CASE STUDY
Mapping Human Neuronal Diversity in the Search for New Therapeutics: Using Real Human Neuron Data Sets to Build Student Quantitative Skills

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Case studies are a high impact educational practice that engage students in collaborative problem solving through storytelling. HITS, an NSF funded research coordination network dedicated to exposing students to high-throughput discovery science, drove creation of this case. In this case, students imagine themselves as researchers developing new therapeutic drugs for epilepsy. Specifically, students work with the Allen Cell Types Database, which is the result of collaborative, interdisciplinary open science. Neurosurgeons partnered with the Allen institute to provide living human brain tissue for electrophysiological, morphological, and transcriptomic study. Students collaborate to collect and organize data, investigate a research question they identified, and perform fundamental statistical analyses to address their question. By leveraging the unique Cell Types dataset the case enhances student knowledge of epilepsy, illuminates high-throughput scientific approaches, and builds quantitative and research related skills. The case is also versatile and was implemented in two distinct courses. The case can also be taught in different modalities, in person or remote, with a combination of synchronous and asynchronous work. Indirect and direct measures along with quantitative and qualitative approaches were used for case assessment and improvement. Students performed well on case related exam questions, reported high confidence in their achievement of the learning outcomes, and enjoyed the case's link to neurological disease, real research data and advanced technological approaches. Our assessment findings and instructor implementation experiences are also included to facilitate the adoption or adaptation of the case for a variety of courses and/or modalities in neuroscience and STEM related curricula.

Key words: case study; epilepsy; Allen Institute for Brain Science; RNA-Seq; electrophysiology; hybrid learning; high-throughput data; quantitative skills; science process

BACKGROUND AND CONTEXT

Case studies engage students in active, collaborative learning through stories (Herreid, 1997). Cases bring course content to life, stimulate critical thinking and allow instructors to assess student knowledge and their application of that knowledge to "real world" problems (Yadav et al., 2007). They are also more effective than other modes of instruction as students perform better on assessments, report increased learning gains and demonstrate the ability to connect core biological concepts to life outside the classroom (Bonney, 2015). The 'real-world' feature of cases also makes them well suited to neuroscience education, given countless neurological clinical case reports, the rates of neurobiological disease in society (Carroll, 2019), and the incredible investment in neuroscience research (Jorgenson et al., 2015). Recent NSF-funded initiatives such as the Neuroscience CaseNET NSF Award #1624104 and HITS (Robertson et al., 2021) coupled with freely available neuroscience research databases also support the creation of data-focused neuroscience cases (Gilbert, 2018; Shelden et al., 2019 Gaudier-Diaz et al., 2023; Miller et al., 2021). After all, despite calls to action to develop life science student quantitative skills, there is a lack of educational resources that promote such skills for our neuroscience curricula (Aikens and Dolan, 2014; Robertson et al., 2021).

The current case study requires students to imagine themselves as research assistants working on drug development for epilepsy. The research group is in search of therapies that would reduce seizures in the temporal lobe. Epilepsy is a common, often severe brain disorder that affects 1.2% of the population (CDC, 2023). Epilepsy can occur at any stage of life, and it has many different presentations and possible causes (Duncan et al., 2006). The core feature of epilepsy is repeated seizures, which are characterized by uncontrolled synchronous brain activity that can cause a variety of associated symptoms (temporary confusion, staring spells, loss of consciousness, uncontrollable muscle contractions, and various cognitive and emotional symptoms) (Hughes et al., 1993). Distinct types of seizures include generalized seizures and focal seizures, and once a person has two or more seizures, they may be diagnosed with epilepsy. Generalized seizures can occur in both hemispheres of the brain or multiple groups of neurons simultaneously. In some cases, focal seizures in a specific area of the brain can spread across both hemispheres, resulting in a generalized seizure. (Gloor and Fariello, 1988). Through the story of a research assistant, students learn core features of epilepsy, and they also see how cutting-edge neuroscience research is conducted.

