ARTICLE
Sleepy Mice Case Study: Implementation and Assessment

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Case studies are a valuable teaching tool to engage students in course content using real-world scenarios. As part of the High-throughput Discovery Science & Inquiry-based Case Studies for Today's Students (HITS) Research Coordination Network (RCN), our team has created the Sleepy Mice Case Study for students to engage with RStudio and the Allen Institute for Brain Science's open access high-throughput sleep dataset on mice. Sleep is important for health, a familiar concern to college students, and was a basis for this case study. In this case, students completed an initial homework assignment, in-class work, and a final take-home application assignment. The case study was implemented in synchronous and asynchronous Introductory Neuroscience courses, a Biopsychology course, and a Human Anatomy and Physiology course, reflecting its versatility. The case can be used to teach course-specific learning objectives such as sleep-related content and/or science data processing skills. The case study was successful as shown by gains in student scores and confidence in achieving learning objectives. Most students reported enjoying learning about sleep deprivation course content using the case study. Best practices based on instructor experiences in implementation are also included to facilitate future use so that the Sleepy Mice Case Study can be used to teach content and/or research-related skills in various courses and modalities.

Key words: sleep; high-throughput data; case study; Allen Institute for Brain Science; active learning; R studio; science process skill

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Case study-based learning is a high-impact approach that develops students' science process, problem solving, and critical thinking skills. The case study method can be implemented in a variety of ways, but at its core, case-based teaching uses a real-world narrative to engage students in collaboration to solve problems and build analytical skills in a self-directed way. Case studies that combine real research data with relatable narratives also require students to apply quantitative skills, evaluate problems from a variety of perspectives, and consider the human impact of science. The case study approach, therefore, is a powerful tool for neuroscience and other classrooms that aligns with core competencies outlined by Vision and Change (American Association for the Advancement of Science, 2011).

High-throughput research utilizes automation, technological advances, and large-scale experimentation to facilitate discovery. In the field of neuroscience, high-throughput research can take a variety of forms such as single neuron transcriptomics (Boldog et al., 2018; Bandler et al., 2022; Yang et al., 2022), automated image analysis (Thompson et al., 2010), proteomics (Perkel, 2021; Yang et al., 2021; Paulsen et al., 2022), connectomics (Zhang et al., 2020), genomics (Janssens et al., 2022), and drug discovery (Bock et al., 2021; Willsey et al., 2021). Combining various high-throughput approaches to tackle long-standing questions in the field is also becoming increasingly common (Paulsen et al., 2022). Consequently, high-throughput approaches are transforming the way neuroscience research is conducted, requiring a matched evolution of our future neuroscientist training. Case studies that incorporate large, complex datasets offer an evidence-based approach to bolster student quantitative skills while also integrating high-throughput discovery into curricula. Creating such cases, however, is challenging given a variety of barriers such as limited faculty time, required training, and access to high-throughput technology, among others (Williams et al., 2019).

HITS (High-throughput Discovery Science and Inquiry-based Case Studies for Today's Students), a research coordination network sponsored by the National Science Foundation (Robertson et al., 2021), aims to encourage integration of high-throughput discovery science into classrooms through the use of case studies. The network has implemented high-throughput-based case studies in over 18 different courses, reaching thousands of students at a diversity of institutions. Cases are created through working groups of high-throughput researchers and educators whose goal is to design, assess and share their cases broadly with the educational community. The current case was developed by an interdisciplinary HITS case fellow team. HITS fellows commit to the creation of a new high-throughput case, in return the network provides training, structured time, and financial support for case development. Our case fellow group saw a need for introductory level cases that require R programming and general quantitative skill development. As neuroscience and physiology instructors, we chose to focus on the topic of sleep.

