CASE STUDY
Epilepsy and the Action Potential: Using Case Based Instruction and Primary Literature in a Neurobiology Course

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Epilepsy and seizure generation are at the center of this case study narrative. By exploring the nature of genetic mutations in voltage-gated sodium channels students will solidify fundamental concepts involving action potential generation and roles for excitatory and inhibitory neurons in the central nervous system. Students will wrestle with primary data, developing analytical and quantitative skills, and generate evidence-based hypotheses and predictions. As written here, the case is used in an upper-level undergraduate course, but because the case focuses on basic fundamental neuroscience concepts, the narrative could be easily adapted for uses in introductory neuroscience courses or potentially first-year graduate courses. Full text of the case study and the classroom implementation notes are available at cases.at.june@gmail.com.

Key words: case study, active learning, primary literature, action potential, voltage-gated sodium channels, epilepsy

Background and Context

Case-based instructional methods use realistic narratives to engage students and allow for the integration of discipline-specific content knowledge with scientific skills development. Cases can be especially effective in building skills like quantitative literacy, understanding neuroscience as an evidence-based discipline, understanding neuroscience as a collaborative, interdisciplinary process, and understanding the relationship between science and society (AAAS, 2010; NRC, 2011). With both content- and skill-based objectives, the case study presented here centers around epilepsy, one of the most common and disabling neurological conditions. By using epilepsy as the focal point for this case, students are introduced to a common neurological disorder while at the same time they investigate both the molecular-level and systems-level dysfunctions that can result in this disorder. Students often struggle with the mechanistic explanation between the expression of specific genes and the generation of a specific phenotype (Marbach-Ad and Stavy, 2000; Lewis and Kattmann, 2004), and a strength of this particular case is that it can be used to tie together multiple topics relevant for a deeper understanding of the nervous system function - from how genetics can affect cellular function to how cellular function (or dysfunction) can affect a wider network of neurons. Furthermore, this case can also promote increased awareness of the process of science by encouraging students to follow along in the footsteps of actual scientists trying to solve a mystery. Students will see that experiments don't always return expected results, and results that at first may seem confusing can ultimately provide new information as to how the nervous system functions.

The impetus behind creating the *Epilepsy and the Action Potential* case study was to incorporate neurobiological core concepts and primary literature to increase proficiency with quantitative reasoning and critical thinking skills. Tying these key concepts and skill development to a narrative about the molecular mechanisms of epilepsy and how these molecular mechanisms can affect the overall function of a network engages undergraduates, especially students with biomedical career goals. This case can be utilized to meet a variety of learning goals, including delving into molecular processes, discussing neural circuits and effects on behavior, or tying molecular processes to the development of patient-centered therapies.

Learning Objectives

Content Objectives:
At the end of the case, students will be able to:

- Describe genetic mutations involved in the etiology of certain types of epilepsy
- Define the fundamental role(s) of the voltage-gated sodium channels (VGSCs) in neurons
- Characterize interneurons and pyramidal neurons, in terms of small molecule neurotransmitters and influence in neural circuits
- Draw the structure of VGSCs and describe basic structure-function relationship
- Compare and contrast the effects of two different VGSC mutations on firing rates of neurons
- Compare and contrast animal models of epilepsy, highlighting the advantages and disadvantages of using animals to model disease states
- Predict the effect of gene mutation(s) on protein function and on neuronal function
- Predict the influence of novel genetic mutations in VGSC genes on neuronal firing rates

Skill/Process Objectives:
At the end of the case, students will have improved in their ability to:

- Interpret graphical representations of published data
- Use data to make quantitative, supported hypotheses

and predictions
- Evaluate web information for accuracy
- Apply knowledge in novel situations
- Effectively work in groups towards a mutual goal

Classroom Management Overview

Epilepsy and the Action Potential has been implemented in an upper-level undergraduate neurobiology course at Emory University with approximately 90% of the students in the Neuroscience and Behavioral Biology major and the remaining 10% predominately in a Biology major, with a sprinkling of students from other STEM disciplines. Prerequisites for enrollment in this course are a year of undergraduate introductory biology and introductory chemistry. This case is designed to reinforce concepts of voltage-gated sodium channel biology, action potential generation, and roles for excitatory and inhibitory neurons in the central nervous system. The data in the case come directly from published literature and thus allow students to grapple with interpretation of graphical representations of real data.

This case could be utilized in any biology, psychology, or physiology course that has already discussed action potential mechanisms in molecular detail as a means to reinforce these concepts. Alternatively, this case could serve as a springboard for introducing and engaging students in this topic, particularly for students in upper-level undergraduate or introductory graduate courses who might have prior knowledge of these concepts.