Students access the Allen Cell Types Database to determine the effects of a hypothetical drug on non-epileptic, healthy neurons in the temporal lobe. Before they collect or analyze data, students explore how interdisciplinary, open science is conducted at the Allen Institute for Brain Science. Local neurosurgeons partner with Allen Institute scientists to obtain rare living human brain tissue for research (Tompa, 2019). These tissue samples would be removed anyway during necessary brain surgery because tissue is removed to gain access to the surgical target site. This tissue is not needed for pathological analysis and is donated for research purposes. This dataset has been used in other teaching resources (Juavinett, 2020; Ho et al., 2021), but has not been previously used in a case study.

In this case, students discover how electrophysiology, morphology and RNA sequencing approaches are combined to create open access research databases from the tissue. Students specifically work with the electrophysiology dataset. Thus, the case study narrative illuminates the high-throughput discovery science process for students. Interdisciplinary teams rely on multifaceted methodology to generate big data sets that can be used by anyone for various research purposes. This combination of a clinical research story and analysis of real data from the Allen Cell Types Database keeps students deeply engaged.

Neuroscience case studies can be employed to achieve a variety of pedagogical goals: engaging students with specific course content (Lemons, 2021), exposing students to primary scientific literature (Rollins, 2020), enhancing science process and critical thinking skills (Ogilvie, 2019; Bindelli et al., 2021), etc. The primary goals of this case are to (1) enhance student understanding of epilepsy etiology, (2) engage students in the process of high-throughput discovery science and, most importantly, (3) to build fundamental quantitative and research related skills. The case focuses on basic statistical analyses and collaboration to manipulate large data sets. Students collect and analyze data from the Allen Cell Types Database in the same way researchers in the field might use it. Students also pose and investigate their own research questions. This unique opportunity to do hands-on research with high-quality, real data requires students to build their quantitative analysis skills and may potentially yield novel research insights.

The case is also quite adaptable and was implemented in both introductory (100) and advanced (400) level neuroscience courses, in person and via remote instruction (Bixler et al., 2021). It can be condensed to a single 50-minute session or expanded to at least two 50 minute sessions, both with required outside student preparation and homework. The case also emphasizes the interdisciplinary nature of neuroscience research, showcasing how collaboration between neurosurgeons and basic researchers of multiple research specialties yielded a large, rich complex data set. Students emulate this collaborative approach, working as a class to collect data and in teams of four to analyze and address their research questions. In summary, by using real human neuron data and a story of a common neurological disease, students gain biological insights as well as quantitative and science process skills that will better prepare them for the neuroscience workforce (Coil et al., 2010). Student materials and implementation notes are available from the corresponding author (sabrinae@email.unc.edu).

CASE OVERVIEW

This case was designed for NSCI 423 Neurotechnology in Modern Neuroscience Research and implemented in four sections of the course across three semesters (Fall 2020, Spring 2021 and Fall 2021; 126 Students). NSCI 423 addresses the fundamental challenges inherent in studying the brain and explores the theory, applications, and limitations of new and traditional neurotechnology. Unique ethical issues and the significance of interdisciplinary approaches in modern neuroscience research are also highlighted. Students analyze research literature and focus on cellular and molecular approaches that are essential staples in the neuroscientist's toolkit. Students also design experiments, utilize publicly available resources, and analyze big data generated by high-throughput approaches as exemplified by this case. Prerequisite courses include NSCI 175 Introduction to Neuroscience or PSYC 101 General Psychology and PSYC 220 Biopsychology. NSCI 423 students were either juniors (11%) or seniors (89%) and the majority were neuroscience majors (75%). Psychology (15%), Biology (8%) and single students from Chemistry, Exercise and Sport Science, and Biomedical Engineering majors also participated. The case was implemented over two 50-minute class periods with required pre- and post-group work in the first quarter of the semester as the class discussed the first course theme based on the NIH BRAIN Initiative (Jorgenson et al., 2015): Generating a census of cell types and a map of their connections.