We selected the topic of sleep for two primary reasons: (1) sleep deprivation is a scourge of modern society that has deadly consequences especially for the typical college-aged student and (2) the Allen Institute for Brain Science offers an open access high-throughput gene expression dataset based on a sleep deprivation study in mice (Allen Institute for Brain Science, 2007; Thompson et al., 2010). Chronic sleep deprivation increases risk of all-cause mortality and risk of cardiovascular disease, neurodegenerative disease, depression, and car accidents, among others (Cappuccio et al., 2010; Yin et al., 2017; Zamore and Veasey, 2022). In fact, sleep deprivation is a major risk factor for two of the top three most common causes of death for individuals aged 15 to 25, suicide (Harris et al., 2020) and car accidents (American Academy of Sleep Medicine Board of Directors et al., 2015; Gottlieb et al., 2018; Tefft, 2018; CDC, 2022a; National Highway Traffic Safety Administration, 2022). Sleep deprivation is also detrimental to memory function, attention, and emotional regulation (Alhola and Polo-Kantola, 2007; Chee and Chuah, 2007; Saghir et al., 2018); all critical brain functions for successful academic performance. Yet, college students report alarming rates of sleep deprivation (Hershner and Chervin, 2014; CDC, 2022b). Sacrificing sleep time is routine for students juggling academics, extracurriculars, jobs, key social needs, and more. As neuroscientists, we must educate students and our community on the devastating consequences of sleep deprivation. Our case meets this need by engaging students in a tale of sleep deprivation while also bolstering student quantitative and science process skills through the collection and analysis of a real sleep deprivation high-throughput data set readily available through the Allen Brain Institute

CASE OVERVIEW

The case was designed to reinforce knowledge of sleep and the consequences of sleep deprivation, expose students to primary scientific literature as well as R, and require students to apply knowledge learned in class to their personal lives. The case included three parts: pre-case work, class activities, and post-case reflection. Students independently completed pre-case work which consisted of researching and summarizing how sleep deprivation can affect attention, emotion, memory or neurological diseases from primary scientific literature. Additionally, students downloaded R and used this program to explore the sleep deprivation literature and create a histogram of sleep deprivation papers through 2021. During the in-person class sessions, students typically worked in groups to collect gene expression data from the Allen Mouse Brain Atlas in an excel sheet, import data into RStudio, and use R to create a graph comparing brain gene expression in sleep-deprived and control conditions. Students were challenged to analyze their results to determine if there were any specific patterns of gene expression between control animals and sleep-deprived animals, as well as patterns specific to a brain region. For the in-class sessions held remotely, students completed class activities individually. Post-case reflections were completed individually and allowed students to apply their knowledge to their own lives by writing a letter to enact local policy change in school times

Students should be able to…

Content

- Discuss the reasons why we sleep and the consequences of sleep deprivation *(Pre-work, Q1-2)*
- Understand the impact of sleep deprivation on attention, emotion, memory, and neurobiological disease *(Pre-work, Q3-4)*
- Explain how the Allen Mouse Brain Atlas was created through high-throughput approaches *(In-class, Q1)*
- Diagram how *in situ* hybridization works *(Prior course content related to case-study, assessed in exam Qs)*
- Summarize the best sleep hygiene practices and how they promote sleep from a biological perspective *(Prior course content related to case-study, assessed in exam Qs & Post-work Q3)*
- Apply their knowledge to write a persuasive letter to enact local policy change *(Post-work, Q1)*

Skill

- Read and interpret scientific literature *(Pre-work, Q1-4)*
- Create a histogram of sleep deprivation literature using R *(Pre-work, Q5)*
- Collect and analyze expression of a gene in the brain using the Allen Mouse Brain Atlas *(In-class, Q1-2)*
- Create and interpret a graph comparing brain gene expression in sleep-deprived and control conditions using R *(In-class, Q3-4)*

Table 1. Content and Skills Learning Objectives for the Sleepy Mice Case Study. Next to each learning objective is the associated assessment question.

Course	Course Enrollment	Classroom Modality	Course Requirements	Implementation Notes
Biopsychology 200-level Psychology UNC at Chapel Hill	42 students	Face-to-Face Meetings 2x/week (75 min)	Pre-Req: Introduction to Psychology 1 of 3 options required for Psychology major	The case was presented after the instructor had covered material on brain rhythms and sleep (biology of sleep). The case was the first exposure to the use of R programming presented in the course.
Introduction to Neuroscience 100-level Neuroscience UNC at Chapel Hill	118-120 students per section	Section 1: Remote, asynchronous Section 2: Hybrid, synchronous Meetings 2x/week (75 min) Section 3: Hybrid, synchronous Meetings 3x/week (50 min)	Pre-Req: none (Knowledge of biology and chemistry at the high school level is assumed) Required for neuroscience major and minor	The case was presented after the instructor had covered material on brain rhythms and sleep (biology of sleep). The case was the first exposure to the use of R programming presented in the course.
Human Anatomy and Physiology 200-level Crown College	19 students in joint lecture and 2 lab sections	Face-to-Face, in person Meetings 3x/week (50 min) + Lab 1x/week (100 min)	Pre-Req: Introductory Biology or Introductory Chemistry/Biochemistry course Required for some majors	Although the nervous system is covered in the course, the neurobiology sleep content emphasized in the case is not a part of the course. The goal for implementing the case study in this course was for students to gain science competency by practicing data processing, thus, only a subset of the learning objectives listed in Table 1 was relevant.