Prior to case implementation, students had been assigned appropriate readings that covered action potential mechanisms, had classroom mini-lectures, and had participated in other in-class activities that supported their understanding of the concepts that would be addressed in the case. Students received the case narrative with the imbedded questions at the start of class and worked in groups (usually three students/group). The case was implemented in one 75-minute classroom period and most groups were able to complete the questions within the class period, though the answers to the questions were not officially due until the next class meeting. A portion of the subsequent class period was used to address any questions that might remain and to reiterate the learning objectives of the case.

Case Evaluation

Epilepsy and the Action Potential has been implemented in the Introduction to Neurobiology course each spring semester since 2013 (30-45 students/semester; five semesters total). Direct assessment and collection of the exam data has only occurred in one semester (Spring 2016; 34 students).

Assessment of the learning objectives:
The questions within the case are not graded and the students are encouraged to review the case, the case learning objectives, and the provided answer key in preparing for an exam on this material. In Spring 2016, one question from a summative exam came directly from the *Epilepsy and the Action Potential* case study. This exam question had five parts (A – E) and the scores from each part were collected and analyzed, since each part of the question had independent goals. Of the 34 students, four students received less than 25% on this exam question and their data was not included in the subsequent analysis because they either did not participate in the case study and/or did not use the case study answer key in preparation for the exam. Thus, we argue that these students' data do not accurately represent an assessment of the learning objectives.

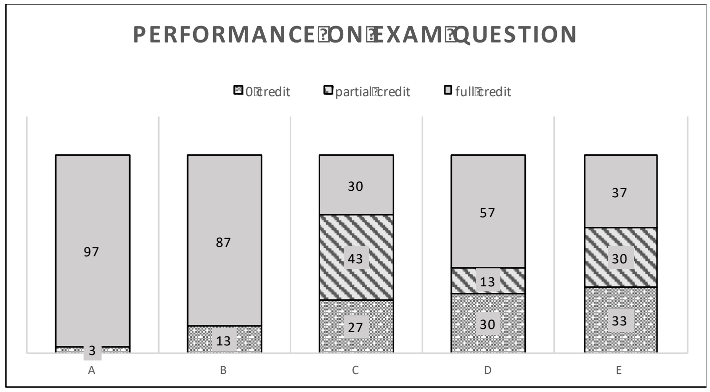

Figure 1: Performance on a case-based summative exam question. The exam question had five sub-questions (A – E) and each sub-question could earn zero, partial (50% or greater) or maximum credit. Numbers in each column stack represent the percentage of students who earned zero, partial or maximum credit.

Students could earn a maximum of 12 points on this question and the average score was 8.5/12 points (71%). For questions A and B, students either received full points (1.5 points) or 0 points. For questions C-E, students received a range of grades that increased in increments of 0.5 points from 0 – 3 points.

In part A of the exam question, the question was designed to determine if the students could accurately interpret data they had seen previously in the case study. Of 30 answers, 29 of 30 students (97%) received full points for this question (Figure 1). The basis for questions for Parts B-E were paraphrased from the case study. Question B is a low-level Bloom's taxonomy question designed to assess students' ability to remember an answer from the case study answer key. Twenty-six of 30 students (87%) received full credit, suggesting students used the case study in studying for the summative exam and could remember the answer. Question C and D of the question are worded different from the text in the case study and are designed to assess students' ability to analyze and synthesize various key elements of the case study, including understanding structure-function relationships in voltage-gated sodium channels, how the mutations can affect channel function and ultimately lead to epilepsy. Twenty-two (73%; Question C) and 21 (70%; Question D) of the 30 students earned full or partial credit on these two questions. Finally, Question E contained data the students had NOT seen in the case study and focused on a genetic mutation in a *different* voltage-gated sodium channel. Students need to interpret these novel data and propose an explanation that ties together firing rates, neuronal subtypes, and epilepsy. Thus, this question requires students to accurately interpret the novel data, synthesize what they had learned about the original genetic mutation with these new data, and draw an accurate conclusion. Twenty of the 30 students (67%) earned full or partial credit (Figure 1). Based on the evidence from these students' performance, we concluded that this case study reasonably meets content and skill learning objectives.

Assessment of students' opinion about the case study: These data were collected from three end-of-semester course evaluations (2015-2017). Students were asked about the effectiveness of the case study in preparing for exam questions. Data from Figure 2 suggest that, on average, students found the case study to be reasonably effective in helping them succeed on summative exams (Mean = 6.2/10; median = 6.3/10; n = 88 responses).