The case was also initially piloted in NSCI 175 Introduction to Neuroscience with 116 students in the Spring of 2020. NSCI 175 provides an introduction to the structure and function of the nervous system and explores fundamental principles regarding neuroanatomy, cellular and molecular properties of the nervous system, sensory and motor systems, neuroscience methodology and how our nervous system produces complex behaviors and cognition. We implemented the case as extra credit at the very end of the semester to see how it worked in the classroom and to collect informal student feedback for case improvement before officially implementing it for credit in Fall 2020 NSCI 423. Implementation at this introductory level was also successful, as student feedback was overwhelmingly positive (see Case Assessment below for details). We also utilized a shortened format in NSCI 175 where a single 50-minute class period with required pre- and post-group work was sufficient for case implementation.

This case was designed to reinforce how scientists at cutting-edge research institutions like the Allen Institute classify neuronal diversity using modern, multifaceted approaches such as electrophysiology, morphology, and high-throughput RNA sequencing. The case requires students to employ basic data management strategies, statistical analyses and to apply their knowledge of neuroscience research methods and epilepsy to a real-world research scenario. The pre-class work included various readings and videos related to epilepsy and the Allen Institute Cell Types morpho-electric cell feature Dataset.

The post-work requires student collaboration as they continue data analyses, pose research questions, and interpret results. This case study can be adapted for either introductory or advanced students in a variety of courses such as neuroscience, psychology, or biology courses with neuroanatomy or neuron physiology units. The case has also been delivered via remote and in-person instruction, and given its quantitative focus, may be especially suitable for a laboratory setting.

Learning Objectives (LOs)

Content Learning Objectives:

1. Describe epilepsy and how seizures occur in the brain
    a. Compare different types of seizures
    b. Analyze new evidence that reveals how acute focal seizures spread in the brain
    c. Explain SUDEP and when to call 911 if someone is having a seizure
2. Discuss how neuronal diversity may impact the therapeutic potential of new drugs
3. Define neuronal excitability and identify factors that influence it
4. Discuss how epilepsy linked mutations and anti-epileptic drugs can alter neuronal excitability
5. Access human neuron electrophysiological, morphological and transcriptomic data from epileptic patients
6. Analyze electrophysiological data from human epileptic patients
7. Discuss the ethical, legal and social implications of this human neuron data set
8. Discuss the advantages and limitations of studying neurons from human patients

Technical Skills based on learning objectives:

1. Apply big data from high-throughput experiments to detect patterns and quantify data
2. Identify and test a new hypothesis
3. Apply appropriate statistics to quantitative results
4. Describe practical considerations of data collection in humans
5. Access data from high-throughput experiments on living human brain tissue in the Allen Institute database
6. Interpret primary science data in the context of pre-translational research

CASE IMPLEMENTATION

NSCI 423 is organized around four central course themes based on the NIH BRAIN initiatives: (1) Generate a census of cell types and map of their connections, (2) Measure the fluctuating patterns of electrical and chemical activity flowing across brain circuits, (3) Understand how this interplay creates our unique cognitive and behavioral capabilities, and (4) Translate to treat neurobiological disorders. The case directly relates to Theme 1, which includes two priority research areas of the BRAIN Initiative, Cell Type and Circuit Diagrams. Students explore how research institutions like the Allen Institute for Brain Science lead the way in our mapping of the brain's rich cell type diversity through multi-pronged approaches. The case does not cover content related to circuit diagram research or the other three course themes. In the session before the case, we discuss methods both classic and cutting edge that are used to classify distinct neuronal cell types (function, anatomy, electrophysiology, morphology, single cell transcriptomics, etc.). The case then showcases the power of the Allen Institute for Brain Science's multifaceted, interdisciplinary, and collaborative approach to study human neurons as students engage with the Allen Cell Types Database (Gouwens et al., 2019). Students collect and analyze human electrophysiology data from the database that is generated from tissue donated by patients with epilepsy and glioblastoma. The cells in the database are collected from tissue removed during surgery that is on the path to the seizure foci or tumor tissue. Previously, such tissue was discarded, but collaboration between local Seattle neurosurgeons and the Allen Institute scientists means the precious human brain tissue can now be used for research. It is important to note that while the tissue is obtained from patients undergoing surgery for epilepsy or glioblastoma tumors, only relatively healthy tissue that needed to be removed during the surgery anyway is used for research (Tompa 2019). The details of how the case is implemented across two 50 minute class sessions is described below. After the case work, the unit concludes with a journal club discussion of (Boldog et al., 2018), where researchers utilized Allen Institute cell types data, transcriptional data and international collaboration with a Hungarian research group to identify a new human neuron not found in rodent species. In other courses, such as an introductory neuroscience course, the case would best fit in units where concepts such as neuronal diversity, electrophysiology, resting membrane potential, action potentials, epilepsy, or research methods are covered.