Table 2. Case Implementation Course Parameters. Summary of parameters across courses in which the Sleep Mice Case Study was implemented.

as well as evaluating their sleep hygiene practices. This case would be appropriate for a neuroscience, psychology, or biology course that includes a unit on sleep biology and/or for the development of science data processing skills.

CASE IMPLEMENTATION

The Sleepy Mice Case Study was designed during Summer 2021 and implemented during Fall 2021 in a series of courses: Biopsychology (1 section) and Introduction to Neuroscience (3 sections) at the University of North Carolina at Chapel Hill and Human Anatomy and Physiology I (2 lab sections/joint lecture) at Crown College. During the
Fall 2021 implementation, 418 college students with a variety of declared majors were enrolled in these courses and were assigned the Sleepy Mice Case Study (Table 2). The Sleepy Mice Case Study was implemented in the Introduction to Neuroscience course at University of North Carolina a second time in Spring 2022 (300 students in 2 sections), and a third time in Summer 2022 (40 students in 2 sections). Thus far, 768 students have been assigned the Sleepy Mice Case Study in a total of 9 sections of 5 courses. Student outcome data for this paper were only collected during the Fall 2021 implementation.

Biopsychology

In-Person with No Remote Option (1 Section)

Implementation of this case differed slightly from others as pre-work, in-class work, and post-work were all completed in groups of 5-6 students. All students in the course completed all three elements of the case. Students divided work such that only one student from each group completed the R section of pre-work. A bulk of the R section pre-work includes instructions on downloading R and familiarizing themselves with the program. Groups' ability to engage with R immediately in class was hampered because multiple group members were unfamiliar with R. Therefore, subsequent implementations of the case required the pre-work to be done on an individual basis to ensure all students downloaded R and used it before class. Despite this initial setback, at the end of class, all groups submitted a bar graph of mean *in situ* hybridization (ISH) values of their gene of interest.

In the post-case reflection, about 75% of students reported enjoying working with RStudio to generate a bar graph while about 25% of students reported that working with RStudio was confusing and difficult. Students cited other enjoyable aspects of the case, including searching for and reading literature related to sleep deprivation, connecting the material to their sleep practices, and the change from lecture to an activity. Other less enjoyable parts for students were writing the policy letter and the volume of work required.

Introduction to Neuroscience

Remote, Asynchronous (1 section)

Students were responsible for completing the pre-case work individually, class activities in groups of 3-4 students, and post-case reflection individually. Approximately half of the students in the course (46%) completed all three elements of the case study. This was unusual for a lesson in the class but is likely because the lowest 20% of assignments in the class pre-work and engagement grade categories of the course are dropped from students' final grades. Also, this lesson was implemented just before the third mid-term exam.

All 72% of students who completed the pre-case activity researched and summarized literature about sleep deprivation and their disorder of choice, but only 73% of those students submitted the literature histogram they created using Rstudio, while 26% did not. Of the 60 students who completed the post-case reflection, half reflected on using Rstudio: 50% reported enjoying working with Rstudio the most out of the activities and the other 50% reported enjoying working with Rstudio the least out of the activities. Other most enjoyable parts of the case study for students were connecting with Nadia, the character in the narrative, and looking for information about sleep deprivation. Other least enjoyable parts of the case study for students were working in groups and the volume of work required by the case study activities. Using Rstudio was a divisive point in the case study for students and may reflect the different proportion of majors in this section compared to other sections. An alternative interpretation is that implementing the case study asynchronously was a barrier for students trying to work with Rstudio.