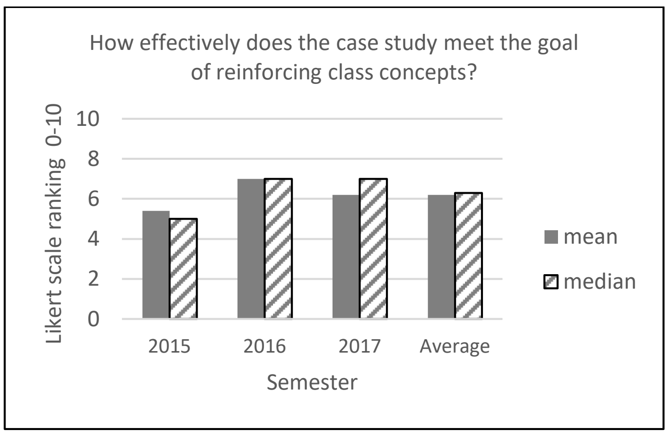

Figure 2. Assessment of content. Likert scale range: 10 = highly effective 0 = not at all effective. N = 88 responses.

This case study *Epilepsy and the Action Potential* is one of 5-6 case studies that are generally used in this course and thus comprises one of the activities where student have opportunities to interpret data and draw conclusions from data. When asked about their confidence in analyzing data on the end-of-semester evaluation, students rated their confidence in their ability quite high (Figure 3; Mean = 7.6/10; median = 8/10; n = 89 responses). In rating their confidence in working with peers to discuss data, the average response was also quite high (Figure 4; Mean = 7.3/10; median = 7.7/10, n = 92 responses).

The summative exam data demonstrate that this case study meets content goals, and we interpret these data as evidence that the case study helped students solidify concepts that include voltage-gated sodium channel biology, action potential generation, and roles for excitatory and inhibitory neurons in the central nervous system. As well, we interpret the student self-report data to mean that the students improved in the process objectives of improving their skills in analyzing data and in sharing and discussing data with peers.

Summary and Future Directions

Overall, this case is an interesting and effective way to introduce fundamental neuroscience concepts and allow for students to analyze and interpret primary data. By leveraging the strengths of a case-based teaching method, students not only master the content objectives, but also build quantitative and critical thinking skills.

One future goal for this case is to modify the narrative to incorporate a focus on translational research for genetic forms of epilepsy since many of the students have a keen interest in this area. As well, we are going to use this case as a tool to summarize a whole teaching unit, and not just the portion on action potential mechanism. Thus, we would use the case after the students have completed the teaching unit, which includes action potential mechanisms and synaptic communication, to additionally solidify concepts of excitatory and inhibitory neuronal function.

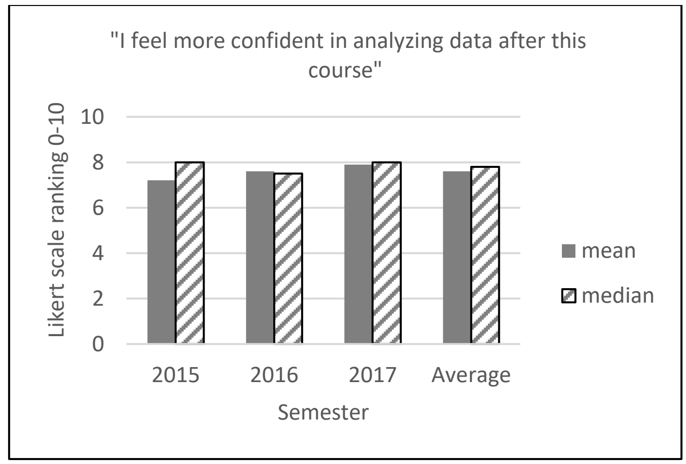

Figure 3. Assessment of student opinion about data analysis skills. Likert scale range: 10 = Strongly agree 0 = strongly disagree. N = 89 responses.

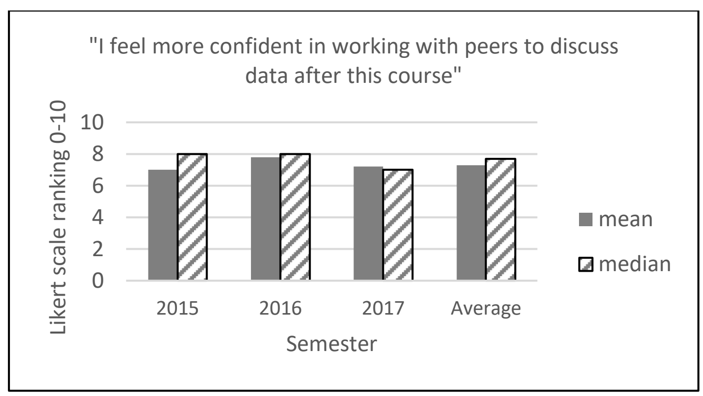

Figure 4. Assessment of student opinion about working with groups. Likert scale range: 10 = Strongly agree 0 = strongly disagree. N = 92 responses.

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