In our neurotechnology course, students engaged with the case over two 50-minute class periods, and the case required independent student work prior to the sessions and student collaboration outside of class (Table 1). Direct measures of student learning were assessed through pre-class homework activities, case study questions, and exam questions on case study content. Prior to the first session, students: (1) read a textbook summary of seizures in epilepsy, (2) watched a video on epilepsy, (3) read excerpts about the Allen Cell Types Database and collection of human brain tissue, and (4) answered case pre-work questions. In the first session, we began with a lecture related to the learning objectives (LOs) to elaborate on topics from the pre-work and to clarify any misconceptions. Table 1 provides an overview of the lecture topics. After the lecture, students worked in their semester-long teams of four to collect data for our entire class in a collaborative Google Sheet (Supplementary Material 2). Our class goal was to collect data from all the human neurons in the medial temporal gyrus (MTG) and frontal lobe (FroL) neurons in the database, a total of 332 cells. Students recorded the ID, brain region, layer, firing rate, and resting potential for every neuron. On average, students collected data from 10 cells to meet our goal since the typical class size was 32 students.

Using a class Google Sheet was essential to this collaborative data collection, allowing us to mine data from many cells quickly. The Google Sheet also ensured we could detect and delete any duplicate cell data accidentally entered by two different students. The cell ID column highlights identical neuron ID numbers. Instructors could certainly choose different brain regions for data collection, allow students to select, or require students to collect more data, or collect data independently. Instructors could also consider using cell data from other species, different electrophysiological parameters (resistance, rheobase, etc.) or the morphology data that is available for some cells. The database contains a multitude of measurements from 2333 cells so instructors can be creative in how they might tailor data collection to suit their classroom goals. By the end of the first 50-minute session, the majority of students finish data collection for all 10 of their assigned cells. Prior to the next session, students must have finished their data collection and they are encouraged to begin data analysis with their group.

The second 50-minute session again begins with content delivery through lectures about neuronal excitability, seizures, sudden unexpected death in epilepsy (SUDEP), and seizure emergencies. After this discussion, students work in their groups to analyze the whole class collected neuron dataset. Students calculate the mean and standard deviation for firing rate and resting potential for all the cells in the FroL or MTG brain regions. Students make the same calculations for each layer within these regions and create a table or graph to display the data. Next, students compare