In-person, Combination of Asynchronous and Synchronous Work (2 Sections)

For implementation, students completed the pre-case work individually and the class activities in groups of 4-6 students. The post-case reflection was also completed as a team. More than 85% of students participated and submitted the case study work. The increased case participation in these in-person versions of *NSCI 175* is interesting. More students may have participated because the opportunity to work with their team in person made the Rstudio work less intimidating. Again, a key implementation strategy for our synchronous offerings of the case was to require students to individually complete the pre-work. This ensured that the majority of students had successfully downloaded R and created a histogram before our classroom activity day. In the 50-minute class period, the majority of student groups had a data figure exploring their gene of interest expression before leaving for the day. In the 75-minute class period, all groups completed the in-class activity and many had finished the post-class reflection.

A total of 87% of student groups reported enjoying the case study. Students cited a variety of aspects of the case as the most enjoyable: using R studio to conduct data analysis and create graphs, having the freedom to choose what genes to analyze, working with real data, collaborating with their peers, and learning about sleep deprivation. Students also mentioned how using a story (i.e., the case narrative) was more engaging than just a list of questions. Students' least favorite aspects of the case included struggling with R studio and understanding the purpose of the coding steps as novices, writing the letter, the time required for the in-depth case, particularly the pre-work, the timing of the case study (on the last day of class for one section and right before an exam for the other) and the tedious process of gathering and organizing data from the brain atlas.

The majority, 93% of student groups, also reported a commitment to change their sleep practices to achieve better sleep hygiene and avoid the consequences of sleep deprivation, although many students pointed out the practical constraints to adopting better sleep hygiene when many students juggle academics, work, and extracurriculars.

Human Anatomy & Physiology I

In-Person (1 section)

The students were given the pre-case work as a take-home assignment to complete. In this iteration, some of the students had computer-related issues and so a part of a subsequent lab was then used to help resolve these issues before moving on to the next step. The goal was to get everyone to the step where they had generated the

Major	Percentage of Students
Neuroscience	39%
Psychology	18%
Biology	16%
Chemistry	13%
Exercise & Sport Science	8%
Computer Science	4%
Nursing	2%
Education	1%

Table 3. Cumulative Major Demographics of Students in Fall 2021 Implementation. The overall percentage of students in all of our courses with each major. N = 418 students

graph using R. The students then completed the in-class work using the Allen Mouse Brain Atlas during a 50-minute lecture and this was enough time for some students but not all. The students subsequently submitted the graphs, graph analysis, and the letter writing assignment as part of the post-case reflection. The use of this activity in a non-Neurobiology course highlights that it can be used in multiple course contexts, even with students with minimal content background knowledge.

CASE ASSESSMENT

Participant recruitment and data collection procedures were reviewed and exempted by the University of North Carolina at Chapel Hill Institutional Review Board (PROTOCOL #21-2266). This UNC-exempted IRB protocol was then reviewed and approved by the Crown College Institutional Review Board. Quantitative and qualitative data were collected from student work submitted as part of the Sleep Mice Case Study implementation and an anonymous post-case study survey. The post-case study survey assessed student enjoyment (Figure 1) and student perceptions on the achievement of learning outcomes (Figure 2), whereas quiz/exam questions assessed content knowledge gained (Figure 3). This assessment data only includes data from Introduction to Neuroscience and Biopsychology students.

Figure 1 summarizes student feelings and enjoyment of the case. Eighty-two percent of students strongly agree/agree that they enjoyed learning about sleep deprivation in the case format while only 45% strongly agree/agree they would have preferred a lecture. A majority of students (58%) also strongly agree/agree that they gained more knowledge about sleep deprivation from the case study format than from our textbook or lecture. Writing a persuasive letter was enjoyed and disliked by almost identical proportions of students 39%, and 22% felt neutral about this requirement of the assignment. A strong majority of students (70%) felt the case should be used again to learn about sleep deprivation, while only 11% felt it should not. In summary, the majority of students enjoyed the case format and felt they learned more from this pedagogical approach. Students were divided in their enjoyment of the letter writing, and many students mentioned this as a time-consuming aspect of the case in our open-ended questions. Accordingly, instructors should consider whether letter writing is essential for their classrooms and whether it aligns with their overall learning objectives and course goals.

To assess perceptions on the achievement of learning outcomes (Figure 2), students were asked to retrospectively rate their confidence level for each of the case study learning objectives with the exception of "reading and interpreting primary literature". When students compare their perceptions from before and after completion of the Sleepy Mice Case Study, they report significant increases in confidence for all content and skill-related learning objectives.

