUMMARY AND FUTURE DIRECTIONS

In summary, we felt that the incorporation of case studies enriched the course experience for all students and allowed us to better teach the more complex concepts. Students that actively worked on case studies prior to lecture were already invested in the content and came up with better questions during the lecture portion of the class, allowing for more in-depth explanations of potential misconceptions.

In the future, we are considering embedding the case studies into an online platform that can provide immediate feedback to students about their answers as well as detailed analysis about student work habits to the instructor. In this way students can work on case studies individually and at their own pace outside of class time. Ideally, this would allow more flexibility in the way we use case studies can be used going forward and afford even more class time for active learning, discussion and instruction.

REFERENCES

American Association for the Advancement of Science (2011) Vision and change in undergraduate biology education: a call to action. (Brewer CA, Smith D; eds) Washington, DC: Science.

Bloom BS, Englehart MD, Furst EJ, Hill WH (1956) Taxonomy of educational objectives: handbook I. Cognitive domain. New York: McKay.

Freeman S, Haak D, Wenderoth MP (2011) Increased course structure improves performance in introductory biology. CBE Life Sci Educ 10:175–186.

Grilly DM, Salamone J (2011) Drugs, brain and behavior. 6th ed. *Scholarship Collection.* Book 94.

Herreid CF, Schiller NA (2013) Case studies and the flipped classroom. J Coll Sci Teach 42:62-66.

Ledbetter ML (2012) Vision and change in undergraduate biology education: a call to action presentation to faculty for undergraduate neuroscience. J Undergrad Neurosci Educ 11:A22–26.

Nagel A, Nicholas A (2017) Don't believe the gripe! Increasing course structure in a large non-majors neuroscience course. J Undergrad Neurosci Educ 15:A128-A136.

Stevens C (2011) Integrating community outreach into the undergraduate neuroscience classroom. J Undergrad Neurosci Educ 10:A44-A49.

Wiertelak EP, Frenzel KE, Roesch LA (2016) Case studies and neuroscience education: tools for effective teaching. J Undergrad Neurosci Educ 14:E13–E14.

Yadav A, Lundeberg M, DeSchryve, M, Dirkin K, Schiller NA, Maier K, Herreid CF (2007) Teaching science with case studies: a national survey of faculty perceptions of the benefits and challenges of using cases. J Coll Sci Teach 37:34–38.

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