	Day 1	**Day 2**
Pre-Work	1. Read "The Seizures of Epilepsy" from *Neuroscience Exploring the Brain* 2. Watch 2-min Neuroscience: Epilepsy Video 3. Read "**Introduction to the case**" and "**Experimental design of the Allen Cell Types Database and your experiment"** in the case study document. 4. Answer the "**Pre-work Questions**" in the case study.	1. Ensure data collection is complete. 2. OPTIONAL: Begin data analysis with group
In-Class: Background Material and Introduction	Instructor introduces related topics: 1. Seizures vs. epilepsy 2. Types of seizures 3. How seizures spread in the brain 4. Neuronal diversity 5. Allen institute and local neurosurgeon partnerships	Instructor introduces related topics: 1. Neuronal excitability (firing rates, resting potentials, etc.) 2. Seizures and neuronal excitability 3. Explain SUDEP and what to do in a seizure emergency.
In-Class: Data Collection and Analysis	Students collect data as a class using the Google sheet 1. Assign ~10 cells per student for data collection. *Note the number of cells per student depends on the brain regions your group decides to explore and how many neurons from those regions are in the database.* 2. Explain what data to collect and the organization of the sheet 3. A sample Google spreadsheet can be found in supplemental materials (Supplementary Material 2).	In small groups (4 students) analyze class data from the Google Sheet 1. Calculating means and standard deviation for the **firing rate** and **resting potential** for each brain region and cortical layer within the region 2. Compare two regions (MTG and FroL) with a two-sample Wilcoxon/Mann-Whitney U-test. 3. Discuss why a U-test and not T-test 4. Interpret the results or the statistical comparison. 5. Ask a new research question and design a way to test the new hypothesis, show results with a table or graph, and interpret the statistical comparison.
Post-Work	Complete data collection if students did not finish during class.	Complete unfinished data analysis and the post-data analysis questions in the case study (Supplementary Material 1).

Table 1. Case implementation plan broken down into pre-class, in-class, and post-class work for two 50-minute class session.

the FroL and MTG firing rates and resting potential averages using a two-sample Mann-Whitney U-Test. After the U-test, students interpret their results and answer the discussion questions in the case study (S1). Finally, students apply their learning to make a new comparison from the dataset (ex. Comparison of the average firing rate of neurons between two layers within the MTG). Students describe their rationale for the new comparison, apply the Mann-Whitney U-Test, and interpret their findings. At the end of day 2, any unfinished data analyses or case study questions are completed outside of class as a group. The final case study document is submitted as a group.

The case can be condensed to a single 50-minute session that requires more work outside of class hours. We offered the condensed version to introductory level students but required less analyses. We also offered the case in both remote and in-person versions due to the COVID-19 pandemic. It is easily adaptable to either learning format. The case could also be an excellent fit for a longer laboratory period. The Allen Cell Types Database is a rich dataset so the type of data, story connected to the data (examining data from epilepsy vs. glioblastoma patients), and many other features of our case could be easily adapted to a variety of neuroscience and general biology courses. The student handout (Supplementary Material 1) and data collection sheet are provided (Supplementary Material 2). Any other case materials (Lesson PowerPoints, Case Study Key, etc.) are available from the corresponding author (sabrinae@email.unc.edu).

CASE ASSESSMENT

Student learning was assessed using both direct and indirect measures. Quantitative and qualitative student feedback was also used to improve the case study after grading of group case study documents and assessment of questions on an exam. While the case was piloted in a 100 level course, NSCI 175 Introduction to Neuroscience, case assessment data was only collected and analyzed from students in NSCI 423 Neurotechnology in Modern Neuroscience Research. A total of 126 students from four distinct sections and three semesters of NSCI 423 completed the case study.

Indirect measures of student learning included a post-case survey used to evaluate students' retrospective perceptions of their achievement of the case learning objectives before and after the case using Likert scale questions (Figure 1). Collectively, fifty-two students from the three semesters of *NSCI 423* participated in this survey. Direct measures included group case study document (Supplementary Material 1) grades (90% average score), midterm exam data and multiple-choice questions in the pre- and post-course survey (Table 2). The case study document also included prompts for student feedback. This qualitative data allowed assessment of students' enjoyment of the case and descriptions of why they enjoyed the case, how it could be improved, and what kind of research they would do to expand the case. The reported averages of group case study document grades, midterm exam data, and qualitative responses on the case study document include data from all