To assess content knowledge gains (Figure 3), we had our students complete three multiple-choice content questions in the form of a quiz before covering the Sleep

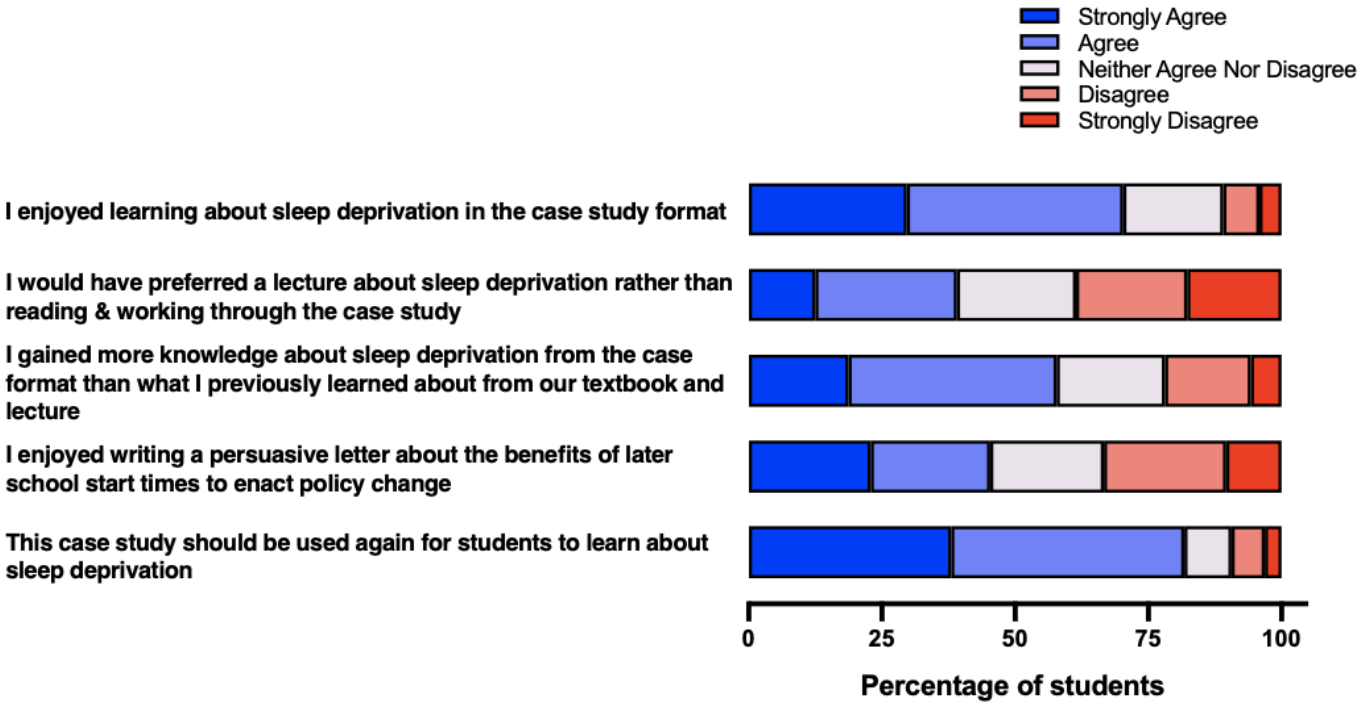

Figure 1. Student perceptions of the case study. Students responded with strongly agree (blue), agree (light blue), neither agree nor disagree (grey), disagree (light red), or strongly disagree (red) to five statements about the case study. The five statements are on the left and corresponding cumulative bar plots are on the right (n = 192 students).

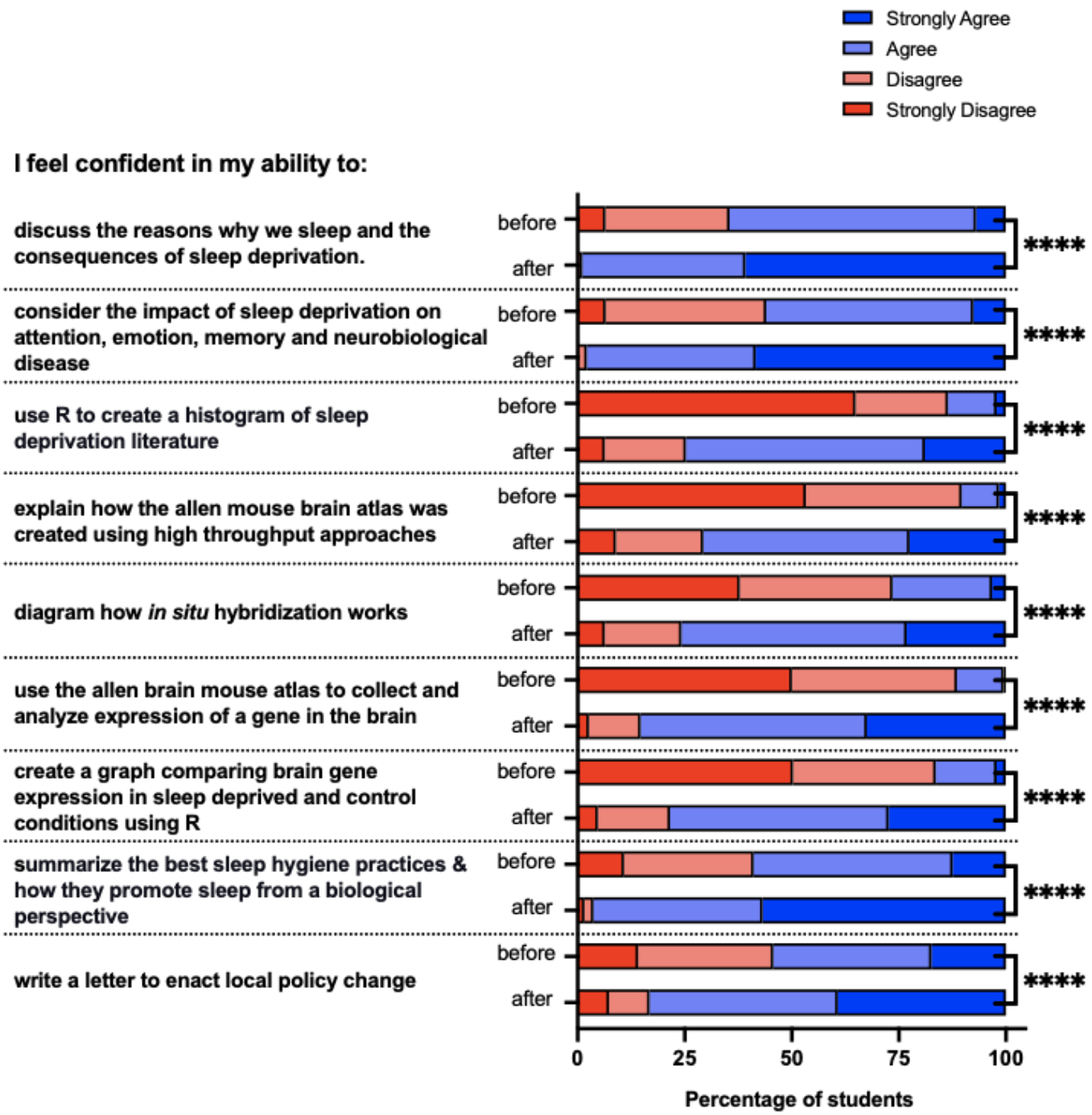

Figure 2. Retrospective Student Perceptions of the Achievement of Learning Outcomes. Students retrospectively responded with strongly agree (blue), agree (light blue), disagree (light red), or strongly disagree (red) to nine statements of confidence in their ability to meet Learning Objectives before and after completing the case study. The statements are on the left and corresponding cumulative bar plots are on the right (n = 182 students, Friedman with Dunn's Multiple Comparisons Test, ****p< 0.0001).

units. The same questions were later administered as part of an exam. For each question, we tallied the total correct responses and compared the values before and after the implementation of the case study.

The first two multiple choice questions focused on sleep biology content and the third on assessing their ability to interpret results and analyze a figure similar to the graphs generated in the case study assignment. Paired data were obtained from 276 students. The fraction of students answering each question correctly increased for all 3 questions and these increases were all statistically significant using Sidak's multiple comparison test (Figure 3). The overall quiz score also increased from 46.14% +/- 1.98% to 67.25% +/- 1.42% and this change was statistically significant using a two-tailed paired t-test (Figure 3).