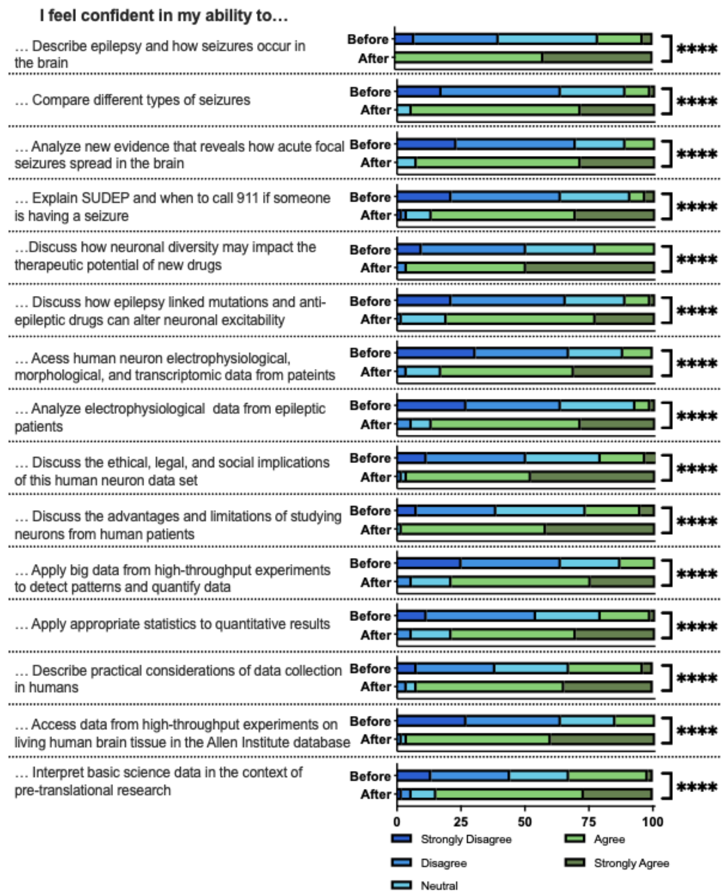

Figure 1. Cumulative percent of students attitudes of the learning objectives before and after completing the case study. All LOs had a significant increase between the two groups, using Wilcoxon signed rank test (****p < 0.001).

126 *NSCI 423* students. The pre- and post-course survey multiple choice questions include responses from 61% of those students. The institutional review board (IRB) at the University of North Carolina at Chapel Hill approved our assessment IRB protocol number 17-1196.

To assess student perceptions of their achievement of learning objectives, students retrospectively rated their confidence for each case study objective before and after the case. Students ranked their confidence using a 5-point Likert scale (1 = Strongly Disagree, 5 = Strongly Agree); the results are shown in Figure 1. Overall, students reported a significant increase in their perception of their achievement across all LO's, both content and skill based, after completing the case study ($p < 0.001$, Wicoxon signed rank test, $n = 52$). The average confidence rating for all the LOs before completion of the case study was 2.47, compared to after completing the case study, the average confidence rating was 4.21 ($p < 0.001$, $n = 52$). In summary, after working through the case study, students feel highly confident in their ability to perform the case's major objectives.

The case study document (Supplementary Material 1) includes open ended questions that directly address both the content and technical skills related learning objectives.

The case study document is done collaboratively in groups, and students have performed well. The average case study document scores were 90% (individual course averages F2020 91% (32 students), S2021 89% (63 students), F2021 92% (31 students)). To directly assess individual student knowledge, we tested seven learning objectives (Table 2) in a mid-term exam using multiple choice questions which are available upon request from the corresponding author (sabrinae@email.unc.edu). These questions were a small subset of the material tested in the exam. For five of the seven learning objectives tested, the percent of students who selected the correct answer was equal to or greater than 90%. Questions linked to three learning objectives were more challenging for students to address correctly and yielded 68% (LO1c) to 70% (LO4) correct responses (Table 2).

A subset of objectives (Table 2: LO1,2,3and4) were also assessed directly in the pre- and post-course survey. The percent of students who answered correctly increased after the case for all but one LO. This increase, however, reached significance only for the first objective. A decrease in the percent of correct responses for LO3 was observed in the post-course survey. This result was surprising given the high performance on the midterm exam on the learning objective. The post-case survey however was administered at the very end of the semester. The case was delivered in the first few weeks of the semester and there is no final cumulative exam in the course which could have led to this discrepancy.

In summary, 126 students from four course sections across three semesters and spanning remote and in person learning offerings performed well on the case, and our direct assessment shows evidence of their learning. Direct assessment of the case study document itself revealed a 90% average across all of these courses. Direct assessment of specific LOs on exams shows individual students achievement of a subset of the case study learning objectives (Table 2). And our pre- and post course survey data show some learning gains at the very end of the course. The early delivery of the case in the semester and very late delivery of the post-course survey may have impacted students' performance on these survey items. Also note that our response rates on the post-course survey data were low (61%) and do not as accurately reflect overall student performance as the midterm exam data included data from all 126 students. To fully assess and iteratively improve our case over time, we also collected qualitative data. We collected student feedback by including four questions in the case study document itself (1) Did you enjoy this case study? Why or Why not? (2) How could we improve the case? (3) Were there questions or steps in the experimental procedure that you found confusing? (4) Are there other research questions you are interested in exploring with this dataset?

Student feedback information was used to continually improve the case after each offering, and again this information was collected from all 126 *NSCI 423* students. 95% of students described their enjoyment of the case. 59% of students described the case as interesting and enjoyed the link to a neurological disease like epilepsy and 53% mentioned enjoying working with real research data from the Allen Institute for Brain Science. Below is a sample quote that captures this student feedback:

> *"The case was enjoyable because it was interesting to gain more knowledge as to the neural happenings behind epilepsy. Additionally, the case study allowed us to get a better idea of what information the Allen Brain Institute dataset has and how researchers may be able to use this public knowledge for their own experiments."*

Students also had many constructive ideas to improve the case that we incorporated over time. For example, 9% of students described how the layout of the case document could be optimized for ease of use. We took these suggestions to improve the current version of the case study

Learning Objective Addressed by Multiple Choice Questions	**% correct response on exam**	**% correct response on Pre- and Post-course Survey (n=32)**
1.Describe epilepsy and how seizures occur in the brain	95% (n=96)	53%, 78% *(p=0.043)
1.a.Compare different types of seizures	100% (n=31)	N/A
1.c.Explain SUDEP and when to call 911 if someone is having a seizure	68% (n=31)	N/A
2. Discuss how neuronal diversity may impact the therapeutic potential of new drugs	96% (n=127)	69%, 84% (p>0.05)
3.Define neuronal excitability and identify factors that influence it	90% (n=96)	44%, 41% (p>0.05)
4.Discuss how epilepsy linked mutations and anti-epileptic drugs can alter neuronal excitability	70% (n=127)	47%, 63% (p>0.05)
6. Analyze electrophysiological data from human epileptic patients	98% (n=127)	N/A

Table 2. Direct Assessment of Individual Student Learning. Seven case study learning objectives were also assessed using multiple choice questions on a midterm exam and the pre- and post-course survey. Midterm exam results include data from 126 students total (Fall 2020 (32 students), Spring 2021 sections 001 (31 students) and 002 (32 students), Fall 2021 (31 students)). Pre- and post-course survey results include data from only 77 students total (61% response rate). A two tailed McNemar chi-square test was used to identify significant changes in pre- to post-course results *p<0.05.

document (Supplementary Material 1). Students also suggested clearer in-class instruction on how to collect data (19%) and more time for discussion of background material related to the case (16%). While 22% of students state they had no confusion while working through the case, asking students to highlight confusing steps in the case procedure also helped iteratively improve the case over time. 56% of students described the statistical test as a point of confusion. Many of these comments also described how, once the students explored the accompanying case resources and learned more about the statistical test, they were able to work through this aspect of the case.