CONCLUSIONS

After integrating our case in five distinct classrooms, we compiled a summary of best practices (Table 4). First, we

highly recommend that instructors carefully consider the timing of case implementation during the semester. There is significant time, both in and out of the classroom, required for the case. Ensuring that other major course assignment deadlines or exams are not near the case study due dates is key. We also found students struggled to fully engage with the case when it was offered in the last week of class. Communication about the assignment is also essential. All of our courses are highly structured. For example, in *Introduction to Neuroscience*, students are required to read the text and take a quiz before each class session. The case study, however, breaks this tradition. Many students suggested that advanced discussion of the case requirements and posting of case materials would have been beneficial. We also compared how the case was delivered across our classrooms. Using a combination of asynchronous pre-work and synchronous class sessions yielded the best results. Every student, on their own, should watch an Rstudio tutorial video and download R to create a graph prior to class. Also, offering an office hour for R troubleshooting prior to the synchronous session will ensure that students arrive to synchronous session ready to collaborate or troubleshoot roadblocks they encountered with R. During the synchronous session, it is ideal if the instructors and assistants can circulate in the room or online break rooms to check in with all the groups. As an instructor, building your confidence with R is also important. Some of us were novice R users but by working through the case on our own we were adequately prepared to lead the synchronous session and troubleshoot. Instructors and students should also be aware that R and RStudio program updates may alter the steps listed in the student handout over time. Recruiting learning assistants that have significant R experience can also be valuable, especially for large classroom environments as they can circulate and assist students.

In summary, our team created the Sleepy Mice Case Study as a part of the HITS network to develop student quantitative skills while exposing them to the power of high-throughput approaches, R Studio, and

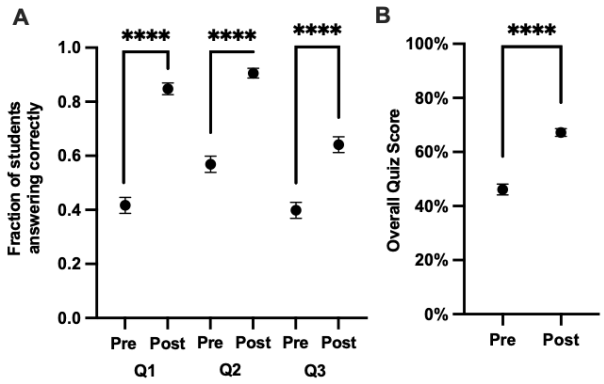

Figure 3. Student scores on a short content quiz were improved following the case study. *A.* The fraction of students correctly answering three questions on a content quiz given pre-case and post-case (n = 276 students; Repeated Measures One-Way ANOVA, F = 70.73, ****p < 0.0001; Šidák's multiple-comparisons test ****p < 0.0001 for each pre-case vs. post-case comparison). *B.* The average overall quiz score for students pre-case and post-case (n = 276 students; two-tailed paired t-test, ****p < 0.0001). Error bars are +/- SEM

Institute for Brain Science's open access datasets. We also used the case to convey the central role of sleep to human health and the significant consequences of sleep deprivation with hopes of impacting student sleep hygiene. By implementing the case in synchronous and asynchronous Introductory Neuroscience courses, a Biopsychology course, and a Human Anatomy and Physiology course, we've demonstrated its versatility. We've assessed our case, illustrating its ability to increase student scores and confidence in achieving learning objectives. Our students also generally enjoyed learning about sleep deprivation through the case study and many reported a commitment to change their sleep practices. We welcome adoption or adaptation of the Sleep Mice Case Study. The classroom implementation notes, full case narrative, and answer key are available upon request from cases.at.june@gmail.com. Instructors seeking additional case information are encouraged to contact any of the co-authors.

Curriculum Integration
Consider the high case workload and due dates for other course assignments and exams carefully *Avoid implementation in the last weeks of class* *Mentally prepare students for the assignment and prepare materials and due dates in advance*
Case Delivery
Use a combination of asynchronous pre-work and synchronous class sessions *Require student collaboration* *Instructors should check-in with all groups* *Do the case yourself well in advance!*
R Support
Provide a video of how to use Rstudio in the pre-class work *All students should do the pre-work of downloading R and creating a graph individually* *Consider offering office hours for R troubleshooting before the synchronous session* *Recruit learning assistants that have significant R experience for troubleshooting*

Table 4. Summary of Best Practices.

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