Below is a quote that captures this realization:

> *"Our group initially found the Whitney-Mann U-Test results difficult to interpret. Though none of us were familiar with the statistical test and after doing some individual research, we were able to break down our results."*

Finally, 94% of students expressed an interest in exploring other research questions after the case. Students cited interest in analyzing data from diseased tissue both epileptic and other neurological disease, utilizing the morphology data provided in the Allen Institutes cell feature database, assessing the impact of aging on the electrophysiological properties we measured, etc. In summary, our qualitative analysis shows that students enjoyed the case, especially the real-life application of the case and were inspired to think creatively about the next research they might want to conduct as a continuation of the activity.

CONCLUSIONS/DISCUSSIONS

Case studies are highly effective pedagogical tools that help students gain new content knowledge and skills. The current case hooks students through the story of a researcher working with real human brain tissue to uncover novel therapeutics for epilepsy, a disease that afflicts 1.2% of the population. The case is unique as it develops students' quantitative skills through analysis of real human neuron data from the freely accessible Allen Cell Types Database. The case study narrative also reveals how high-throughput, cutting edge neuroscience research is conducted collaboratively and by employing a multitude of approaches such as electrophysiology, morphology, RNA sequencing etc. Ultimately, the case goals are to enhance student understanding of epilepsy, engage students in high-throughput discovery science and build students' science process and quantitative skills.

We assessed the effectiveness of the case using both indirect and direct measures. The data indicates that students generally perform well on the case and related exam questions. Students are also confident in their achievement of the case's LOs, and 95% of students enjoy the case. Students particularly appreciate the case's connection to a neurological disease, epilepsy, and working with real research data. We also leveraged student's feedback to improve the case study narrative document and to inform how the case is implemented in the classroom.

Qualitative data used for Iterative Case Improvement	
Question	*Student Feedback*
Did you enjoy this case study? Why or Why not?	**95%** enjoyed the case **59%** enjoyed the epilepsy link **53%** enjoyed working with real research data
How could we improve the case?	**9%** suggested changes to the layout of the case document **19%** advised clearer class instruction for data collection **16%** advised more discussion of background content
Were there questions or steps in the experimental procedure that you found confusing?	**22%** stated no confusion **56%** described the statistical test as a point of confusion, but also described working through this struggle with the case resources
Are there other research questions you are interested in exploring with this dataset?	**94%** expressed interest in exploring new research questions with the dataset

Table 3. Summary of Qualitative Analysis used to Iteratively Improve the Case Study. Responses from >120 students analyzed from the four different sections of the course from 2020 to 2021. Percentages represent the number of similar student feedback responses out of the total number of comments for that question. Student responses were leveraged to improve the case study over time and create the case study document (Supplementary Material 1).

In summary, we implemented the case in two highly distinct neuroscience courses, emphasizing the case's adaptability to different classroom and university settings. The case was piloted in an introductory level course and then offered in four distinct sections over three semesters in an upper level course. We used the multiple offerings to iteratively improve the case over time. The case can be condensed to a single 50 minute session in an introductory neuroscience course with pre- and post-student work, or it can be expanded significantly to multiple days of work in an upper level neuroscience course. We also offered the case in remote, hybrid and in-person learning formats due to the COVID-19 pandemic. It is easily adaptable to any of these modes of instruction. The effectiveness of the case in a 100 level setting is noteworthy, given that the majority of published neuroscience cases have been designed for more advanced students (Roesch and Frenzel, 2016; Cook-Snyder, 2017; Sawyer and Frenzel, 2018; Mitrano, 2019; Watson, 2019). Given the data analysis focus of the case, it may also work nicely as a laboratory module to accompany an introductory neuroscience or biology lab. The case would also be effective in general biology focused courses as the only requisite knowledge for students is an understanding of resting membrane potential and action potentials, both topics covered in most introductory biology courses.

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